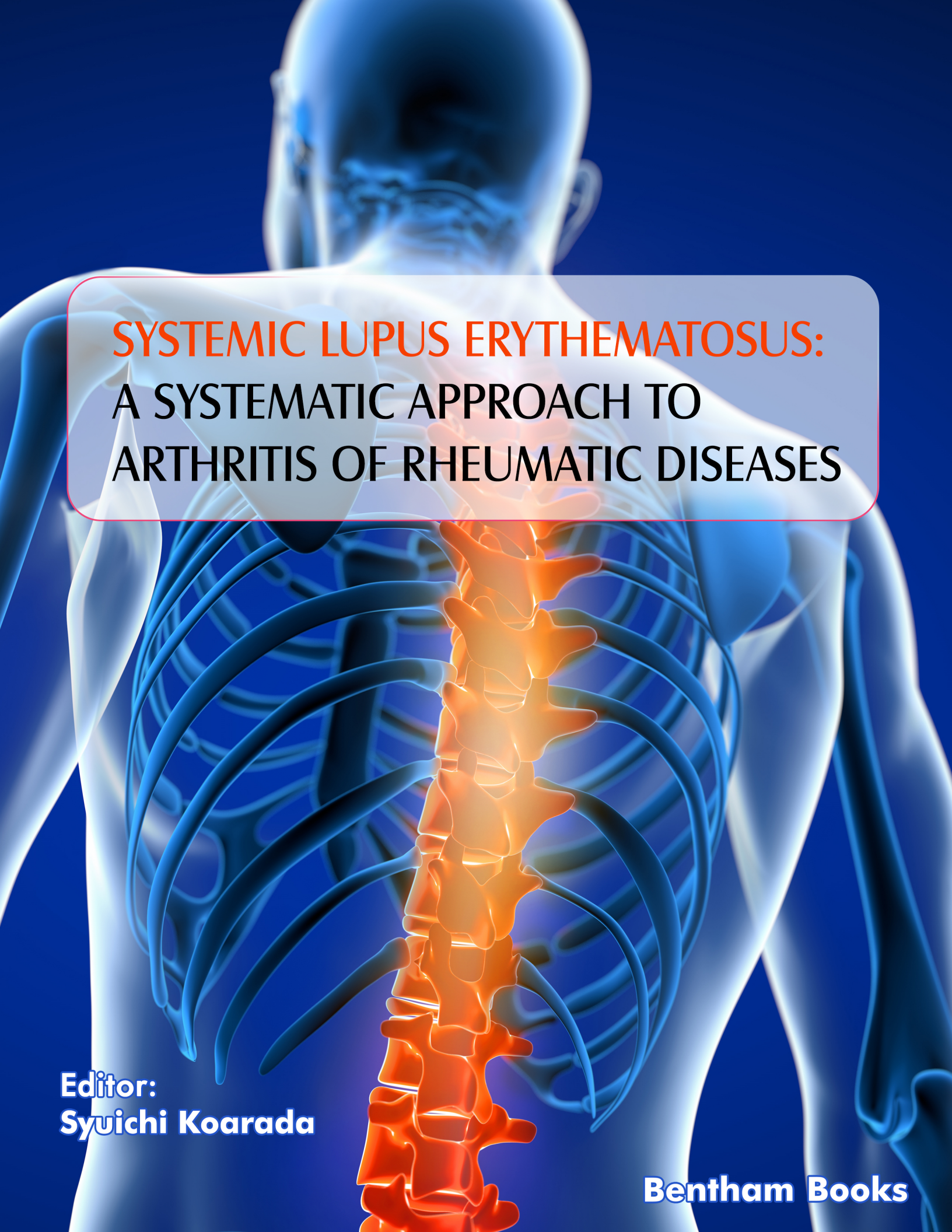

SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC APPROACH TO ARTHRITIS OF RHEUMATIC DISEASES

Editor:
Syuichi Koarada

Bentham Books

Frontiers in Arthritis

(Volume 4)

Systemic Lupus Erythematosus: A Systematic Approach to Arthritis of Rheumatic Diseases

Edited by

Syuichi Koarada

Department of Medical Technology and Sciences
International University of Health and Welfare
Okawa
Japan

Frontiers in Arthritis

Volume # 4

Systemic Lupus Erythematosus: A Systematic Approach to Arthritis of Rheumatic Diseases

Editor: Syuichi Koarada

ISSN (Online): 2468-6670

ISSN (Print): 2468-6662

ISBN (Online): 978-981-5050-65-3

ISBN (Print): 978-981-5050-66-0

ISBN (Paperback): 978-981-5050-67-7

need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.

3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

Bentham Science Publishers Pte. Ltd.
80 Robinson Road #02-00
Singapore 068898
Singapore
Email: subscriptions@benthamscience.net

CONTENTS

PREFACE i

LIST OF CONTRIBUTORS ii

CHAPTER 1 INTRODUCTION OF DIAGNOSTIC APPROACH FOR SYSTEMIC LUPUS ERYTHEMATOSUS 1

Syuichi Koarada and *Yoshifumi Tada*

1. INTRODUCTION 1

2. CLASSIFICATION OF LUPUS ARTHROPATHY 3

2.1. Frequency of Arthritis Subtypes 4

2.2. Arthritis Subtypes 4

2.2.1. Non-erosive Arthritis 4

2.2.2. Erosive Arthritis 5

2.3. Osteonecrosis, Avascular Osteonecrosis (AVN) 6

2.4. Osteoporosis 7

2.5. Insufficient Fractures 7

3. APPROACHES TO DIAGNOSIS OF SLE 7

3.1. Approach to Hand X-rays 8

3.1.1. Posteroanterior View, Posterior-anterior View (PA View) 8

3.1.2. Oblique View 10

3.1.3. Ball-catcher's View, Norgaard's View 11

3.1.4. Lateral View 14

CONCLUSION 14

CONSENT FOR PUBLICATION 15

CONFLICT OF INTEREST 15

ACKNOWLEDGEMENTS 15

REFERENCES 15

CHAPTER 2 ALIGNMENT OF MUSCULOSKELETAL SYSTEM IN SYSTEMIC LUPUS ERYTHEMATOSUS 18

Syuichi Koarada and *Mitsuteru Akahoshi*

1. INTRODUCTION 18

2. NON-EROSIVE ARTHROPATHY, JACCOUD'S ARTHROPATHY 19

3. CHRONIC FIXED DEFORMITIES 20

4. MECHANISM OF DEFORMITIES OF JOINTS 20

5. HANDS 20

5.1. Deformities of Metacarpophalangeal Joints 20

5.1.1. Ulnar Deviation of Metacarpophalangeal Joints 21

5.1.2. Flexion Deformities of MCP Joints 24

5.2. Deformities of DIP and PIP Joints 24

5.2.1. Boutonniere Deformities 24

5.2.2. Swan-neck Deformities 25

5.3. Dislocation 28

5.4. Flexion Contracture of Digits 29

5.5. Osteoarthritis of Hands in SLE 31

5.6. Thumbs 31

5.6.1. Swan-neck Deformities 31

5.6.2. Z-thumbs, Boutonniere Deformities 32

6. WRISTS 34

6.1. Radial Deviation of Wrists 34

6.2. Carpal Collapse 35

7. SHOULDERS 35
8. HIPS 35
8.1. Osteonecrosis of Hips 35
9. KNEES 37
10. FEET 38
10.1. Hallux Valgus 38
10.2. Hammer Toes, Mallet-toes, and Claw-toes 38
10.2.1. Hammer Toes 39
10.2.2. Crossover Toe Deformities 40
10.2.3. Mallet-toes 42
10.2.4. Claw-toes and Curly Toes 43
10.3. Tailor's Bunion, Digitus Quintus Varus 44
10.4. Flat Feet and Pedes Spinatus 45
10.5. Widening of Forefeet 45
11. SPINE 46
11.1. Lumbar Spine 46
11.2. Cervical Spine 46
12. FRACTURES 47
12.1. Hands 47
12.2. Feet 48
12.3. Spine 48
12.4. Pelvis 49
12.4.1. Fractures of Pubic Bones 49
12.4.2. Fractures of Ischiopubic Ramus 50
CONCLUSION 50
CONSENT FOR PUBLICATION 50
CONFLICT OF INTEREST 50
ACKNOWLEDGEMENTS 50
REFERENCES 50

CHAPTER 3 BONE LESIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS 52
Syuichi Koarada and *Akihito Maruyama*
1. INTRODUCTION 52
2. BONE MINERALIZATION 52
2.1. Periarticular (Juxta-articular) Osteoporosis 52
2.1.1. Hands 55
2.1.2. Wrists 67
2.1.3. Elbows 68
2.1.4. Shoulders 70
2.1.5. Knees 70
2.1.6. Ankles 70
2.1.7. Feet 71
2.2. Generalized Osteopenia, Generalized Osteoporosis 72
3. OSTEOSCLEROSIS 74
3.1. Hands 74
3.1.1. Acro-osteosclerosis 74
3.1.2. Osteosclerosis of Tufts 74
3.1.3. DIP Joints 74
3.1.4. IP joints 75
3.1.5. PIP Joints 75
3.1.6. MCP Joints 76

3.2. Hips 76
3.3. Knees 76
3.4. Feet 77
3.4.1. MTP Joints 77
3.5. Sacroiliac Joints 77
3.6. Vertebral End Plates 78
4. BONE SHAPE 78
4.1. Erosions 78
4.1.1. Erosions in Rhupus 78
4.1.2. MRI 80
4.1.3. Hands 81
4.1.4. Wrists 88
4.1.5. Feet 90
4.2. Cystic Changes 92
4.2.1. Hands 92
4.4.2. Hips 95
4.4.3. Feet 95
4.3. New Bone Formation: Osteophytes and Syndesmophytes 95
4.3.1. Osteophytes 95
5. AVASCULAR NECROSIS OF BONES 101
CONCLUSION 102
CONSENT FOR PUBLICATION 102
CONFLICT OF INTEREST 102
ACKNOWLEDGEMENTS 102
REFERENCES 102

CHAPTER 4 CARTILAGINOUS AND CAPSULAR CHANGES IN SYSTEMIC LUPUS ERYTHEMATOSUS 104
Syuichi Koarada and *Sachiko Soejima*
1. INTRODUCTION 104
2. SYNOVITIS 105
2.1. Jaccoud's Arthropathy 105
2.2. DIP Joints 105
2.3. IP Joints 106
2.4. PIP Joints 107
2.4.1. Second PIP Joints 107
2.4.2. Third PIP Joints 108
2.4.3. Fourth PIP Joints 111
2.4.4. Fifth PIP Joints 112
2.5. MCP Joints 113
2.5.1. First MCP joints 113
2.5.2. Second MCP Joints 114
2.5.3. Third MCP Joints 116
2.5.4. Fourth MCP Joints 120
2.5.5. Fifth MCP Joints 121
2.6. Wrists (Fig. 52) 122
2.6.1. First Digit Line of Wrist 123
2.6.2. Second Digit Line of the Wrist 124
2.6.3. Third Digit Line of the Wrist 125
2.6.4. Fourth Digit Line of the Wrist 130
2.6.5. Ulna Line of the Wrist 131

2.7. Elbows 134
2.8. Knees 135
2.9. Ankles 135
2.10. Feet 136
2.11. Sacroiliac Joints 138
3. JOINT EFFUSIONS 138
3.1. Hands 138
3.1.1. MCP Joints 138
3.2. Wrists 139
3.3. Elbows 140
3.4. Knees 140
4. JOINT SPACES 145
4.1. Rhupus 145
4.2. Joint Space Narrowing 145
4.2.1. Hands 145
4.2.2. Elbows 150
4.2.3. Knees 150
4.2.4. Sacroiliac Joints 151
4.3. Joint Space Widening (JSW) 151
4.4. Pseudo Joint Space Narrowing 151
5. CALCIFICATIONS 152
5.1. Calcifications of Joint Capsules 152
5.1.1. DIP Joints 152
5.1.2. IP Joints 153
5.1.3. PIP Joints 153
5.1.4. MCP Joints 154
5.1.5. Carpal Joints 155
CONCLUSION 155
CONSENT FOR PUBLICATION 155
CONFLICT OF INTEREST 155
ACKNOWLEDGEMENTS 155
REFERENCES 156

CHAPTER 5 DISTRIBUTION, PATTERN OF JOINT INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS 157
Syuichi Koarada and *Mariko Sakai*
1. INTRODUCTION 157
1.1. Gallium Scintigraphy 159
1.2. Bone Scintigraphy 162
2. DISTRIBUTION OF ARTHRITIS 163
2.1. General Distribution 163
2.1.1. Distribution of Arthritis by Subtypes 164
2.1.2. Distribution of Bone Cysts 164
2.1.3. Distribution of Osteonecrosis 164
2.1.4. Distribution of Osteonecrosis in Antiphospholipid Antibody Syndrome (APS) 165
2.1.5. Distribution of Bone Infarcts 165
2.1.6. Distribution of Insufficient Fractures 165
2.1.7. Distribution of Myositis 165
2.1.8. Distribution of Infection 165
2.2. Distribution in Regions 166
2.2.1. Hands 166

2.2.2. Lower Limbs 169
2.2.3. Sacroiliac Joints 169
2.2.4. Tenosynovitis (Distribution of Tenosynovitis in the Hands) 169
2.2.5. Axial Skeleton 170
2.3. Distribution in Joints 171
2.4. Distribution of Timeline 171
2.4.1. Early Phase 171
2.4.2. Active Phase 171
2.4.3. Terminal Phase 172
CONCLUSION 172
CONSENT FOR PUBLICATION 172
CONFLICT OF INTEREST 173
ACKNOWLEDGEMENTS 173
REFERENCES 173

CHAPTER 6 EXTRA-ARTICULAR SOFT TISSUE AND MUSCULAR INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS 175
Syuichi Koarada, Makiko Takayama, Kouki Takedomi, Jun Hirano, Hijiri Hirose, Yuumi Maeda, Yuiko Miyajima, Honoka Mouri and *Yukiko Takeyama*
1. INTRODUCTION 175
2. PERIPHERAL SOFT TISSUE SWELLING 176
2.1. Hand 176
2.2. Wrists 181
2.3. Knees 182
2.4. Ankles 183
3. CALCIFICATIONS 184
3.1. Soft Tissue Calcifications 184
3.2. Calcification Around Joints 185
3.3. Arterial Calcifications 185
4. BURSAE 185
4.1. Knees 186
4.2. Ankles 189
4.2.1. Lateral Premalleolar Bursitis 189
5. TENDONS 193
5.1. Involvement of Tendons 193
5.2. Tendon Sheaths, Tenosynovitis 194
5.2.1. Hands and Wrists 194
5.2.2. Digits 200
5.2.3. Wrists 207
5.2.4. Knees 208
5.3. Peritenon Extensor Tendon Inflammation (PTI) 209
6. LIGAMENTS 212
6.1. Digits 212
7. ENTHESITIS / ENTHESEAL INVOLVEMENTS 213
7.1. DIP Joints 213
7.2. PIP Joints 215
7.3. MCP Joints 217
7.4. Knees 217
8. LUPUS MYOPATHY 218
CONCLUSION 218
CONSENT FOR PUBLICATION 218

CONFLICT OF INTEREST 218
ACKNOWLEDGEMENTS 219
REFERENCES 219

CHAPTER 7 SKIN MANIFESTATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS 221
Syuichi Koarada and *Tetsuhiro Maesaki*
1. INTRODUCTION 221
2. ACUTE CUTANEOUS LUPUS ERYTHEMATOSUS (ACLE) 222
2.1. Lupus Malar Rash 222
2.1.1. Typical Malar Rash 223
2.1.2. Mild Malar Rash 224
2.1.3. Atypical Malar Rash 225
2.2. Maculopapular Lupus Rashes, Widespread Erythematous Maculopapular Lesions 226
2.2.1. Hands 226
2.2.2. Forearms 231
2.2.3. Elbows 231
2.2.4. Upper Arms 232
2.2.5. Faces 233
2.2.6. Necks and Jaws 234
2.2.7. Backs 236
2.2.8. Abdomens 237
2.2.9. Thighs 237
2.2.10. Knees 237
2.2.11. Lower Limbs 238
2.2.12. Feet 239
2.3. Palmar Erythema 241
2.4. Bullous LE Skin Rashes, Bullous Lesions (BSLE), Bullous Lupus Erythematosus 241
2.5. Toxic epidermal necrolysis (TEN) 243
2.6. Photosensitivity 244
2.7. Periungual Erythema 244
2.8. Periungual Telangiectasias 246
3. SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS (SCLE) 247
3.1. Annulare SCALE, large polycyclic lesions or small cyclic lesions 248
3.2. Mixed form with both annular and psoriasiform lesions 248
3.3. Papulosquamous Psoriasiform Lesions 251
3.3.1. Hands 251
3.3.2. Wrists 253
3.3.3. Elbows 253
3.3.4. Upper Arms 254
3.3.5. Feet 254
4. CHRONIC CUTANEOUS LUPUS 255
4.1. Classic Discoid Rashes, Discoid Lupus Erythematosus (DLE) 255
4.1.1. Ears 255
4.1.2. Hands 255
4.1.3. Elbows 256
4.1.4. Knees 257
4.1.5. Backs 257
4.1.6. Abdomens 258
4.2. Chilblain Lupus Erythematosus, Chilblain Lupus 258

4.2.1. Hands 259
4.2.2. Feet 261
4.3. Hypertrophic or Verrucous Lupus 262
4.3.1. Hands 262
4.3.2. Elbows 263
4.3.3. Knees 264
4.3.4. Feet 264
4.4. Lupus Erythematosus Profundus 265
4.5. Mucosal Lupus 267
4.5.1. Oral Ulcers 267
4.5.2. Cheilitis 268
4.5.3. Angular Cheilitis 269
4.6. Nodular Cutaneous Lupus Mucinosis; NCLM 269
5. OTHER MANIFESTATIONS OF SKIN 270
5.1. Urticarial Vasculitis in SLE 270
5.2. Livedo Reticularis 271
5.3. Raynaud's Phenomenon 272
5.4. Acrocyanosis 275
5.5. Erythromelalgia 275
5.6. Gangrene of Extremities 276
5.7. Subcutaneous Hematoma 277
5.8. Internal Bleeding 278
5.9. Subcutaneous Nodules 278
5.10. Necrotizing Fasciitis 278
5.11. Subcutaneous Edema 278
5.12. Soft Tissue Calcifications 279
5.13. Nonscarring Alopecia, Hair Loss/alopecia 280
6. NON-SPECIFIC SKIN LESIONS 281
7. INFECTIONS 281
7.1. Herpes Zoster 281
CONCLUSION 283
CONSENT FOR PUBLICATION 283
CONFLICT OF INTEREST 283
ACKNOWLEDGEMENTS 283
REFERENCES 283

CHAPTER 8 RESPIRATORY INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS 286
Syuichi Koarada and *Yoshinobu Nakao*
1. INTRODUCTION 286
2. PLURA 287
2.1. Pleural Effusions 287
2.1.1. Imaging Findings 287
2.2. Pleuritis 289
3. PARENCHYMA 289
3.1. Interstitial Pneumonia, Interstitial Lung Disease (ILD) 289
3.1.1. Lupus Pneumonitis 289
3.1.2. Chronic Lupus Pneumonitis 291
3.2. Diffuse Alveolar Hemorrhage (DAH) 292
3.2.1. Imaging Findings 292
3.2.2. Chest CT Scans 293
4. BRONCHI 294

4.1. Bronchiectasis 294
5. DIAPHRAGM 294
5.1. Diaphragmatic Dysfunction 294
5.1.1. Imaging Findings 295
6. PULMONARY INFECTIONS 295
6.1. Bronchopulmonary Infections 295
6.1.1. Pneumonia 296
6.1.2. Pneumocystis Pneumonia (PCP) 298
6.1.3. Aspergillus Pneumonia, Pulmonary Aspergillosis 300
6.1.4. Cryptococcal Pneumonia 302
6.1.5. Legionella Pneumonia 303
6.1.6. Pulmonary Tuberculosis 304
CONCLUSION 309
CONSENT FOR PUBLICATION 309
CONFLICT OF INTEREST 309
ACKNOWLEDGEMENTS 309
REFERENCES 309

CHAPTER 9 NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (NP-SLE) 311
Syuichi Koarada and *Yuri Shirahama*
1. INTRODUCTION 311
2. CENTRAL NERVOUS SYSTEM 312
2.1. Cerebral Atrophy 312
2.2. Diffuse Cerebral Edema with Leukoencephalopathy 313
2.3. White-matter Lesions in Central Nervous System (CNS) 314
2.4. CNS Ischemia 315
2.4.1. Medial Longitudinal Fasciculus Syndrome 315
2.5. Occlusion of Dural Venous Sinuses and Deep Cerebral Veins 317
2.6. Intracranial Hemorrhage (ICH) 317
2.7. Posterior Reversible Encephalopathy Syndrome (PRES) 319
2.8. Lupus Meningitis 319
3. PERIPHERAL NEUROPATHY IN SLE 320
CONCLUSION 320
CONSENT FOR PUBLICATION 320
CONFLICT OF INTEREST 320
ACKNOWLEDGEMENTS 320
REFERENCES 320

CHAPTER 10 CARDIOVASCULAR AND RENAL DISEASES IN SYSTEMIC LUPUS ERYTHEMATOSUS 322
Syuichi Koarada and *Satoko Tashiro*
1. INTRODUCTION 322
2. PERICARDITIS 323
3. MYOCARDITIS 324
3.1. Libman-Sacks Endocarditis 324
3.2. Valvulopathy 324
4. CORONARY VESSELS 325
4.1. Left Anterior Descending (LAD) 325
4.2. Right Coronary Artery (RCA) 325
4.3. Left Circumflex Artery (LCx) 326
5. AORTA AND ITS BRANCHES 326
6. PULMONARY ARTERIAL HYPERTENSION (PAH) 326

6.1. Radiography 326
6.2. Electrocardiogram (ECG) 327
6.3. Echocardiography 328
6.4. Pulmonary Embolism (PE) 329
7. RENAL SYSTEM 329
CONCLUSION 329
ACKNOWLEDGEMENTS 329
REFERENCES 330

CHAPTER 11 GASTROINTESTINAL SYSTEM IN SYSTEMIC LUPUS ERYTHEMATOSUS 331
Syuichi Koarada and *Yukihide Ono*
1. INTRODUCTION 331
2. SEROSITIS 332
3. GASTRITIS 332
4. LUPUS ENTERITIS 333
5. CHOLECYSTITIS 333
6. SPLEEN 334
7. SALIVARY GLANDS 335
CONCLUSION 335
CONSENT FOR PUBLICATION 335
CONFLICT OF INTEREST 336
ACKNOWLEDGEMENTS 336
REFERENCES 336

SUBJECT INDEX 337

PREFACE

Systemic lupus erythematosus (SLE) is a chronic multisystem inflammatory connective tissue disease with immunologic abnormalities producing autoantibody, including anti-ds (double strand)-DNA antibodies. In SLE, joint symptoms are the most common and one of the first signs.

The objective of our monograph is to integrate information on musculoskeletal and systemic pathophysiology in SLE. Although SLE is one of the rheumatic diseases, lesions extend not only to joints but to the whole body, causing inflammation in diverse organs, such as the skin, lungs, nervous system, serous membranes, kidneys and virtually all organs of the body. Therefore, patients with SLE have various presentations of disorders of organs. It is necessary to understand the findings of various organs throughout the body for proper diagnosis and treatment of patients with SLE.

Early diagnosis and treatment are required for rheumatic diseases, but early diagnosis is often difficult due to the enormous and diverse findings. Therefore, we are widely advocating a methodology called the ABCDEFGHI method as a comprehensive diagnostic approach based on the clinical, imaging, and immunological characteristics of rheumatic diseases.

The ABCDEFGHI method consists of A (Alignment): malalignment and deformation, B (Bone): bone changes, C (Capsular lesions): cartilage and intra-articular lesions, D (Distribution): four-dimensional altered distribution: 1 intra-articular, 2 intra region, 3 intra-body, 4 timeline, E (Extra-bone): extra-articular soft tissue, F (Further information): further additional medical information, G (Goal): general analysis and diagnosis, I (Integration): integrated and comprehensive diagnosis from the above data and information, H (Heal and Heath): treatment and prognosis, and I (Immunological analyzes): immunological interpretations (cytokines and immune cell phenotypes).

It is a method of making a comprehensive diagnosis by individually performing interpretations based on various symptoms, images, laboratory findings, and immunological analysis. This diagnostic procedure is being approved by medical students and evaluated from various fields.

The cases and images of patients with SLE discussed in this book are only a small part of the cases we have experienced. In the future, we would like to consider adding more cases to make the contents more complete. If there are any inadequacies in this book, we would like to receive suggestions from valuable readers. We would also be happy to receive suggestive cases and images from readers so that we can compose even better content.

I dedicate this book to my parents and my beloved Miwako and Sakura.

Syuichi Koarada

Department of Medical Technology and Sciences
International University of Health and Welfare
Okawa, Japan

List of Contributors

Akihito Maruyama	Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan
Hijiri Hirose	Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan
Honoka Mouri	Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan
Jun Hirano	Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan
Kouki Takedomi	Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan
Makiko Takayama	Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan
Mariko Sakai	Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan
Mitsuteru Akahoshi	Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan
Sachiko Soejima	Division of Rheumatology, Takagi Hospital, Okawa, Japan
Satoko Tashiro	Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan
Syuichi Koarada	Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan Division of Rheumatology, Takagi Hospital, Okawa, Japan Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan
Tetsuhiro Maesaki	Division of Rheumatology, Takagi Hospital, Okawa, Japan
Yoshifumi Tada	Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan
Yoshinobu Nakao	Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan
Yuiko Miyajima	Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan
Yukihide Ono	Division of Rheumatology, Takagi Hospital, Okawa, Japan
Yukiko Takeyama	Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan
Yuri Shirahama	Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan
Yuumi Maeda	Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan

CHAPTER 1

Introduction of Diagnostic Approach for Systemic Lupus Erythematosus

Syuichi Koarada[1, 2, 3,*] and **Yoshifumi Tada**[3]

[1] *Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan*

[2] *Division of Rheumatology, Takagi Hospital, Okawa, Japan*

[3] *Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan*

Abstract: Musculoskeletal symptoms occur in up to 90% of systemic lupus erythematosus (SLE) patients. Lesions extend not only to joints but to the whole body, causing inflammation in diverse organs such as the skin, kidneys, lungs, nervous system, serous membranes and virtually across all organs of the body. The ABCDEFGHI method consists of A (Alignment): malalignment and deformation; B (Bone): bone changes; C (Capsular lesions): cartilage and intra-articular lesions; D (Distribution): four dimensional distributions: 1 intra-articular, 2 Intra region, 3 intra-body, 4 timeline; E (Extra-bone): extra-articular soft tissue; F (Further information): further additional medical information; G (Goal): general analysis and integrated, a comprehensive diagnosis from the information; H (Heal and Heath): treatment and prognosis; and I (Immunological analyzes): immunological interpretation (cytokines and phenotypes of immune cells). This chapter outlines a methodology for diagnosing the musculoskeletal and systemic manifestations of SLE.

Keywords: Musculoskeletal symptoms, Systemic lupus erythematosus (SLE), Systemic manifestations.

1. INTRODUCTION

Systemic lupus erythematosus (SLE) is a complex and clinically heterogeneous autoimmune disease. Musculoskeletal symptoms occur in up to 90% of SLE patients [1, 2]. Musculoskeletal disorders cause disabling symptoms in 70% of patients [3].

[*] **Corresponding author Syuichi Korada:** Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan; Email: koarada@iuhw.ac.jp

Despite being one of the most common symptoms, medical and basic researchers do not always pay the utmost attention to musculoskeletal symptoms. Joint symptoms may be neglected in SLE because systemic, cutaneous, and organ lesions are more prominent.

Both directly and indirectly, musculoskeletal symptoms affect patient quality of life (QOL), causing immobility and frailty. Ultimately, the musculoskeletal symptoms have a significant effect on the prognosis of the musculoskeletal system due to osteoporosis, compression fractures, necrosis of the femoral heads, and are irreversible.

Suppose patients with SLE are not diagnosed early. In that case, treatment may be delayed, the lesions and disorders will persist, and delayed diagnosis is often the cause of impaired patient quality of life.

Patients with rheumatoid arthritis always have joint radiography performed at the first visit and on regular examinations thereafter. On the other hand, in SLE patients, even if they have joint symptoms/deformities, radiography of the joints may not always be taken. It is the patient's desire to relieve the pain without using glucocorticoids in the treatment with more attention to lupus arthritis and musculoskeletal symptoms. SLE is a systemic disease, but it is important to recognize that SLE is also a joint disease.

Musculoskeletal involvement is one of the most common manifestations of SLE and is present in 69-95% of lupus patients [4 - 9]. Moreover, joint symptoms are frequently one of the earliest manifestations. Many patients with SLE can develop non-erosive arthritis. Joint lesions range from mild to severe, but clinically and historically, joint symptoms of SLE, including joint pain or arthritis, have usually been considered transient, mild, or moderate [10].

Arthritis in SLE is very important symptomatology, as 58% of patients have active musculoskeletal lesions even at relapse in one cohort study [10]. Historically, in 1872, Kaposi identified SLE arthritis and reported that joint lesions were a precursor to the more severe symptoms of lupus.

However, most researchers did not adequately study arthritis in SLE as a milder symptom compared to systemic symptoms. Even now, in daily practice, joint symptoms in SLE may be milder. Furthermore, it has been reported that arthralgia is one of the most influential symptoms on the quality of daily life from the perspective of the patient [11, 12]. Because it has been shown that joint involvement deeply impacts on quality of life in SLE patients [11]. Recently, many studies have shown that joint deformities also occur in SLE patients,

causing erosive arthritis, the so-called rhupus syndrome, in up to 15% and Jaccoud's arthropathy [10, 13 - 16]. Musculoskeletal ultrasonography and magnetic resonance imaging (MRI) have become useful tools in assessing patients with arthritis.

Surprisingly, these new imaging techniques have shown articular involvement of SLE in an unexpected higher prevalence [12]. The evaluation of various forms of lupus arthropathy with clinical and laboratory functions and images, including conventional radiography, musculoskeletal ultrasound, MRI, and other modalities, is described. In addition, images of musculoskeletal lesions are used to determine overlap with other diseases, rheumatoid arthritis (RA), spondyloarthritis, vasculitis syndrome, fractures, septic arthritis, and osteomyelitis. To diagnose lupus arthropathy, it is necessary to perform and interpret typical conventional and other diagnostic imaging.

The cause of the disease is still unknown. Genetic, hormonal, and environmental factors are thought to play important roles in the pathophysiology of SLE. Multiple genes show genetic susceptibility to SLE. Environmental factors such as ultraviolet (UV) light, viral infections, female gender, and exposure to estrogen-containing drugs induce SLE.

This book will serve as a useful reference in clinical and radiological diagnosis.

2. CLASSIFICATION OF LUPUS ARTHROPATHY

Arthropathy of SLE is clinically extremely diverse. There are two indicating categories: 1) non-erosive or erosive, and 2) non-deformable or deformable. However, it is clinically useful to divide into three categories: non-specific arthritis, non-erosive arthropathy (Jaccoud's arthritis), and erosive arthritis (rhupus) [17]. Moreover, lupus arthropathy is clinically highly diverse and can be divided into at least six clinical forms.

Musculoskeletal abnormalities in SLE patients have tremendous clinical variability and include myositis, fasciitis, symmetric arthritis, non-erosive degenerative arthritis, spontaneous tendon rupture, soft tissue calcification, osteomyelitis, septic arthritis, terminal phalangeal sclerosis, erosion, and osteonecrosis (Table **1**).

CHAPTER 2

Alignment of Musculoskeletal System in Systemic Lupus Erythematosus

Syuichi Koarada[1, 2, 3,*] and **Mitsuteru Akahoshi**[3]

[1] *Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan*

[2] *Division of Rheumatology, Takagi Hospital, Okawa, Japan*

[3] *Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan*

Abstract: Abnormalities of joint alignment in systemic lupus erythematosus (SLE) are characterized by subluxation or dislocation without erosion. Hand deformities ("lupus hands") in SLE patients include ulnar deviation, swan neck deformity, and thumb Z deformity. However, abnormalities in alignment are widespread and can occur in the wrists, shoulders, hips, knees, toes, and spine. Osteonecrosis and fracture can also occur as alignment abnormalities. In addition, rheumatoid arthritis (RA) and other complications such as scleroderma and inflammatory myositis may also occur, making the alignment abnormalities complex. An understanding of alignment abnormalities in SLE is helpful in diagnosing the condition of the disease and establishing a treatment strategy. The purpose of this chapter is to provide an overview of alignment abnormalities in SLE from various perspectives.

Keywords: Hand deformities, Joint alignment, Lupus hands, Systemic lupus erythematosus (SLE).

1. INTRODUCTION

Abnormalities of alignment in systemic lupus erythematosus (SLE) (category "A") are typically characterized by subluxation or dislocation without erosions. However, alignment abnormalities in late arthropathy include severe erosive deformities of the joints, such as rheumatoid arthritis combined with SLE called rhupus. In some cases, severe arthritis with erosive and deforming changes occurs and is clinically indistinguishable from RA.

[*] **Corresponding author Syuichi Koarada:** Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan; Email: koarada@iuhw.ac.jp

The typical alignment abnormality in SLE is Jaccoud's arthropathy is a reversible change. However, fixed deformities of joint changes can also occur in SLE. Hand deformities ("lupus hands") include ulnar deviation, boutonniere deformities, swan neck deformities, and thumb Z deformities.

However, abnormalities in alignment are widespread and can occur in the wrists, shoulders, hips, knees, toes, and spine. Osteonecrosis and fracture lesions can also occur as alignment abnormalities in SLE. In addition, rheumatoid arthritis (RA) and other complications such as scleroderma and inflammatory myositis may also occur. They make the alignment abnormalities in SLE complex. An understanding of alignment abnormalities in SLE is helpful in diagnosing the condition of the disease and establishing a treatment strategy. The objectives of this chapter are to provide a visual overview of alignment abnormalities in SLE from various perspectives.

2. NON-EROSIVE ARTHROPATHY, JACCOUD'S ARTHROPATHY

Deformities of the hands in patients with SLE include ulnar deviation, swan neck deformities, and Z deformities of the thumbs. In Jaccoud's arthropathy, hand deformities can be reduced and do not cause severe functional disability. Therefore, in the posterior-anterior (PA) view of a conventional radiograph, the technicians carefully position the digits, and the mispositioning may disappear. However, some patients may have chronic fixed deformities due to Jaccoud's arthropathy and rhupus (SLE and rheumatoid arthritis) [1].

Jaccoud *et al*. described Jaccoud's arthropathy as characterized by muscular atrophy, ulnar deviation, and flexion of the MCP joints in a patient with rheumatic fever (RF) [2].

Although classically described for rheumatic fever, Jaccoud's arthropathy also occurs in some connective tissue diseases such as SLE, systemic sclerosis, polymyositis/dermatomyositis, vasculitis, other infectious diseaeses, and neoplastic conditions.

In Jaccoud's arthropathy, the severe deformity can mimic rheumatoid arthritis, although erosions are absent. However, in Jaccoud's arthropathy, it is important that the deformities of the joints can be reversed by physical examination.

Bywaters reported a similar case in 1950 and reviewed European literature suggesting that Jaccoud's arthropathy can be distinguished from rheumatoid arthritis. In 1963, Twigg and Smith disseminated the concept by radiologically presenting the findings of Jaccoud's arthropathy observed in two patients at

Georgetown University Hospital. In 1869, Jaccoud first described Jaccoud's arthropathy [2].

Subluxations and/or dislocations of the MCP joints in SLE patients are observed in plain radiographs of the hands. Minor subluxations of the MCP and PIP joints of the digits are found in the plain radiographs of the restored same hands by radiographers. In Jaccoud's arthropathy, the deformities of the hands are reducible and do not cause severe functional disability compared to rheumatoid arthritis. Most patients with Jaccoud's arthropathy can easily correct the deformities on their own in their daily lives.

Unless otherwise instructed, the deformities may disappear in routine radiography as the radiologist carefully repairs the hand deformities. Therefore, it may be necessary to instruct the radiologist to take the image slightly away from the imaging surface in order to evaluate the deformation.

3. CHRONIC FIXED DEFORMITIES

Some patients of SLE have chronic fixed deformities.

4. MECHANISM OF DEFORMITIES OF JOINTS

The mechanism of joint deformities in arthropathy of SLE is caused by the laxity of the joint capsules and ligaments, contractures, and muscular imbalance.

5. HANDS

The main findings of plain radiography are swan-neck deformities, subluxations of the thumbs, ulnar deviation of the metacarpophalangeal (MCP) joints, Z-thumbs, contractures, tendon ruptures, and buttonhole deformities, but there are no signs of bone erosions.

5.1. Deformities of Metacarpophalangeal Joints

Changes in the digits of lupus arthritis show various deformities and deviations of the metacarpophalangeal (MCP) joints. These include ulnar deviation, extensor tendon subluxations, palmar subluxations, and flexion of the joints.

CHAPTER 3

Bone Lesions of Systemic Lupus Erythematosus

Syuichi Koarada[1,2,3,*] and **Akihito Maruyama**[3]

[1] *Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan*

[2] *Division of Rheumatology, Takagi Hospital, Okawa, Japan*

[3] *Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan*

Abstract: Category "B" is a description of bone changes in systemic lupus erythematosus (SLE). Bone lesions in most patients with SLE show only mild changes, including periarticular osteopenia, without erosions or deformities. Therefore, joint and bone destruction is rarely seen. However, bone changes may be evident in some patients with Jaccoud's arthropathy and rhupus. Bone changes include a wide variety of lesions such as bone erosions, bone cysts, osteophytes, and avascular osteonecrosis. The findings of category B are important in the pathophysiology and diagnosis of SLE. Bone lesions of SLE are outlined graphically in this chapter.

Keywords: Avascular osteonecrosis, Bone cysts, Bone erosions, Osteophytes, Periarticular osteopenia, Systemic lupus erythematosus (SLE).

1. INTRODUCTION

Usually, radiographs in systemic lupus erythematosus (SLE) show only mild signs of bone changes. Synovium is the target of SLE, same as rheumatoid arthritis, although erosive structural damage is rare. However, osseous and cartilaginous alterations become evident in some patients with lupus arthropathy [1]. Bone changes in SLE include periarticular osteopenia, generalized osteoporosis, osteosclerosis, erosions, cystic changes, osteophytes, avascular osteonecrosis, and bone infarcts.

2. BONE MINERALIZATION

2.1. Periarticular (Juxta-articular) Osteoporosis

Juxta-articular (periarticular) osteoporosis or osteopenia is one of the prominent

[*] **Corresponding author Syuichi Koarada:** Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan; Email: koarada@iuhw.ac.jp

radiographic abnormalities of the bone (category "B") in SLE. In SLE, juxta-articular osteoporosis and/or soft tissue swelling are often the only findings of radiographs.

Also, juxta-articular osteoporosis, regional osteoporosis, is one of the earliest changes in arthritis of SLE. However, the degree of periarticular osteoporosis varies and is observed in various joints such as the hands and wrists (Figs. **1** - **6**), elbows, shoulders, knees, ankles, and toes.

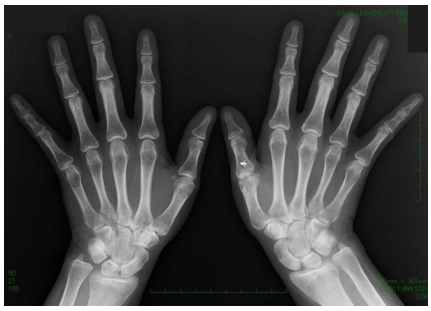

Fig. (1). PA view of the hands in a patient with SLE shows mild periarticular osteoporosis of the MCP joints.

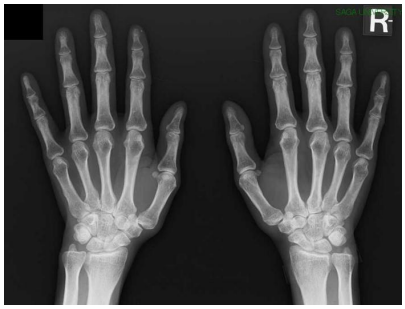

Fig. (2). PA view of the hands in a female with SLE shows mild periarticular osteoporosis of the DIP, IP, PIP, MCP, and carpal joints.

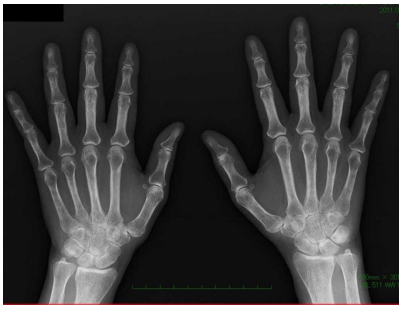

Fig. (3). PA view of the hands in a female with SLE shows moderate periarticular osteoporosis of the DIP, IP, PIP, MCP, and carpal joints.

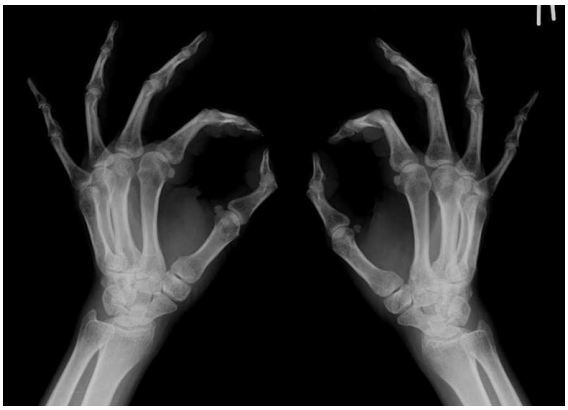

Fig. (4). Oblique view of the hands in a female with SLE shows moderate periarticular osteoporosis of the DIP, IP, PIP, MCP, and carpal joints.

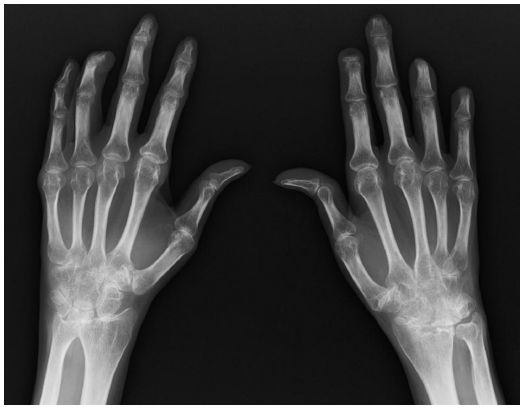

Fig. (5). PA view of the hands in a female with SLE shows severe periarticular osteoporosis of the DIP, IP, PIP, MCP and carpal joints.

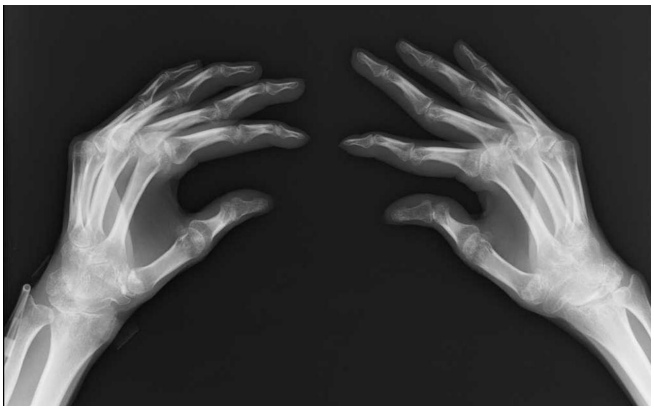

Fig. (6). Oblique view of the hands in a female with SLE shows severe periarticular osteoporosis of the DIP, IP, PIP, MCP and carpal joints.

CHAPTER 4

Cartilaginous and Capsular Changes in Systemic Lupus Erythematosus

Syuichi Koarada[1,2,3,*] and **Sachiko Soejima**[2]

[1] *Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan*

[2] *Division of Rheumatology, Takagi Hospital, Okawa, Japan*

[3] *Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan*

Abstract: Cartilaginous and capsular lesions in systemic lupus erythematosus (SLE), such as diffuse joint space narrowing (JSN) and synovial proliferation, are usually mild. Erosions and pressure cause destruction of cartilages in SLE due to misalignment of joint structures. However, cartilage changes and synovial proliferation are seen in lupus arthropathy. Especially in rhupus, which is thought to be a complication of rheumatoid arthritis, cartilaginous and synovial changes are significant findings. Joint effusions and intra-articular calcifications may also be seen. This chapter will focus on intra-articular lesions, category "C" in SLE.

Keywords: Capsular changes, Cartilaginous changes, Joint effusions, Joint space narrowing, Synovial proliferation, Systemic lupus erythematosus (SLE).

1. INTRODUCTION

In systemic lupus erythematosus (SLE), joint space narrowing (JSN) is not common except for rhupus, which coexists with rheumatoid arthritis. Cartilage destruction can be caused by erosions and pressure from abnormal joint construction. However, in some cases of lupus arthropathy, cartilage and bone changes can be evident. Especially in rhupus (SLE and rheumatoid arthritis), cartilaginous and synovial changes are significant findings. Joint effusions and intra-articular calcifications may also be seen. In this chapter intra-articular lesions, category "C" in SLE is illustrated and discussed.

[*] **Corresponding author Syuichi Koarada:** Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan; Email: koarada@iuhw.ac.jp

2. SYNOVITIS

In the joints of patients with SLE, there is hypertrophy of the synovial membranes and edema of joint capsules.

2.1. Jaccoud's Arthropathy

Jaccoud's arthropathy is one of the major causes of synovitis [1]. Ultrasound findings of synovitis include intra-capsular synovial proliferation (hypertrophic synovial tissue), joint effusions (intra-articular anechoic or hypoechoic fluid collection), capsular distention, and positive power Doppler signals (hyperemia, increased local perfusion). Gabba reported that synovitis was present in 25% of patients with joint effusions and/or synovial proliferation with or without power Doppler signals [2]. The presence of power Doppler signals was found in the joints of 17% of patients [2].

2.2. DIP Joints (Figs. 1 - 3)

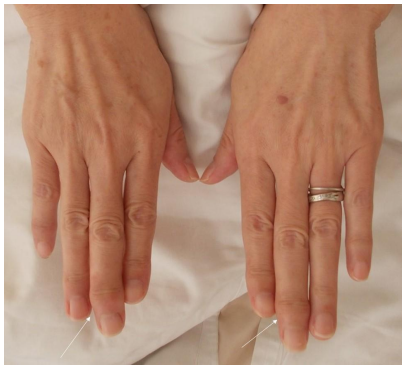

Fig. (1). Swelling of the DIP joints of bilateral third digits in a patient with SLE.

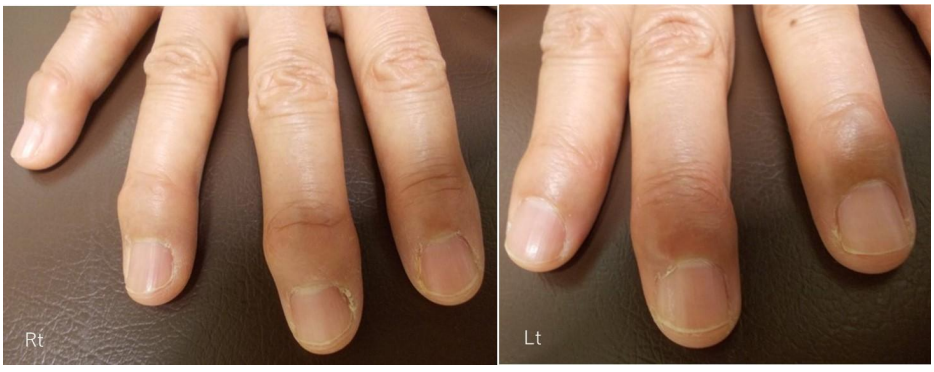

Fig. (2). Swelling of the DIP joints of the digits in a patient with SLE.

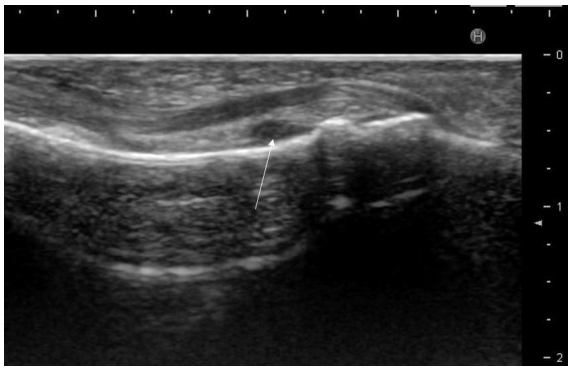

Fig. (3). Palmar longitudinal ultrasound image of the DIP joint of the third digit in a patient with SLE showing synovial hypertrophy (arrow).

2.3. IP Joints (Figs. 4 - 5)

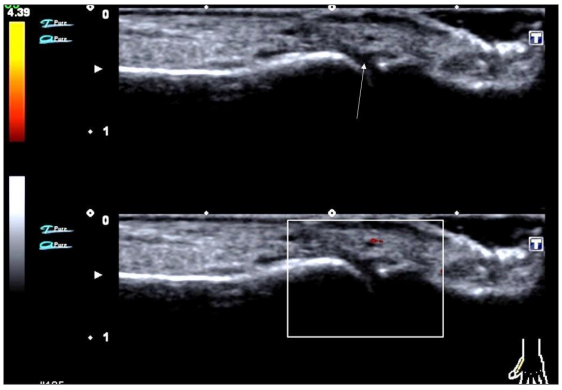

Fig. (4). Dorsal longitudinal ultrasound images of the IP joint of the first digit in a patient with SLE show minimal synovial hypertrophy without power Doppler signals.

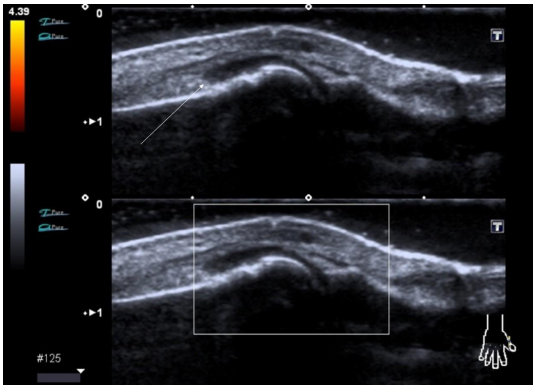

Fig. (5). Dorsal longitudinal ultrasound images of the IP joint of the first digit in a patient with SLE showing moderate synovial hypertrophy without power Doppler signals.

CHAPTER 5

Distribution, Pattern of Joint Involvement in Systemic Lupus Erythematosus

Syuichi Koarada[1,2,3,*] and **Mariko Sakai**[3]

[1] *Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan*

[2] *Division of Rheumatology, Takagi Hospital, Okawa, Japan*

[3] *Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan*

Abstract: There are four concepts of distribution of joint and tendon lesions in systemic lupus erythematosus (SLE): general distribution, regional distribution, intra-articular distribution, and timeline. Usually, joint lesions in SLE are symmetrically, bilaterally, and multiply distributed. However, the distribution varies from case to case. The distribution of the lesions can be ascertained by using bone scintigraphy and gallium scintigraphy. The distribution of the lesions is very important information for the diagnosis of SLE.

Keywords: Distribution of musculoskeletal lesions, General distribution, Intra-articular distribution, Regional distribution, Systemic lupus erythematosus (SLE), Timeline.

1. INTRODUCTION

The target area approach is a concept and a method that is useful for radiographic evaluation of rheumatic diseases. The distribution of joint involvement in systemic lupus erythematosus (SLE) is symmetric and has bilateral polyarthritis [1].

In SLE, joint lesions can occur anywhere [2]. However, the most affected joints in SLE are the metacarpal phalangeal (MCP) joints, proximal interphalangeal (PIP) joints, distal interphalangeal (DIP) joints interphalangeal (IP) joints of the thumbs, wrists, and knees (Fig. **1**) [1 - 4]. Lupus arthritis occurs less often on the shoulders, feet, and elbows [2].

* **Corresponding author Syuichi Koarada:** Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan; Email: koarada@iuhw.ac.jp

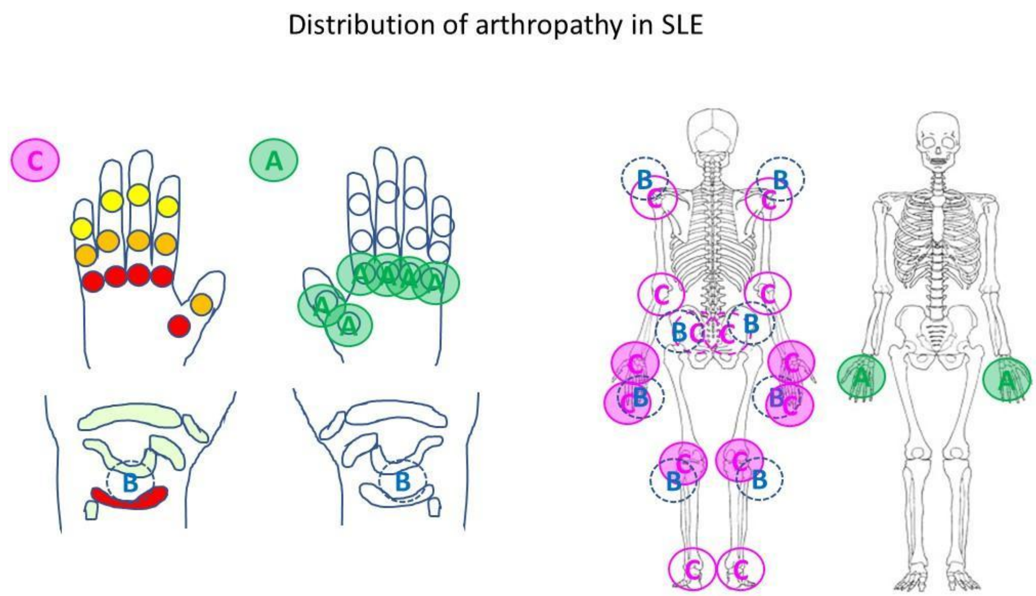

Fig. (1). Distribution of arthropathy in SLE.

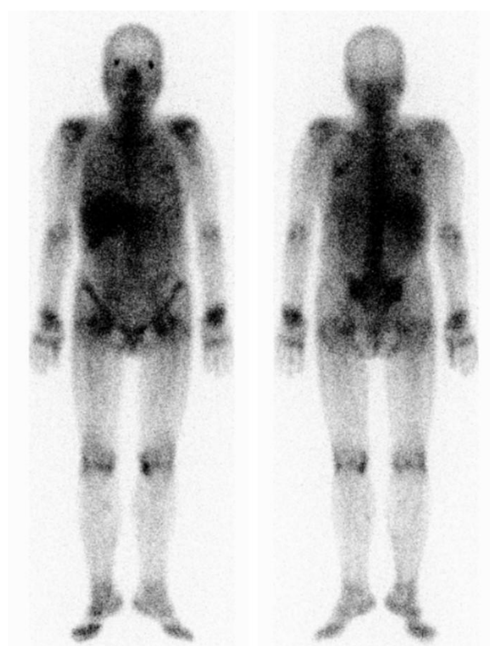

Fig. (2). Gallium scintigraphy can well represent the distribution of severe polyarthritis of the large and small joints in SLE.

1.1. Gallium Scintigraphy (Figs. 2 - 8)

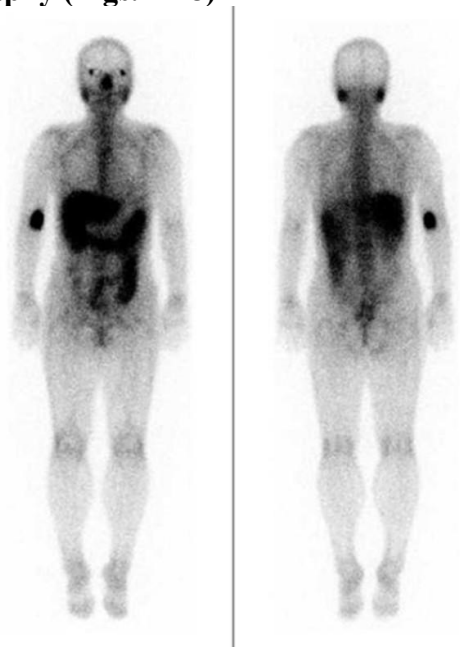

Fig. (3). Gallium scintigraphy shows the distribution of moderate polyarthritis of the large and small joints in SLE.

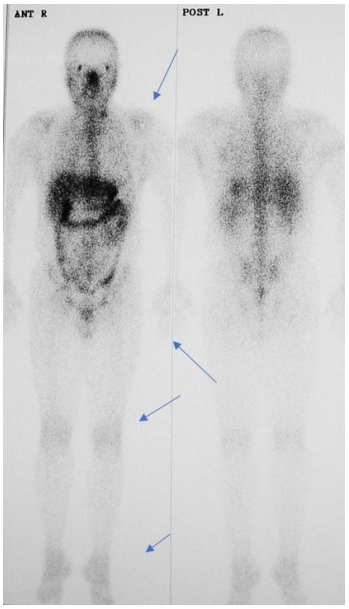

Fig. (4). Gallium scintigraphy shows the distribution of mild polyarthritis of the large and small joints in SLE.

CHAPTER 6

Extra-Articular Soft Tissue and Muscular Involvement in Systemic Lupus Erythematosus

Syuichi Koarada[1,2,3,*], Makiko Takayama[1], Kouki Takedomi[1], Jun Hirano[1], Hijiri Hirose[1], Yuumi Maeda[1], Yuiko Miyajima[1], Honoka Mouri[1] and **Yukiko Takeyama[3]**

[1] *Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan*

[2] *Division of Rheumatology, Takagi Hospital, Okawa, Japan*

[3] *Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan*

Abstract: Soft tissue lesions in systemic lupus erythematosus (SLE) include various lesions such as subcutaneous edema, synovitis of the joint, edema of the joint capsule, tenosynovitis, tendon rupture, muscular, and vascular involvement. The synovium of bursa is also affected. Ultrasound and MRI are especially important for the evaluation of soft tissue lesions because of the low sensitivity of conventional radiography. The soft tissue lesions of SLE are diverse and widespread, and understanding their pathophysiology can help diagnose whether the lesions are of SLE origin or a complication of other factors. Knowing the soft tissue lesions of SLE can also help us to deal with the wide variety of lesions in SLE patients. In this article, we summarize the variety of extra-articular soft tissue lesions.

Keywords: Bursitis, Edema, Peritenon extensor tendon inflammation (PTI), Soft tissue lesions, Systemic lupus erythematosus (SLE), Tenosynovitis.

1. INTRODUCTION

Soft tissue lesions in systemic lupus erythematosus (SLE) include various lesions such as subcutaneous edema, synovitis of the joint, edema of the joint capsule, tenosynovitis, tendon rupture, muscular, bursitis, and vascular involvement. Ultrasound and MRI are useful for the evaluation of soft tissue lesions. Knowing the soft tissue lesions of SLE can also help us to deal with the wide variety of lesions in SLE patients.

[*] **Corresponding author Syuichi Koarada:** Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan; Email: koarada@iuhw.ac.jp

Syuichi Koarada (Ed.)

Joint swelling is due to the growth of synovial tissue and / or synovial fluid. Soft tissue swelling associated with arthritis is more accurately an intracapsular finding and should be included in category "C", but in clinical practice it is often accompanied by inflammation of the soft tissue around the joints. Therefore, the finding also belongs to the category "E" as soft tissue swelling due to arthritis of systemic lupus erythematosus. In most of patients with SLE, soft tissue swelling, and periarticular osteoporosis are usually the only radiographic findings.

Soft tissue swelling of the joints is present in SLE but is less pronounced than in rheumatoid arthritis. As a result of increased intra-articular fluid, synovial hypertrophy, and thickening of adjacent soft tissues, the joints swollen in fusiform or spindle shapes.

2. PERIPHERAL SOFT TISSUE SWELLING

In patients with SLE, periarticular soft tissue swelling, swelling of soft tissue around the joints, is seen at various sites. Periarticular soft tissue swelling varies depending on the underlying condition of each SLE patient.

2.1. Hand (Figs. 1 - 15)

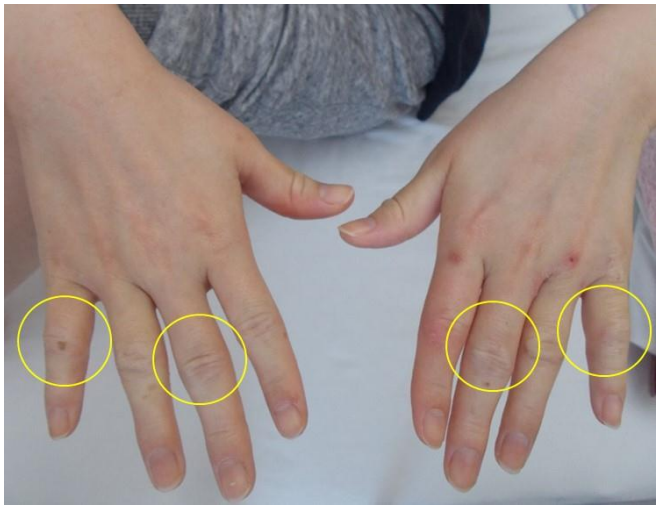

Fig. (1). Fusiform soft tissue swelling in the hands of a patient with SLE. Photograph of the hands shows soft tissue swelling at the PIP joints of a patient with non-deforming non-erosive (NDNE) lupus arthropathy.

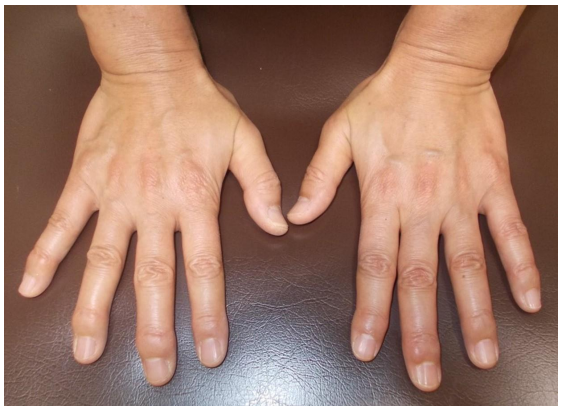

Fig. (2). Joint swelling of the DIP joints in a patient with SLE.

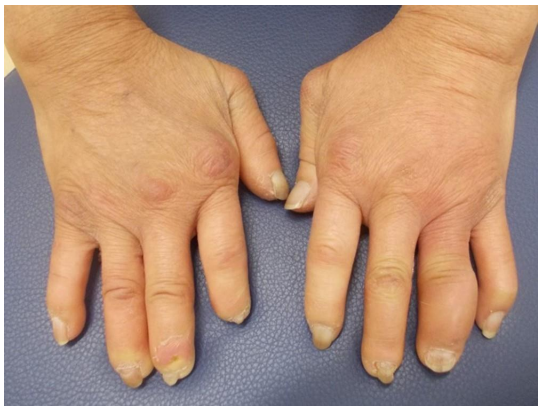

Fig. (3). Joint swelling of the DIP and PIP joints of the left fourth digit in a patient with SLE and scleroderma.

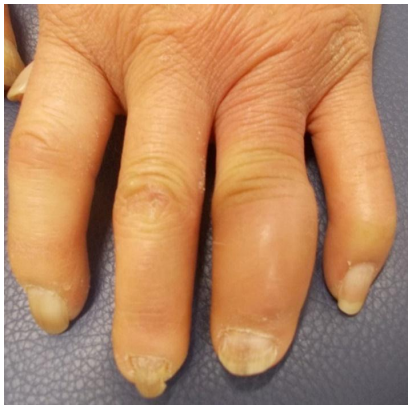

Fig. (4). Enlarged image of the previous figure. Joint swelling of the DIP and PIP joints of the left fourth digit in a patient with SLE and scleroderma.

CHAPTER 7

Skin Manifestations in Patients with Systemic Lupus Erythematosus

Syuichi Koarada[1,2,3,*] and **Tetsuhiro Maesaki**[2]

[1] *Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan*

[2] *Division of Rheumatology, Takagi Hospital, Okawa, Japan*

[3] *Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan*

Abstract: Skin manifestations are one of the most common presenting symptoms in systemic lupus erythematosus (SLE). Skin lesions are seen in more than 80% of patients with SLE at some point during the disease and are also the initial manifestations. The skin manifestations of SLE are varied. Skin lesions of SLE include lupus malar rash, maculopapular lupus rashes, palmar erythemas, bullous rashes, subacute cutaneous lupus erythematosus, chilblain lupus and discoid rashes. These skin lesions can be classified as acute, subacute, and chronic lesions. Specific skin lesions are important for the diagnosis of SLE. This review will outline and illustrate the skin lesions of SLE.

Keywords: Chilblain lupus, Discoid rashes, Maculopapular rashes, Malar rash, Palmar erythema, Subacute cutaneous erythematosus, Systemic lupus erythematosus (SLE).

1. INTRODUCTION

Skin symptoms are one of the most common manifestations of systemic lupus erythematosus (SLE). Various lesions of the skin and mucous membranes are often found in more than 80% of SLE patients at some point during the disease. The symptoms of the skin in SLE are diverse [1]. Importantly, cutaneous symptoms are the first signs of SLE in up to 25% of cases [1].

The American College of Rheumatology (ACR)-SLE classification criteria and the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria include mucocutaneous signs and are used for the SLE classification.

* **Corresponding author Syuichi Koarada:** Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan; Email: koarada@iuhw.ac.jp

SLE is associated with a wide range of oral mucosal lesions, including cheilitis, erythematous patches, “honeycomb” plaques, discoid lesions, lichen planus-like lesions, and discrete ulcers.

In 1979, Sontheimer *et al.* classified cutaneous lesions of LE based on their morphologic features and duration [2]. They classified the lesions into three types: the chronic type, which is typical of discoid lupus erythematosus (DLE); the acute type, which is fixed and scarring lupus erythematosus (LE) and in severe SLE; and recurrent, superficial, non-scarring LE was classified as subacute cutaneous lupus erythematosus (SCLE). SCALE is classified into papulo-squamous type and annular-polycyclic type.

Specific skin lesions of SLE are classified into acute, subacute, and chronic types and further into localized, disseminated, and generalized [3]. These specific skin lesions are important for the definitive diagnosis of SLE, and if present, at least a diagnosis of LE can be made. More than one type of skin lesion is often seen in the same patients. LE with an acute type of rashes is usually the lesions of SLE. Although significant improvements have recently been performed in the classification of skin lesions in SLE, there are some major limitations due to differences in terminology depending on the classification criteria [1].

2. ACUTE CUTANEOUS LUPUS ERYTHEMATOSUS (ACLE)

Butterfly erythema, butterfly rash, or lupus malar rash, is the most common skin rash in acute cutaneous lupus erythematosus (ACLE); however, there is also a skin rash of similar significance on the hands. LE with these types of skin rashes is usually associated with systemic symptoms of SLE. ACLE includes lupus malar rash, bullous lupus, toxic epidermal necrolysis variant of SLE, maculopapular lupus rash, and a photosensitive lupus rash.

2.1. Lupus Malar Rash

Patients with acute cutaneous lupus erythematosus (ACLE) have classic malar or butterfly rash, which is a flat or raised fixed erythema over the malar eminences and tends to preserve the nasolabial folds. The butterfly rash is the most common and well-known skin lesion in SLE patients.

Regarding the distributions of rashes, erythemas are on the cheeks and bridge of the nose but not on the nasolabial folds. The rashes may also appear around the mouth and on the forehead. The rashes may have erythema at the bridge of the nose (butterfly rash) or may not (malar rash). Butterfly rash is rarely formed on the apex of the nose, but it may be seen with photosensitivity. It may be accompanied by erythema of the palpebral superior. In addition, ACLE can cause

lesions on the chin, earlobes, scalp, and neck. Skin lesions of ACLE may be accompanied by erosions and ulcers of the oral and/or nasal mucosa.

Malar rash often appears after exposure to sunlight. Butterfly rash may occur transiently and be the first sign of SLE, which can precede the onset by weeks or months. Butterfly rash can persist for months without systemic lesions.

Facial rashes are characterized by small, discrete erythematous macules, papules, and plaques, or widespread congestive erythemas. Lesions of malar rash become confluent and have scales, erosions, and crusting, but may also be accompanied by dermatitis, ulcers, and blisters.

At the first visit, it may be necessary to distinguish it from parvovirus infection, but parvovirus-induced rashes are transient. Since childhood, some healthy people have always had red cheeks, but they are not pathological findings. Sometimes, severe facial edema resembling dermatomyositis may occur [4]. Although erythemas of the upper eyelids may resemble dermatomyositis, it is possible to distinguish by general findings other than rashes. Conversely, dermatomyositis may cause butterfly rash; however, if they do not meet the classification criteria for SLE, including serum data and symptoms, they should be diagnosed as rashes due to dermatomyositis. Erythemas of the anguli oculi medialis are characteristic of dermatomyositis rather than SLE. In patients with SLE, in contrast to dermatomyositis, lesions usually do not occur in the nasolabial folds and periorbital regions.

2.1.1. Typical Malar Rash (Figs. 1 - 3)

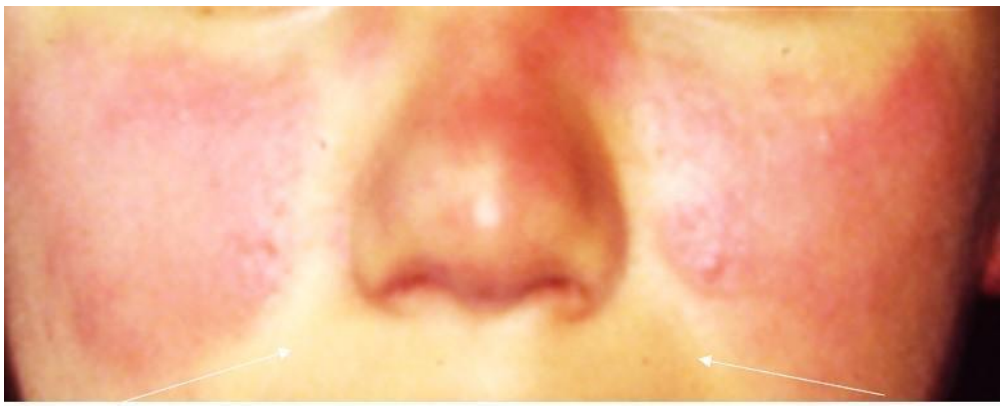

Fig. (1). Malar rash on the cheeks of a patient with SLE. Facial rashes are accompanied by erythema at the base of the nose. The butterfly distribution is typical, sparing the nasolabial folds and orbital regions.

CHAPTER 8

Respiratory Involvement in Systemic Lupus Erythematosus

Syuichi Koarada[1,2,3,*] and **Yoshinobu Nakao**[3]

[1] *Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan*

[2] *Division of Rheumatology, Takagi Hospital, Okawa, Japan*

[3] *Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan*

Abstract: Respiratory lesions in systemic lupus erythematosus (SLE) are relatively common. Pleurisy (pleuritis) is a frequent pulmonary disease in SLE. Sometimes interstitial pneumonia (IP, lupus pneumonia), alveolar hemorrhage, and pulmonary infarction are seen. Pleurisy is usually mild but can sometimes be a severe refractory disease. Interstitial lung disease includes acute IP due to SLE and chronic pulmonary fibrosis. Diaphragmatic dysfunction is also seen. Some cases become chronic after acute lupus pneumonia. Alveolar hemorrhage can be a cause of death depending on the degree. Pulmonary infarction is not uncommon in SLE. This chapter provides an overview of respiratory involvement in SLE.

Keywords: Diaphragmatic dysfunction, Diffuse alveolar hemorrhage (DAH), Lupus pneumonitis, Pleuritis, Respiratory involvement, Systemic lupus erythematosus (SLE).

1. INTRODUCTION

Respiratory lesions are relatively common in systemic lupus erythematosus (SLE) [1]. Between 40% to 57% of patients have symptoms of dyspnea and decreased exercise tolerance [2]. These respiratory symptoms result from pulmonary dysfunction due to lung lesions in SLE. The secondary pulmonary lesions are from infections and other organ lesions such as renal failure [1]. Pleural, lung, and respiratory muscle lesions can occur due to SLE, all of which cause respiratory dysfunction [1].

[*] **Corresponding author Syuichi Koarada:** Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan; Email: koarada@iuhw.ac.jp

Pleuritis frequently occurs in SLE. Lung lesions, sometimes interstitial pneumonitis (lupus pneumonitis), alveolar hemorrhage, and pulmonary infarction may be observed.

2. PLURA

2.1. Pleural Effusions

Pleural effusion is the most common symptom of SLE in the respiratory system and is bilateral in approximately half of the patients [3]. Pleural effusion in SLE is generally small and exudative but contains lupus erythematosus cells, immune complexes, and anti-DNA antibodies [1]. Pleural effusion may also be secondary to pulmonary infarction, infection, and congestive heart failure [4]. To distinguish between transudative and exudative pleural effusions is required when they have pleural effusion.

2.1.1. Imaging Findings

2.1.1.1. Conventional Chest Radiography (Figs. 1 - 4)

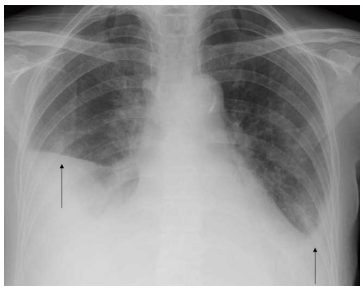

Fig. (1). Extensive bilateral pleural effusions (arrow) are seen on chest radiograph, PA view, of a patient with SLE, worsening on the right side.

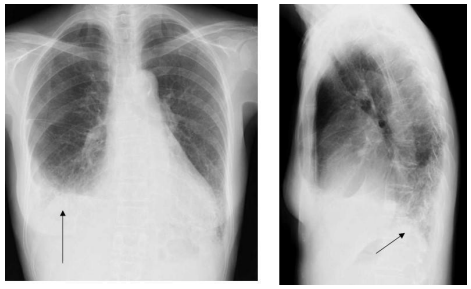

Fig. (2). Chest radiographs (Left panel: PA view, right panel: lateral view) showing moderate pleural effusion in the right lung field in a patient with SLE.

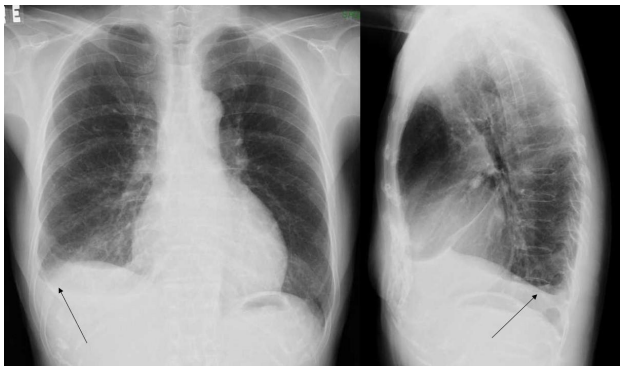

Fig. (3). Chest radiographs (left panel: PA view, right panel: lateral view) of a patient with SLE demonstrate right small pleural effusion.

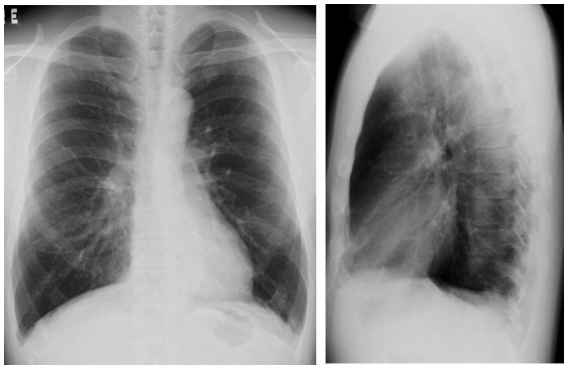

Fig. (4). Chest radiographs, PA, and lateral views, of a patient with SLE demonstrating bilateral mild pleural effusions.

2.1.1.2. Chest CT (Fig. 5)

Chest CT shows pleural effusions, pleural thickening, and subjacent atelectasis [5].

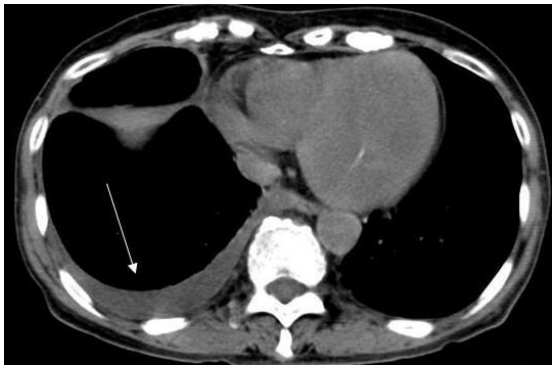

Fig. (5). Axial CT image of the chest of a patient with SLE demonstrates right pleural effusion (arrow).

CHAPTER 9

Neuropsychiatric Systemic Lupus Erythematosus (NP-SLE)

Syuichi Koarada[1,2,3,*] and **Yuri Shirahama**[3]

[1] *Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan*

[2] *Division of Rheumatology, Takagi Hospital, Okawa, Japan*

[3] *Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan*

Abstract: Neuropsychiatric systemic lupus erythematosus (NP-SLE) is one of the most serious organ complications of SLE, affecting health, quality of life, and prognosis of life in patients with SLE. Neurological symptoms are various. Among the pathological conditions of SLE, those including neurologic syndromes of the central nervous system, peripheral nervous system, and diffuse psychiatric and neuropsychiatric syndrome are called NP-SLE in the American College of Rheumatology (ACR) nomenclature. In NP-SLE, such a variety of pathophysiology should be considered when selecting a treatment. In this article, we describe the neurological lesions of SLE with illustrations.

Keywords: Cerebral atrophy, Diffuse cerebral edema, Neuropsychiatric-SLE (NP-SLE), Posterior reversible encephalopathy syndrome, Systemic lupus erythematosus (SLE).

1. INTRODUCTION

Neuropsychiatric (NP) systemic lupus erythematosus (SLE) occurs in 30% to 80% of SLE patients. Neurological symptoms are various. Among the pathological conditions of SLE, those including neurologic syndromes of the central nervous system, peripheral nervous system, and diffuse psychiatric and neuropsychiatric syndrome are called NP-SLE in the American College of Rheumatology (ACR) nomenclature [1]. The ACR Nomenclature for NPSLE provides case definitions for 19 neuropsychiatric syndromes seen in SLE, with

* **Corresponding author Syuichi Koarada:** Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan; Email: koarada@iuhw.ac.jp

reporting standards and recommendations for laboratory and imaging tests. However, glucocorticoids and some immunosuppressants for the treatment of SLE can induce psychosis, depression, anxiety, and mania. NP-SLE is primarily caused by angiopathy, direct neuro-autoimmune damage, demyelination, and thromboembolism. To complicate matters, antiphospholipid antibody syndrome in SLE patients can induce thromboembolic events. Arterial thromboembolism can cause stroke, seizures, and diffuse cognitive impairment.

2. CENTRAL NERVOUS SYSTEM

2.1. Cerebral Atrophy (Figs. 1 - 2)

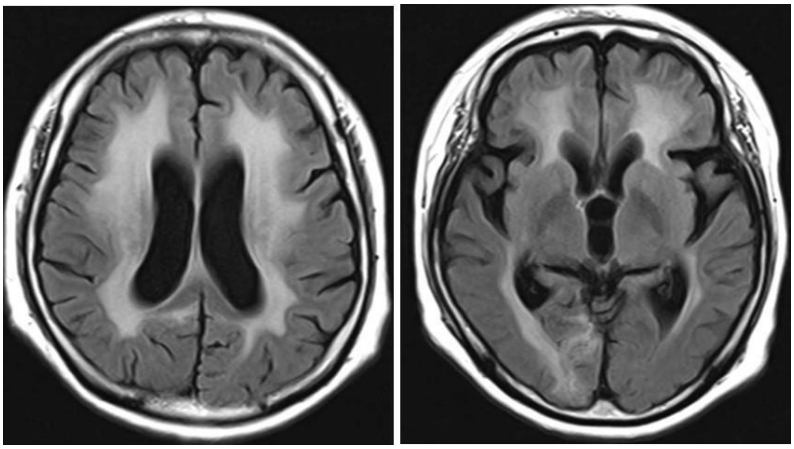

Fig. (1). Axial MRI images of the brain show age-inappropriate frontal and parietal lobe severe atrophy in a young female patient with longstanding SLE.

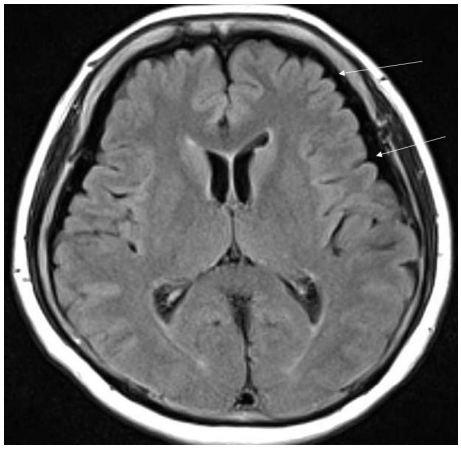

Fig. (2). Axial MRI image of the brain shows mild cerebral atrophy in a patient with SLE.

Cerebral atrophy is one of the most common abnormalities in 8.7-32% of patients with SLE [2 - 5]. Cerebral atrophy is more likely to occur in SLE patients with a long history, history of cerebral ischemia, and cognitive impairment.

2.2. Diffuse Cerebral Edema with Leukoencephalopathy (Figs. 3 - 6)

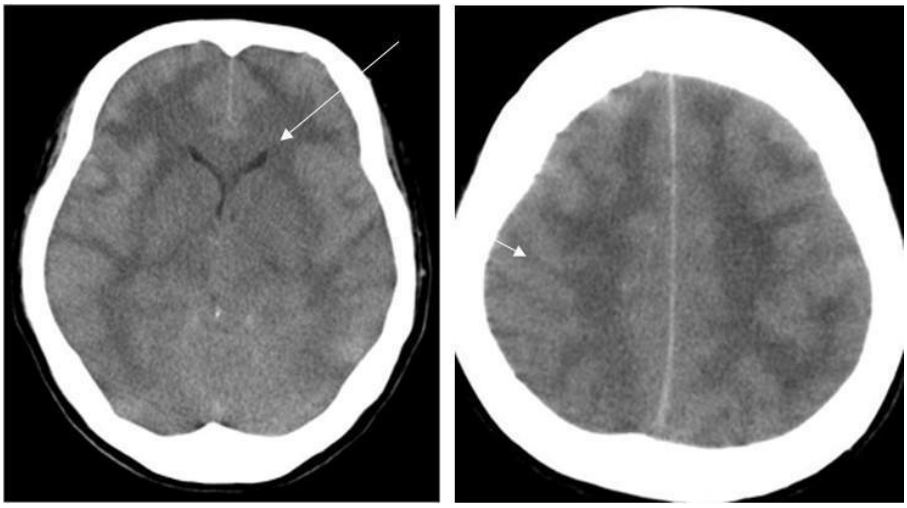

Fig. (3). Diffuse cerebral edema with leukoencephalopathy in a patient with SLE. Axial head CT scans showing severe brain edema, reduction of cerebral ventricles, and disappearance of cerebral sulci.

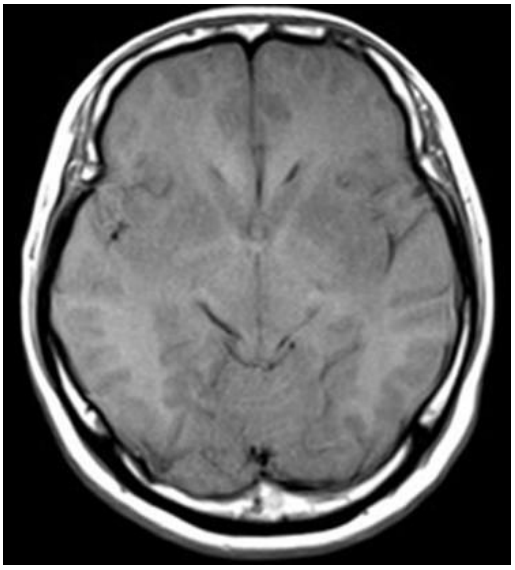

Fig. (4). T1-weighted brain MRI of a patient with SLE showing cerebral edema.

CHAPTER 10

Cardiovascular and Renal Diseases in Systemic Lupus Erythematosus

Syuichi Koarada[1,2,3,*] and **Satoko Tashiro**[3]

[1] *Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan*

[2] *Division of Rheumatology, Takagi Hospital, Okawa, Japan*

[3] *Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan*

Abstract: Cardiovascular disease occurs in systemic lupus erythematosus (SLE). Cardiovascular diseases are important in SLE. Cardiovascular diseases involve the myocardium, pericardium, cardiac valves, and coronary arteries. Pericarditis is often accompanied by pleurisy, tachycardia, and cardiac enlargement. Verrucae on the valve leaflets cause a heart murmur. Myocarditis, coronary artery inflammation, and pulmonary arterial hypertension may be seen. Lupus nephritis is the main cause of renal damage in SLE. The kidney is the most important organ that determines the prognosis of SLE. In this section, cardiovascular involvement in SLE is illustrated.

Keywords: Cardiovascular diseases, Libman-Sacks endocarditis, Pericarditis, Pulmonary arterial hypertension, Systemic lupus erythematosus (SLE).

1. INTRODUCTION

Cardiovascular involvement often occurs in systemic lupus erythematosus (SLE). SLE causes cardiovascular involvement in 58% to 77% of cases while the disease. Cardiovascular diseases can involve the myocardium, pericardium, cardiac valves, and coronary arteries. Pericarditis is found as cardiomegaly. However, symptomatic cases of pericarditis are rather rare. Pericarditis is often accompanied by pleurisy. Tachycardia, cardiac enlargement, and negative T on ECG are non-specific findings of myocarditis. Myocarditis can cause arrhythmia and heart failure. Verrucae on the valve leaflets cause heart murmur (Libman-Sacks endocarditis). It is common on the mitral valves. Myocarditis and coronary artery inflammation may be seen. Pulmonary arterial hypertension is an important

* **Corresponding author Syuichi Koarada:** Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan; Email: koarada@iuhw.ac.jp

disease that affects the prognosis of patients with SLE. The kidney is one of the most important organs that determine the prognosis of SLE. In this section, we will outline the cardiovascular and renal involvement in SLE.

2. PERICARDITIS (FIGS. 1 - 2)

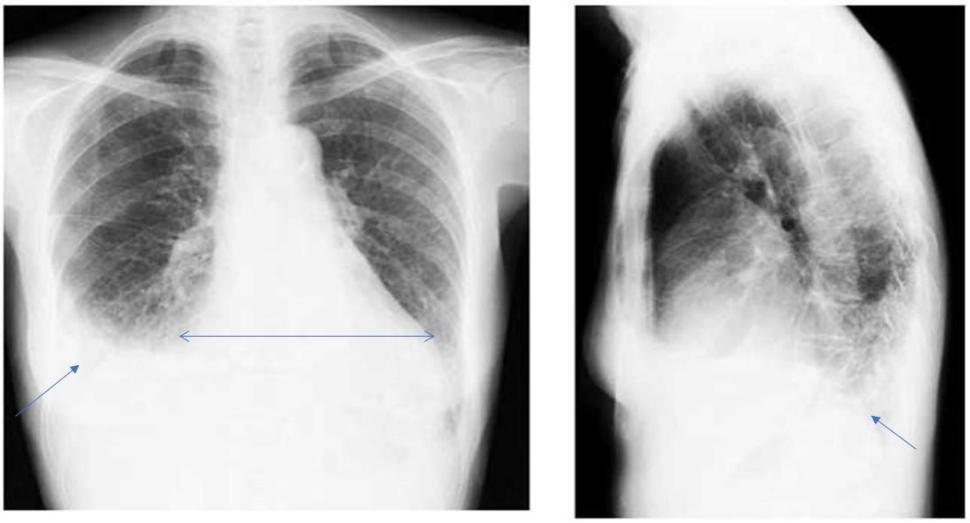

Fig. (1). Lupus pericarditis in a patient with SLE. Posteroanterior (PA) chest radiograph demonstrates moderate cardiomegaly, pericardial effusions, and bilateral pleural effusions. The lateral view also shows pleural effusions.

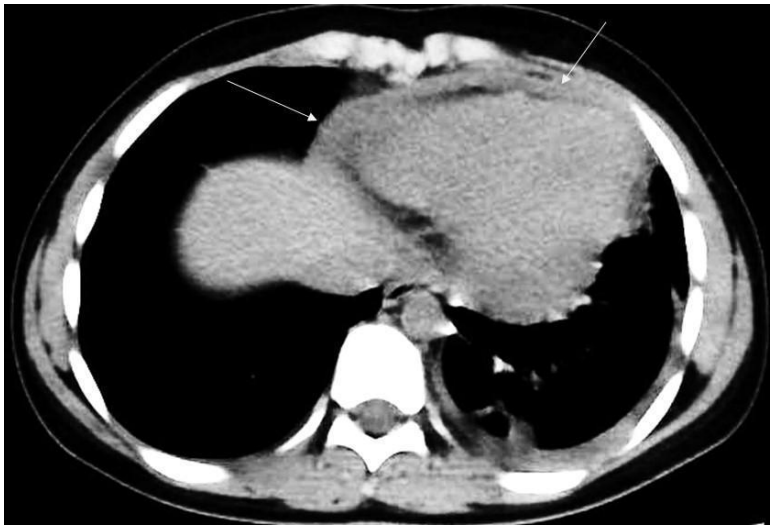

Fig. (2). Lupus pericarditis. Axial chest CT image of a patient with SLE showing a moderate pericardial collection and pleural effusion of the left lung.

Pericarditis is frequently seen in 17% to 50% and is the most common cardiac manifestation of patients with SLE [1, 2]. Electrocardiography can be useful in diagnosing pericarditis. However, in some cases, pericarditis is without effusion, and echocardiography is useless for diagnosis. Chest CT may show abnormal thickening of the pericardium and pericardial effusion.

3. MYOCARDITIS

Myocarditis is a rare condition that is often clinically asymptomatic [2]. Myocarditis may be due to an immune-mediated inflammatory process against striated muscles, or it may be due to drug toxicity from antimalarial drugs (chloroquine and hydroxychloroquine) [3]. If left untreated, it can lead to arrhythmias, dilated cardiomyopathy, total left ventricular dysfunction, and even death [3].

3.1. Libman-Sacks Endocarditis

Diseases of cardiac valves are also common disorders of the cardiac system in patients with SLE. Valvular disease is found in 18% to 74% of patients with SLE. The incidence depends on the duration and severity of the disease and the method of diagnosis. Valvular disease in SLE ranges from thickening of the valve leaflets to Libman-Sacks endocarditis.

3.2. Valvulopathy (Figs. 3 - 4)

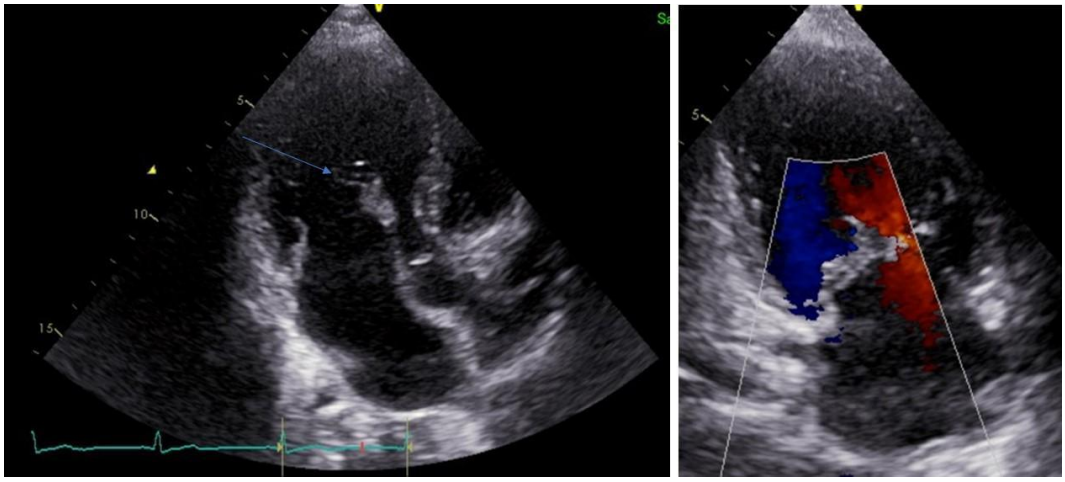

Fig. (3). Mitral valve Libman-Sacks endocarditis in a patient with SLE. Transthoracic echocardiogram demonstrates a mobile mass of the mitral valve consistent with vegetation.

CHAPTER 11

Gastrointestinal System in Systemic Lupus Erythematosus

Syuichi Koarada[1,2,3,*] and **Yukihide Ono**[2]

[1] *Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan*

[2] *Division of Rheumatology, Takagi Hospital, Okawa, Japan*

[3] *Division of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan*

Abstract: In systemic lupus erythematosus (SLE), gastrointestinal symptoms, including nausea, vomiting, abdominal pain, diarrhea, hematemesis, melena, ileus, ascites, and elevated hepatic and pancreatic enzymes are frequently observed. The gastrointestinal manifestations of SLE are diverse, including lupus peritonitis, gastritis, acute pancreatitis, cholecystitis, and lupus enteritis. This chapter provides an overview of the gastrointestinal manifestations of SLE.

Keywords: Gastrointestinal symptoms, Lupus enteritis, Lupus peritonitis, Systemic lupus erythematosus (SLE).

1. INTRODUCTION

Gastrointestinal symptoms, including nausea, vomiting, abdominal pain, diarrhea, hematemesis, melena, ileus, ascites, and elevated hepatic and pancreatic enzymes, are frequently observed in patients with systemic lupus erythematosus (SLE). Among gastrointestinal lesions, intestinal ischemia, infarction, peritonitis, and perforation of the digestive tract are the most dangerous and fatal complications of SLE and require an early diagnosis.

There are no specific gastrointestinal lesions that occur only in SLE. However, small intestinal lesions are not common as gastrointestinal diseases in general subjects, and when they occur in SLE patients, it is strongly suggested that they are lesions due to SLE.

[*] **Corresponding author Syuichi Korada:** Department of Medical Technology and Sciences, International University of Health and Welfare, Okawa, Japan; Email: koarada@iuhw.ac.jp

Generalized abdominal pain is a common symptom of lupus gastrointestinal disease, and computed tomography (CT) is useful in the diagnosis of undiagnosed abdominal pain.

2. SEROSITIS (FIG. 1)

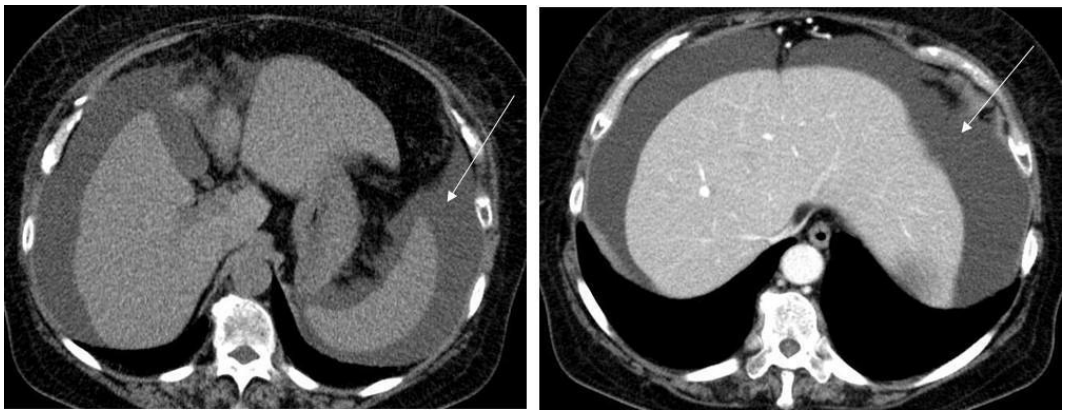

Fig. (1). Non-contrast-enhanced (left panel) and contrast-enhanced (right panel) computed tomographic (CT) scans of the abdomen showing marked amount of abdominal ascites (arrows) with fluid surrounding the spleen and the liver in a patient with SLE.

Ascites, a symptom of serositis of the abdomen, occurs in SLE patients with abdominal pain. Other causes of ascites include pancreatitis, hypoalbuminemia, glomerulonephritis, and nephrotic syndrome, constrictive pericarditis, and inflammatory peritonitis due to vasculitis.

3. GASTRITIS (FIG. 2)

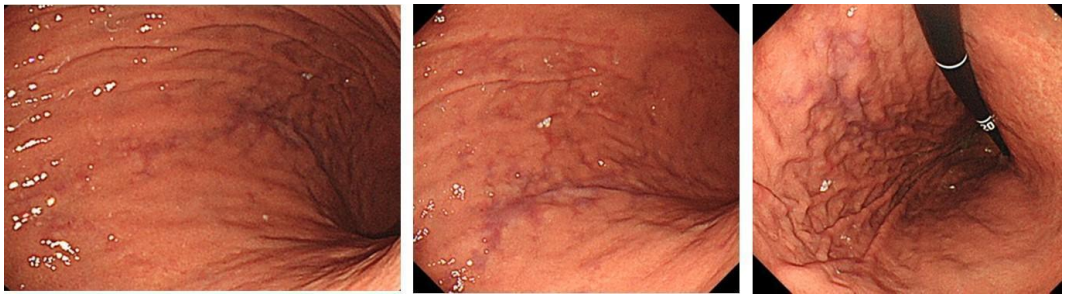

Fig. (2). Gastrointestinal endoscopy shows gastric antral vascular ectasia (GAVE) or lupus gastritis in a patient with SLE.

It has been reported that lupus gastritis, which is thought to be caused by SLE rather than drug-induced, was improved by treatment with glucocorticoid [1]. Then, in 1991, Musaey *et al.* described that SLE itself causes gastritis [2]. Gastric antral vascular ectasia (GAVE) or lupus gastritis in SLE is a rare cause of gastrointestinal bleeding. However, the pathogenesis of GAVE is not fully elucidated [3, 4].

4. LUPUS ENTERITIS (FIG. 3)

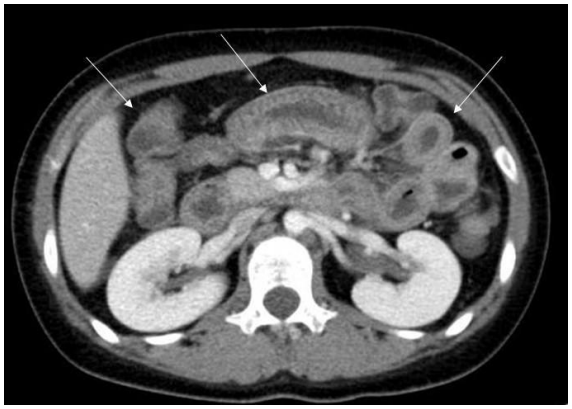

Fig. (3). Contrast-enhanced computed tomographic (CT) scans of the abdomen in a patient with SLE demonstrate small bowel mucosal edema and enhancement when seen en face (target sign) and in longitudinal view.

Lupus enteritis is a visceral vasculitis involving the small intestine, especially the jejunum and ileum. Lupus enteritis is usually difficult to detect with radiography or barium studies, but abdominal CT can be useful in detecting the disease.

5. CHOLECYSTITIS (FIG. 4)

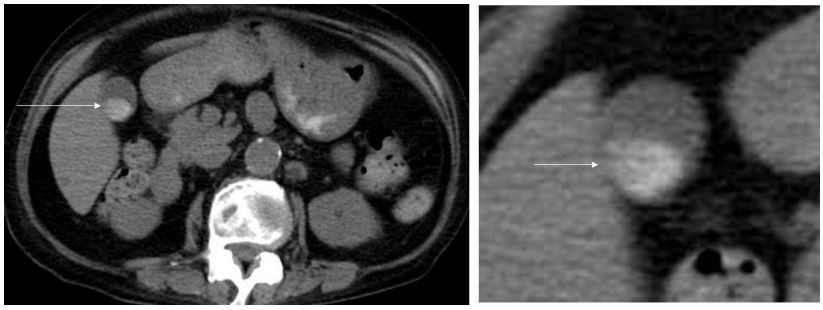

Fig. (4). Non-contrast-enhanced CT scans of the abdomen in a lupus patient with abdominal pain demonstrate a distended gallbladder with biliary sludge. Immediately surgery was performed, and then the histopathology of the resected gallbladder specimen confirmed the diagnosis of acalculous cholecystitis.

SUBJECT INDEX

A

Abdominal 331, 332, 333
  CT 333
  pain 331, 332, 333
Abductor pollicis longus (APL) 194, 195
Abnormalities 18, 19, 35, 53, 193
  joint 35, 193
  of alignment in systemic lupus erythematosus 18
  of joint alignment in systemic lupus erythematosus 18
  radiographic 53
Abnormal 104, 317
  joint construction 104
  neurological signs 317
Achilles tendons 170, 194
Acrocyanosis 275
Acrosclerosis 4
Acute 221, 222, 223, 224, 226, 243, 247, 290, 293, 320
  alveolitis 290
  cutaneous lupus erythematosus (ACLE) 221, 222, 223, 224, 226, 243, 247
  inflammatory demyelinating polyradiculoneuropathy 320
  pulmonary hemorrhage 293
Acute lupus pneumonitis 289, 290
  manifests on chest radiographs 289
  progress 290
Adenosine deaminase 289
Adipose tissues 265
Alignment abnormalities 18, 19, 50
Alopecia 280, 281
  androgenic 281
  severe 280
Alopecia areata 281
Alveolar 286, 287, 290, 292, 293, 294, 309
  capillary injury 290
  hemorrhage 286, 287, 292, 293, 294
  diffuse 286, 292, 309
  hemorrhage in SLE 294
Anatomical snuffbox 194, 197
Anguli oculi medialis 223
Ankle 189, 190
  bursitis 190
  instability 189, 190
Ankylosis 150
Antibodies 6, 243, 247, 287
  anti-collagen VII 243
  anti-DNA 287
  anti-U1RNP 247
  circulating anti-CCP 6
Antibody syndrome (APS) 165, 245, 271, 312, 315, 317
Antiphospholipid 165, 271, 312
  antibody syndrome 165, 271, 312
AP and lateral radiographs 48
Arrhythmias 324
Arterial thromboembolism 312
Arthritis 3, 4, 5, 13, 14, 18, 80, 95, 160, 163, 171, 172, 209, 267
  additive 171, 172
  affected 163
  crystal-induced 172
  early 80
  gonococcal 172
  migratory 171, 172
  mild 5
  non-erosive degenerative 3
  psoriatic 13, 14, 171, 172, 209
  reactive 267
  secondary degenerative 95
  septic 3, 4
  severe 18
  symmetric 3
  symmetrical mild multiple 163
  systemic 160
Arthropathy 5, 3, 4, 19, 101, 158, 163, 164, 171
  deformed 4
  non-erosive 3, 4, 19
  secondary degenerative 101
Aspergilloma 301

Aspergillus pneumonia 300
Atelectasis 295
Atypical malar rash 225
Autoimmune 1, 185, 243, 258
  bullous diseases 243
  disease 1
  inflammatory disease 185, 258
Autonomic disorder 320

B

Baker's cysts 189
Behçet's 267
  disease 267
  syndrome 267
Bilateral 300, 319
  occipital hyperintense signals 319
  patchy infiltrates 300
Biliary sludge 333
Blood hemorrhage 294
Bone(s) 1, 6, 7, 10, 20, 38, 39, 47, 52, 53, 72, 73, 76, 78, 79, 95, 101, 102, 118, 138, 157, 162, 163, 164, 165, 169
  cysts 52, 95, 102, 164
  density 73
  destructions 52, 78
  erosions 6, 20, 39, 52, 79, 102, 118, 138, 169
  involvement in systemic lupus erythematosus 102
  ischemic 6
  lesions of SLE 52
  mineral density 72
  mineralization 52
  scintigraphy 6, 157, 162, 163
  shape 78
  tumors 78
Bone changes 35, 52
  in osteonecrosis 35
  in SLE 52
Boutonniere deformities 19, 24, 31, 32
Bronchiectasis 294, 304
Bronchopulmonary Infections 295
Bullous 241, 242, 243
  lesions (BSLE) 241, 242, 243
  lupus erythematosus 241
  pemphigoid 243
Bursae 186, 189
  anatomical 186
  communicating 186
  synovial 189
Bursitis 7, 175, 185, 186, 189, 190, 218
  occupational 189

C

Calcific atherosclerosis 325
Calcifications and osteophytes 213, 214, 215
Cardiac system 324
Cardiovascular 322, 329
  and renal lesions in SLE 329
  diseases 322
Carpometacarpal Joints 128
Cartilage 104, 145
  changes 104
  destruction 104, 145
CCMC 122, 128
  and CMC Joints 128
  compartment 122
Central nervous system (CNS) 311, 312, 314, 319
Cerebral 311, 312, 313, 317
  atrophy 311, 312, 313
  edema 313
  sulci 313
  venous sinus thrombosis 317
Cheilitis 222, 268, 269
Chest CT 288, 290, 291, 293, 297, 298, 299, 300, 302, 306, 324, 325, 326, 329
  contrast-enhanced 329
  enhanced 325, 326
  images 291, 299, 302, 306
  scans 290, 293, 300
Chest radiograph abnormalities 294
Chilblain lupus erythematosus 258, 259, 260, 261
Cholecystitis 331, 333, 334
  acalculous 333, 334

Circulatory disorders 271, 281
peripheral 271
CNS Ischemia 315
Cognitive impairment 313
Cold-induced microvascular injury 259
Colles fracture 47, 48
Computed tomography (CT) 6, 294, 316, 317, 325, 332, 333
Coronal chest CT images 307
Coronary artery inflammation 322
Corticosteroid therapy 6, 101
Cough 290, 292
Cranial neuropathy 320
CT 49, 50, 265, 299, 301
images 49, 50, 265, 301
scan 299
Cutaneous lupus erythematosus 222, 224, 226, 258
acute 222, 224, 226
chronic 258
Cutaneous lupus mucinosis 270
Cyclophosphamide 101
Cystic lesion 92, 93, 94, 95, 171
Cytomegalovirus 296

D

Dactylitis 30, 193
Damage 292, 304, 312, 322, 329
direct neuro-autoimmune 312
parenchymal 304
renal 322, 329
Deforming 4, 5
arthritis 4, 5
erosive arthritis 4
Deformities 2, 4, 5, 6, 9, 18, 19, 20, 21, 22, 23, 24, 25, 26, 28, 31, 40, 42, 43, 171, 172
congenital 43
joint 2, 20, 28, 171, 172
mild 5
non-erosive 4
of DIP and PIP Joints 24
of Metacarpophalangeal Joints 20
severe erosive 18
Degenerative spondylolisthesis 46
Demyelinating neuropathy 294
Demyelination 312
Dermal-subcutaneous tissue interface 271
Dermatitis 223, 243
interfacial vacuolar 243
Dermatomyositis 181, 223, 275
Destruction 80, 278
joint 80
rapid local tissue 278
Diabetes mellitus 101
Diffuse 74, 286, 292, 309
alveolar hemorrhage (DAH) 286, 292, 309
sclerosis 74
Discoid lupus erythematosus (DLE) 222, 247, 255, 256, 257, 258
Disease 2, 3, 6, 18, 19, 31, 35, 194, 221, 246, 276, 281, 289, 290, 294, 295, 322, 323, 324, 326, 331
collagen 246
gastrointestinal 331
infectious 289, 290
joint 2
lung 295
parenchymal 294
rheumatoid 194
Dislocated total hip replacement implant 37
Dislocations and misalignment 37, 169
Disorders, systemic 269
Distribution of 157, 158, 161, 163, 164, 165
arthropathy in SLE 158
bone cysts 164
inflammation 161
insufficient fractures 165
joint involvement 157, 163
Distribution of arthritis 7, 162, 163, 167, 168
and tenosynovitis in SLE 168
Drug(s) 3, 101, 281, 324
antimalarial 101, 324
estrogen-containing 3
toxicity 324
Dural venous sinuses 317
Dysfunction 5, 286, 294, 295
diaphragmatic 286, 294, 295

immunological 295
pulmonary 286
respiratory 286
Dyspnea 286, 290, 292, 294

E

Early erosions 9, 10, 11, 13, 80
detecting 13
hands and location of 9, 10, 11
ECG of pulmonary arterial hypertension 327
Echocardiography 324, 328
Edema 105, 137, 175, 218, 290, 333
mucosal 333
Electrocardiogram 327, 328
Electrocardiography 324
Enthesitis 213, 216, 217
Enthesopathy 7
Erosions 5, 7, 9, 10, 12, 13, 18, 52, 78, 79, 80, 83, 84, 86, 87, 88, 90, 91, 104, 223
and pressure cause destruction of cartilages 104
definite 13
detecting 80
in Jaccouds Arthropathy and Non-deforming 79
sclerotic 79
Erosive 3, 4, 5, 6, 18, 38, 52, 78, 80, 145
arthritis 3, 5, 6, 80
arthropathy 4, 78, 145
Erythema 222, 223, 224, 241, 242, 243, 246, 247, 260, 261, 262, 265, 266, 269
nodosum 266
widespread congestive 223
Erythema annulare 247
in neonatal lupus erythematosus 247
of SCALE 247
of SCALE and erythema annulare 247
Erythematous macules 247
Erythromelalgia 275, 276
Extensor 194, 197, 199
compartment 199
digitorum 197
indicis (EI) 197
pollicis brevis (EPB) 194
Extensor carpi 195, 196, 199
radialis brevis (ECRB) 195, 196
ulnaris (ECU) 199

F

Facial rashes 223, 225
Fat 95, 101
embolism syndrome 101
suppressed (FS) 95
Femoral 7, 95, 164, 165
condyles 164, 165
head morphology 7
head necrosis 7
neck 95
Fever 19, 172, 290, 292
rheumatic 19, 172
Fibrosis 137, 289, 291, 295
pulmonary 291, 295
Flexion 24, 27, 29, 193
contracture of Digits 29
deformities 24
deformities of MCP Joints 24
restriction 27, 193
Flexor digitorum 42, 204, 207
longus (FDL) 42
profundus (FDP) 204, 207
Fluorescence microscopy 305
Fractures 2, 3, 8, 14, 18, 47, 48, 49, 50, 73, 78, 278
biconcave 48
comminuted intra-articular 47
compression 2
distal radius 47
of Ischiopubic Ramus 50
of pubic bones 49
pathological 47, 48, 73
Functional 19, 20, 275
disability, severe 19, 20
peripheral vasculopathy 275

G

Gadolinium 137
Gallium scintigraphy 157, 158, 159, 160, 161, 218, 302
Gastritis 331, 332, 333
Gastrocnemius 189
Gastrointestinal endoscopy 332
Genetic susceptibility 3
Gingivitis 268
Glomerulonephritis 332
Glossitis 268
Glucocorticoids 2, 312, 333
Guillain-Barré syndrome 320

H

Haemophilus influenza 297
Hair 280, 281
  fragility 281
  loss/alopecia 280
Hammer toes 38, 39, 40
Hand X-rays 8
Heart failure 287, 322
  congestive 287
Heart murmur 322
  valve leaflets cause 322
Hematemesis 331
Hemidiaphragms 295
Hemoptysis 290, 292
Hemorrhage 290, 292
  massive pulmonary 292
Hemosiderin-laden macrophage 292
Herpesvirus 267
Honeycombing 291
Hook erosions 79
Hydroxychloroquine 324
Hyperextension 24, 25, 26, 28, 31, 32, 43
Hyperlipidemia 101
Hyperperfusion encephalopathy 319
Hyperpigmentation 247, 271
  post-inflammatory 247
Hypertension 101, 295
  pulmonary 295
Hypoalbuminemia 332
Hypopigmentation 247

I

IgM anticardiolipin antibodies 101
Images of B-mode ultrasound scans 142
Images of dorsal longitudinal B-mode 83
Images of dorsal longitudinal scans 125
Images of longitudinal B-mode and power Doppler ultrasonography 144, 145
Images of longitudinal B-mode ultrasonography 142, 143
Images of longitudinal B-mode ultrasound scans 141
Images of longitudinal ultrasound scans 140, 143
Images of transverse B-mode ultrasound scans 143
Imaging tests 312
Immune abnormalities 295
Immune-mediated inflammatory process 324
Immunosuppressants 312
Infarction 286, 287, 309, 315, 331
  midbrain 315
  pulmonary 286, 287, 309
Infections 3, 6, 138, 165, 185, 223, 267, 281, 286, 287, 292, 295, 296
  fungal 6
  parvovirus 223
  respiratory tract 296
  viral 3, 6
Infectious bronchopneumonia 295
Infectious diseaeses 19
Inflammation 1, 137, 161, 176, 184, 185, 189, 194, 200, 209, 265, 268
  peritenon 209
Inflammatory 204, 205, 207, 267
  bowel disease 267
  tenosynovitis 204, 205, 207
Interphalangeal 31, 32, 40, 78, 163, 226
  joints 31, 226
  metatarsal 40
Interstitial 286, 287, 289, 291

lung disease (ILD) 286, 289, 291
pneumonitis 287
Intracranial 317, 318
aneurysms 318
hemorrhage 317
Intracranial hypertension 314
isolated 314
Intraventricular hemorrhage 317
Iron deficiency 281
Ischemia 101, 313, 315, 331
cerebral 313
intestinal 331

J

Jaccoud's 3, 4, 5, 21, 24
arthritis 3, 4, 5, 21, 24
Jaccoud's arthropathy 3, 4, 6, 19, 20, 21, 22, 23, 38, 39, 52, 78, 79, 80, 102, 105, 137, 151, 164, 166
and NDNE arthritis 78
and NDNE lupus arthritis 6, 79
and rhupus 19, 52, 102
of SLE 166
Joint(s) 6, 38, 126, 145, 157, 170, 176, 177, 178, 80
interphalangeal 157
metatarsophalangeal 38
radiocarpal 6, 126, 145
swelling 176, 177, 178, 180
synovial 170
Joint effusions 104, 105, 138, 139, 140, 141, 142, 143, 144, 145, 155
mild 139, 143, 144
moderate 138, 142
Joint space 6, 7, 104, 145, 146, 147, 148, 149, 150, 151, 155
narrowing (JSN) 6, 7, 104, 145, 146, 147, 148, 149, 150, 151, 155
widening (JSW) 151

K

Knee pathologies 189

L

Leptomeninges 319
Lesions 1, 2, 5, 6, 92, 104, 145, 157, 164, 165, 170, 172, 175, 185, 191, 192, 221, 222, 223, 243, 244, 248, 249, 250, 257, 259, 266, 267, 268, 269, 271, 286, 291, 304, 311, 331
annular and psoriasiform 248, 249, 250
capsular 1, 104
cutaneous 266
erosive 268, 269
gastrointestinal 331
irreversible lung 291
joint 2, 5, 6, 145, 157, 164, 172, 185
lytic 92
monoarticular 165
neurological 311
oral mucosal 222
respiratory muscle 286
small cavity 304
small cyclic 248
small intestinal 331
systemic 223
tendon 157, 170
urticaria 271
Lesions of malar rash 223
Leukoencephalopathy 313, 314
Libman-sacks endocarditis 322, 324
Livedo reticularis 271
Localized DLE-type eruptions 255
Lung 286, 287, 289, 293
lesions 286, 287, 293
parenchyma 289
Lupus 2, 3, 5, 6, 20, 24, 25, 28, 37, 39, 41, 45, 52, 79, 104, 135, 138, 145, 157, 163, 176, 218, 221, 222, 244, 247, 255, 258, 266, 267, 268, 278, 281, 286, 287, 289, 290, 296, 297, 298, 299, 300, 303, 314, 319, 322, 323, 329, 331, 332, 333,
arthritis 2, 5, 6, 20, 24, 25, 28, 45, 79, 157, 163
arthropathy 3, 37, 52, 104, 138, 145, 176
bullous 222

chilblain 221, 255, 258
cutaneous 247
gastritis 332, 333
gastrointestinal disease 332
malar rash 221, 222
meningitis 319
mucosal 255, 267, 268
myopathy 218
neuropsychiatric 314
nephritis 322, 329
panniculitis 255, 266
pericarditis 323
peritonitis 331
pneumonia 286
pneumonitis 286, 287, 289, 290
Lupus erythematosus 255, 287
cells 287
tumidus 255

M

Maculopapular lupus rashes 221, 222, 226, 227, 228, 229, 230, 231, 233, 234, 235, 236, 237, 238, 239
Magnetic resonance imaging (MRI) 3, 6, 7, 49, 79, 80, 95, 137, 175, 192, 294
Malar rash 221, 222, 223, 224
Malignant tumors 289
Mallet toes 38, 40, 42
Marginal erosions 78, 171
MCP joints and Jaccoud's arthropathy 23
Mechanism of deformities of joints 20
Medial longitudinal fasciculus (MLF) 315
syndrome 315
Mediastinal lymphadenopathy 308
Meningitis 319
Metacarpophalangeal joints 20, 21, 226
Metadiaphysis 165
Midcarpal Joints 128
Mild 74, 109, 116, 117, 118, 119, 126, 129, 131, 132, 136, 137, 218, 244, 225, 229, 298, 304,
acro-osteosclerosis 74
and small maculopapular lupus rashes 229
erythema 244
facial rashes 225
interstitial opacities 298
muscle pain 218
pulmonary tuberculosis 304
synovial hypertrophy 109, 116, 117, 118, 119, 126, 129, 131, 132, 136, 137
Mitral 325, 326
annular calcification (MAC) 325, 326
valve calcification 326
MLF syndrome 315
Mononeuropathy 320
MRI images 206, 315, 317
of Jaccoud's arthropathy 137
MR images 88, 89, 125, 130, 133, 140, 319
contrast-enhanced brain 319
MR sagittal images 135
Multiple 165, 255
eruptions 255
lesions 165
Muscle diseases 218
Musculoskeletal 1, 3, 14, 193
abnormalities 3
lesions 3
manifestations of systemic lupus erythematosus 4
ultrasonography 3, 193
Myasthenia gravis 320
Myocarditis 322, 324, 329
and coronary artery inflammation 322
Myocardium 322
Myositis 3, 4, 18, 19, 165, 218
inflammatory 18, 19
typical lupus 165

N

Nausea 331
NDNE 4, 6, 78, 79
arthritis 78
lupus arthritis 4, 6, 79
Necrosis 2, 6, 35, 101, 244, 278
aseptic 6, 101
full-thickness epithelial 244

ischemic 101
Neonatal lupus erythematosus (NLE) 247
Neoplastic 19, 332
conditions 19
syndrome 332
Nervous system 1, 311, 312, 314
central 311, 312, 314
peripheral 311
Neurological syndrome 319
Neuropsychiatric 101, 311
manifestations 101
syndromes 311
Neutropenia 269
Nodular 269, 270, 279, 280
cutaneous lupus mucinosis (NCLM) 269, 270
subcutaneous 279, 280
Non-deforming arthritis 4
Non-erosive arthritis 2, 4, 5, 80, 171, 184
Norgaard's image 11

O

Occluded sinus 317
Oral ulcers 101, 267, 268
Osteoarthritis 6, 31, 38, 80, 101, 135, 170, 189
of Hands in SLE 31
Osteomyelitis 3, 4
Osteonecrosis 3, 4, 6, 7, 35, 36, 37, 101, 102, 163, 164, 165
occurrence of 101, 164, 165
Osteonecrosis 19, 35
and fracture lesions 19
of Hips 35
Osteophytes 14, 52, 75, 78, 95, 96, 97, 98, 99, 100, 102, 213, 214, 215
Osteoporosis 2, 7, 47, 52, 73
mild 73
Osteosclerosis 52, 74, 75, 76, 77, 78, 80, 81, 138
moderate 75
of tufts 74
reactive 138
secondary 80
typical 78

P

Palindromic rheumatism 172
Palmar 20, 221, 241, 229
erythema 221, 241
side of hands 229
subluxations 20
Pancreatic enzymes 331
Pancreatitis 332
Panniculitis 266
lobular 267
Papulosquamous psoriasiform lesions 247, 251, 252, 253, 254
Paramagnetic effects 294
Patchy 299, 303, 304
consolidations 303, 304
interstitial opacities 299
Pathogenic microorganisms 296
Periarteritis nodosa (PN) 271
Periarticular osteopenia 7, 52, 102
Periarticular osteoporosis 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71
mild 53, 68
moderate 53, 54, 68, 69
severe 54, 69
Pericardial effusions 323, 324
Pericarditis 322, 323, 324, 329, 332
constrictive 332
Peripheral 176, 320
neuropathy 320
soft tissue swelling 176
Peritenon extensor tendon inflammation 175, 209, 210, 211, 212
Peritonitis 331, 332
inflammatory 332
Periungual erythemas 178, 244, 245, 246
mild 245
Periungual telangiectasias 246, 247
and erythema 246, 247
mild 247
Phrenic nerve palsy 294

Pleural 287, 288, 289, 290, 307, 308, 323
effusions 287, 288, 289, 290, 307, 308, 323
fibrosis 289
Pneumocystis jiroveci 296
Pneumocystis pneumonia (PCP) 298, 299
Pneumonia 286, 289, 290, 291,295, 296, 297, 298, 309
community-acquired 296
fibrosis 291
interstitial 286, 289, 309
pneumocystis 298
Pneumonic process 289
Polyarthritis 4, 5, 157, 158, 159, 162, 163
bilateral 157
intermittent asymmetric 5
mild 159
moderate 159
severe 158
Polycyclic lesions 251
Polyneuropathy 320
Posterior 8, 134, 311, 319
leukoencephalopathy syndrome 319
longitudinal power Doppler ultrasound scan 134
reversible encephalopathy syndrome 311, 319
reversible encephalopathy syndrome (PRES) 8, 311, 319
Power doppler 105, 106, 109, 110, 114, 117, 118, 120, 129, 144, 145, 191, 195, 196, 208, 209
scans 129
signals 105, 106, 109, 110, 114, 117, 118, 120, 191, 195, 196, 208, 209
ultrasonography 144, 145
Psoriasiform lesions 248, 249, 250, 251, 252, 253
early changes of papulosquamous 252, 253
large papulosquamous 251
Pulmonary arterial hypertension (PAH) 322, 326, 327, 328, 329
abnormalities of 327, 328
Pulmonary 292, 294, 295, 300, 301, 304, 305, 306, 307, 308
Aspergilloma 301
Aspergillosis 300
diffuse alveolar hemorrhage 292
embolism (PE) 329
function tests 294
infections 295
infiltrates 295
tuberculosis 304, 305, 306, 307, 308

R

Radiographic images 138
Radiography 2, 5, 289, 326, 333
joint 2
Rashes 221, 222, 223, 224, 225, 232, 243, 244, 258, 259, 269, 282, 283
bullous 221
maculopapular 221, 232
parvovirus-induced 223
photosensitive lupus 222
pruritic 259
Raynaud's phenomenon 6, 101, 272, 273, 274, 275
RC 68, 126, 123, 131,
and MC joints 131
and ST joints 123
Joints 68, 126
Reactive sclerosis 169
Redness 44, 275, 276, 282
severe 276
Relapse 2, 171
acute 171
Renal 286, 329
failure 286, 329
lesions 329
system 329
Respiratory system 287
Reversible swan-neck deformities 25
Rheumatic diseases 6, 9, 13, 14, 50, 157, 189, 193, 194
Rheumatoid 2, 3, 5, 6, 7, 13, 14, 18, 19, 29, 78, 104, 142, 168, 209
arthritis (RA) 2, 3, 5, 6, 7, 13, 14, 18, 19, 29, 78, 104, 142, 168, 209
factor (RF) 6, 19

Rhupus syndrome 3
Right 315, 325, 327, 328
coronary artery (RCA) 325
internuclear ophthalmoplegia 315
ventricular hypertrophy (RVH) 327, 328

S

Sacroiliac joints 77, 138, 151, 169
Sacroiliitis 170
Salivary gland scintigraphy 335
Sarcoidosis 172
Scapholunate dissociation 7
Scleroderma 18, 19, 177, 178, 246
Serositis 101, 332
Sialadenitis 335
Single photon emission computed tomography (SPECT) 316, 317
Sjogren's syndrome (SS) 6, 247, 271, 335
Skin 1, 165, 190, 200, 207, 221, 258, 267, 270, 271, 275
biopsy 271
edematous 258
symptoms 221
Skin lesions 221, 222, 223, 257, 262, 266, 281, 283
of ACLE 223
of SLE 221, 222, 262, 283
Skin rashes 222, 226, 241, 244, 281, 282
of herpes zoster 281, 282
SLE 2, 3, 6, 19, 20, 46, 70, 71, 101, 104, 151, 155, 157, 164, 286, 289, 309
active 101
and chronic pulmonary fibrosis 286
and Jaccoud's arthropathy 151
and rheumatoid arthritis 6, 19, 46, 70, 71, 104
arthritis 2
arthropathy 3, 6, 20
derived diseases 289
induced pneumonia 289
joint lesions in 155, 157
osteonecrosis in 101, 164
respiratory involvement in 286, 309
SLE and pulmonary 304, 305, 306, 308, 328
arterial hypertension 328
tuberculosis 304, 305, 306, 308
Soft tissue 3, 4, 184, 175, 218, 278, 279, 280
and subcutaneous calcifications 184
calcifications 3, 4, 184, 279, 280
infection 278
lesions 175
lesions of SLE 175, 218
Spondyloarthritis 3
Spondylolisthesis 46
Sporadic chilblain lupus erythematosus 259
Squamous cell carcinomas 262
Staphylococcus aureus 296
Steroid myopathy 218
Stress 80, 101, 189, 277
mechanical 80, 189, 277
Subacute cutaneous lupus erythematosus (SCLE) 221, 222, 247, 251
Subarachnoid hemorrhage 318
Subchondral cysts 4, 92
multiple well-defined 92
Subcutaneous 171, 175, 185, 194, 210, 218, 266, 278, 279, 277
edema 171, 175, 194, 210, 218, , 278, 279
fat tissue 266
hematoma 277
tissue 185
Swan-neck deformities 5, 20, 21, 25, 28, 31, 32
Swelling 30, 105, 107, 108, 137, 178, 179, 181, 182, 183, 189, 198, 199, 200, 206, 207, 210, 265
capsular 137
hypoechoic 210
subcutaneous tissue 265
synovial 30
Symptomatic avascular osteonecrosis 101
Symptomatologic bronchial disease 294
Symptoms 1, 2, 6, 14, 222, 271, 311, 314, 320, 331
gastrointestinal 331
musculoskeletal 1, 2
musculoskeletal disorders cause disabling 1
neurological 311, 320

systemic 2, 6, 14, 222, 271, 314
Synovial 106, 109, 111, 113, 114, 115, 117, 118, 123, 128, 131, 135, 136, 186, 195, 196
cysts 186
hypertrophy 106, 109, 111, 113, 114, 115, 117, 118, 123, 128, 131, 135, 136, 195, 196
Systemic 2, 19, 247, 275
disease 2, 247
sclerosis 19, 275

T

Tachycardia 322
Tendon disorders 193
Tendonitis 7, 25, 193, 195, 196, 198, 199, 201, 203, 204, 206, 208, 209
mild 204
severe 203
Tenosynovitis 29, 137, 167, 168, 169, 170, 175, 193, 194, 195, 196, 199, 200, 201, 202, 203, 204, 205, 207
extensor carpiulnaris 199
flexor 29
proliferative 137, 195, 196, 204, 207
Tenosynovitis 170, 207
flexor tendons 207
lesions 170
Terminal phalangeal sclerosis 3
Thromboembolism 277, 312
Thrombolytic therapy 329
Tomography, computed 6, 316, 317, 325, 332
Toxic epidermal necrolysis 243, 244
Transthoracic echocardiogram 324

U

Ulcers 222, 223, 265, 268, 267
discrete 222
nasal 267
Ultrasonography 78, 80
Ultrasound 83, 118, 125, 127
images 118, 125, 127
scans 83
Urticarial vasculitis 270, 271
hypocomplementemia 271
in SLE 270

V

Valvulopathy 324
Vasculitis 3, 6, 19, 101, 267, 271, 277, 332
cutaneous 101, 271
leukocytoclastic 271
syndrome 3
Vasoconstriction 259
Verrucous lupus 262, 263, 264, 265
Vomiting 331

W

Wedge fracture 48
White-matter Lesions 314

Syuichi Koarada

Syuichi Koarada holds a Ph.D. and M.D. in Immunology and Internal medicine from Saga University, Saga, Japan. He worked at UPMC (University of Pittsburgh Medical Center, Pittsburgh, USA) as an Associated Professor. Currently, he is a Professor of IUHW in Japan. He specialized in Rheumatology and Clinical Immunology. He has published more than 100 papers and 11 books. Moreover, he has received the Investigator's Award of Internal Medicine of Saga University, the Japanese Clinical Immunology Association, and many more.