Mastocytosis and the Mast Cell

MASTOCYTOSIS
AND THE MAST CELL

By Felix Sagher, m.d.

Professor of Dermatology and Venereology, Hebrew University-Hadassah Medical School, Head of the Department of Dermatology and Venereology, Hadassah University Hospital, and Director of the Governmental Hospital for Hansen’s Disease, Jerusalem, Israel

and Zvi Even-Paz, M.B., Ch.B

Senior Lecturer, Department of Dermatology and Venereology, Hebrew University Hadassah Medical School; Chief Physician, Department of Dermatology and Venereology, Hadassah University Hospital, Jerusalem, Israel

With 4 color plates, 163 black-and-white illustrations, 9 diagrams, 23 tables and 1361 references

BASEL (Switzerland) S. KARGER NEW YORK

Atlas and Chapter on Roentgenographic Appearances in collaboration with S. Schorr, M.D.
Professor of Roentgenology, Head of the Roentgenologic Department, Ichilov-Municipal Hospital, Tel Aviv, Israel

Distributed simultaneously in North and South America, Australia and the Philippines by
YEAR BOOK MEDICAL PUBLISHERS, INC., Chicago

S. Karger AG, Arnold-Böcklin-Strasse 25, CH-4000 Basel 11 (Switzerland)

All rights, including that of translation into foreign languages, reserved. Photomechanic reproduction (photocopy, microcopy) of this book or part of it without special permission of the publishers is prohibited.

©

Copyright 1967 by S. Karger AG, Basel
Printed in Switzerland by Basler Druck- und Verlagsanstalt, Basel
It is now recognized that urticaria pigmentosa or mastocytosis, once considered a purely benign affection of the skin, may involve internal organs and tissues with sometimes fatal results. The disease has become the concern of the internist, hematologist, roentgenologist, biochemist and pathologist as well as of the dermatologist. Cutaneous manifestations of mastocytosis which were previously unknown have recently been described whilst systemic involvement is being reported with increasing frequency. A reappraisal of the disease, such as we have attempted in the first section of this book, may therefore be timely.

The second section of the book comprises a necessarily limited survey of what is known or conjectured with regard to the tissue mast cell: here emphasis is laid on the participation of this cell in various human physiological and pathological processes. The mast cell is thought to play a major or minor role in numerous regulative mechanisms within the connective tissue, as well as in a wide variety of immuno-allergic conditions. It is subject to hormonal influences and may be concerned in the reaction to stress. Knowledge of the nature of the mast cell thus furthers a more complete understanding of some fundamental biological phenomena.

Acknowledgements

We gratefully acknowledge our debt to many physicians in various countries for their kindness in sending us details of patients under their care, for accounts of their experimental observations, for supplying photographs, and for permission to reproduce published material. For help of this nature we sincerely thank:

Asboe-Hansen, G., M.D., Copenhagen, Denmark;
Atkinson, W.B., M.D., Cincinnati, Ohio, U.S.A.;
Beare, J.M., M.D., Belfast, Northern Ireland;
Bendel, W.L., M.D., Dallas, Texas, U.S.A.;
Berlin, Ch., M.D., Tel-Aviv, Israel;
Bigelow, E.L., M.D., Cincinnati, Ohio, U.S.A.;
Bloom, G., M.D., Stockholm, Sweden;
Braun-Falco, O., M.D., Mainz, W.Germany;
Butterworth, T., M.D., Reading, Pa., U.S.A;
Caplan, R.M., M.D., Iowa City, Iowa, U.S.A.;
Cardama, J.E., M.D., Buenos Aires, Argentine;
Cole, A.R. C., M. D., Toronto, Canada;
Dameshek, W., M. D., Boston, Mass., U. S. A.;
Degos, R., M.D., Paris, France;
Demis D.J. M.D., St.Louis, Mo., U.S.A.;
Efrati, P., M. D., Rehovot, Israel;
Epstein, B., M.D., Pretoria, South Africa;
Findlay, G.H., M.D., Pretoria, South Africa;
Franks, A. G., M. D., New York, N.Y., U.S.A.;
Gatti, J.C., M.D., Buenos Aires, Argentine;
Goldgräber, M.B., M.D., Jerusalem, Israel;
Grupper, C., M.D., Paris, France;
Gusek, W., M.D., Hamburg, W.Germany;
Gutman, A., M.D., Tel-Aviv, Israel;
Holti, G., M.D., Newcastle upon Tyne, England;
Jacobson, C., M.D., Dallas, Texas, U.S.A.;
Johnston, M.M., M.D., Vancouver, Canada;
Jung, J., M.D., Mainz, W.Germany;
Kelsall, M. A., M. D., Boulder, Colo., U. S. A.;
Lennert, K., M.D., Frankfurt am Main, W.Germany;
Lynfield, Y., M.D., Chicago, 111., U.S.A.;
Marshall, J., M.D., St.James, Cape Province, South Africa;
Meneghini, C. L., M.D., Milan, Italy;
Race, G.J., M.D., Dallas, Texas, U.S.A.;
Remy, D., M.D., Bremen, W.Germany;
Riley, J.F., M.D., Dundee, Scotland;
Ross, C. M., M.D., Pretoria, South Africa;
Selye, H., M.D., Montreal, Canada;
Shelley, W.B., M.D., Philadelphia, Pa., U.S.A.;
Sirois, J., M.D., Hull, Quebec, Canada;
Smith, Elizabeth W., M.D., Cincinnati, Ohio, U.S.A.;
Stroud, C.E., M.D., London, England;
Tempsky, Y., M.D., Haifa, Israel;
Weidman, A.I., M.D., New York, N.Y., U.S.A.
For permission to reproduce illustrations, we are also indebted to the editors and publishers of the
Acta Derma to-Venereologica; Actas dermo-sifiliograficas; Acta Pediatrica;
Acta Radiologica; A.M. A. Archives of Dermatology; Annals of the
New York Academy of Sciences; Archives Belges de Dermatologie et de Syphiligraphie; Archives of Diseases of Childhood; Archiv für klinische und experimentelle Dermatologie; Blood; The British Journal of Dermatology;
Clinical Radiology; Ergeb. Inn. Med. Kinderheilkunde; The
Journal of Bone and Joint Surgery; Journal of Investigative Dermatology;

In particular, we especially thank Charles C. Thomas, Publisher, Springfield, Ill., U.S.A., for permission to reproduce text and illustrations from a chapter by the present authors which was published in ‘Cutaneous Manifestations of the Reticuloendothelial Granulomas’, edited by S.Bluefarb, M.D., 1960. This previous work contains about one quarter of the present text, and many of the illustrations.

It is a pleasure to express our thanks to those many people who have rendered valuable assistance in various fields connected with this work:
To S. Schorr, M.D., Tel-Aviv, for his cooperation in the Atlas and chapter on roentgenographic changes; to H.Ungar, M.D., E.Liban, M.D. and E.Rosenmann, M.D. for pathological examinations; to G.Isaac, M.D. and E.Rachmilevitz, M.D. for hematological studies; to Mrs. Belina Lazarova and Mrs. Ruth Ungar for laboratory assistance; to Mrs. Ruth Sagher, Mr. E.B. Kennedy, Mr. M. Comforti and Mr. J. Hoory for photographic work; to Mr. Zvi Cochavy for technical assistance. We particularly wish to thank Mrs. Frances Shlesinger for her secretarial help.

We are much indebted to Frances Pascher, M.D., New York, for her general interest and encouragement during the preparation of the manuscript. For financial assistance in defraying the costs of the color plates we are most grateful to Ciba Ltd., Basel, Switzerland; Dermik Pharmacal Co., Inc., Syosset, N.Y., U.S.A.; and Mrs. Irving Wershaw, Dome Chemicals Inc., New York, U.S.A.

Finally we wish to thank the publishers S. Karger Ltd., for their patience and helpfulness during all the stages of production.
A few reports of special interest, which were published or communicated to us whilst this book was in press, have been referred to in the form of footnotes. This material, however, is not included in the tables or in statistical analyses.

Jerusalem, July 1966 Felix Sagher
Zvi Even-Paz

Contents

Section One: Mastocytosis

Chapter I—Definition 3
Chapter II—History 4
Chapter III—Classification 8
Chapter IV—Etiology and Pathogenesis 10
A congenital or nevoid abnormality, possibly hereditary 10
A metabolic disturbance 11
An infective or toxic state 11
An inflammatory process 11
A blood dyscrasia or a reticuloendotheliosis 11
Mastocytosis associated with other diseases 12

Chapter V—Incidence of Mastocytosis 14
Incidence of various types 14
Age incidence 15
Sex incidence 16
Complexion-type and race incidence 17

Chapter VI—Cutaneous Mastocytosis: Clinical Types and Lesions 18
Solitary mastocytoma 18
Disseminated forms of cutaneous mastocytosis 20
Bullous urticaria pigmentosa 40
Telangiectatic types of urticaria pigmentosa: telangiectasia macularis eruptiva perstans 44
Hemorrhagic lesions 46
Diffuse and erythrodermic forms of cutaneous mastocytosis 47

Chapter VII—Systemic Mastocytosis (Part ) 55
Introduction 55
Benign and malignant systemic mastocytosis 56
Incidence of systemic mastocytosis 56
Incidence of malignant mastocytosis 56

XII Contents

Sex and age onset ratios in systemic mastocytosis 57
Tabulation of findings in 145 cases of 'proved' or 'possible' systemic mastocytosis 58

Chapter VIII—Systemic Mastocytosis (Part 2)93
Liver and spleen involvement 93
Liver function tests and other biochemical changes 94
Lymph node involvement 95
Bone marrow involvement 96
Peripheral blood changes 98

Chapter IX—Systemic Mastocytosis (Part 3)105
Roentgenographic studies in mastocytosis 106
Roentgenographic bone changes 106
The differential diagnosis of roentgenographic bone changes in mastocytosis 114
Roentgenographic lung changes 116
Roentgenographic changes in liver and spleen 117
Roentgenographic changes in the gastrointestinal tract 117

An Atlas of Roentgenographic Appearances in Mastocytosis 120

Chapter X—Symptomatology 148
Pruritus 149
Vascular disturbances—flushing 149
Gastrointestinal symptoms 151
Skeletal symptoms 152
Respiratory tract symptoms 152
Neurological symptoms 153
Ophthalmologic symptoms 153
Otolologic symptoms 154
Hemorrhagic tendency 154
Skin ulceration 155
Hypersensitivity 155

Chapter XI—Clinical Diagnosis and Differential Diagnosis 156
Age of onset 156
Urticaria of the lesions (Darier’s sign) 156
Dermographism of the apparently uninvolved skin 159
Color of the lesions 160
Cytological procedures 160
Intradermal tests 161
Examination of urine and serum for mast cell metabolites 163
Clinical differential diagnosis of cutaneous mastocytosis 164

Chapter XII—Histopathology and Histologic Differential Diagnosis 171
Skin sections 172
Bone sections 182
Histologic examination of other tissues 187

Contents XIII

Chapter XIII—Fatal Cases and Autopsy Findings 189

Chapter XIV—The Treatment of Mastocytosis 229
Histamine and serotonin antagonists 229
Heparin antagonists 231
Histamine and serotonin liberators 231
Hyaluronidase 233
Steroids and corticotrophin 234
Antimitotic drugs 235
Irradiation therapy—external and internal 237
General medical and surgical procedures in patients with mastocytosis 238

Chapter XV—Prognosis 239

Section Two: The Tissue Mast Cell

Chapter XVI—Definition of the Tissue Mast Cell 245

Chapter XVII—Mast Cell Distribution in Animal and Human Tissues 246
Distribution in animal tissues 246
Distribution in human tissues 247
Chapter XVIII—The Origin of Mast Cells 251

Chapter XIX—The Relationship of Tissue Mast Cells to Other Cells 254
Mast cells and blood basophils 254
Mast cells and eosinophils 255
Mast cells and chromaffin cells256
Mast cells and juxtaglomerular cells256

Chapter XX—Morphological Features of Tissue Mast Cells 257
Ordinary light microscopy257
Phase contrast microscopy257
Ultra-violet and polarized light illumination261
Electron microscope studies261
Ameboid movement in mast cells268

Chapter XXI—The Staining of Mast Cells269
Metachromatic staining269
Periodic acid — Schiff (PAS) reaction273
Other stains used for mast cell identification273
Fixation275
Dehydration276

Chapter XXII—Biochemistry of Mast Cells278
Heparin and mast cells279
Hyaluronic acid and mast cells283
Histamine and mast cells285

XIV Contents

Serotonin and mast cells287
Dopamine and mast cells288
Slow reacting substance (SRS) in mast cells288
‘Spreading substance’ and mast cells289
Enzyme systems in mast cells289

Chapter XXIII—Function of Tissue Mast Cells and Their Participation in Various Physiological and Pathological Conditions
Part 1: General Conditions292
Introduction292
Mast cells and the integrity and metabolism of connective tissue293
Mast cells and tissue growth298
Mast cells and tumor growth299
Mast cells in the defense against infectious and noxious agents301
Mast cells and calciphylaxis302
Mast cells and calcergy (mastocalcergy)305
Mast cells and the regional fixation of blood-borne particles306
Mast cells and fat transport307
The effects of some experimental diets on mast cells in animals
Drug induced hypothermia
Antimitotic drugs and mast cells
Radiation and mast cells
The influence of hormones on tissue mast cells
Mast cells in anaphylactic, immuno-allergic and hypersensitivity states
Blood basophil tests and allergic states
Chapter XXIV—Function of Tissue Mast Cells and Their Participation in Various Physiological and Pathological Conditions
Part 2: Special Conditions
Some examples of mast cell participation in allergic and sensitivity states in humans
Atherosclerosis and mast cells
Mast cells in thrombotic and bleeding states
Mast cells and collagen diseases
Mast cells and diseases of the gastrointestinal tract
Mast cells and cirrhosis of the liver
Mast cells and renal disease
Mast cells and alopecia areata
Mast cells and migraine
Mast cells and eye conditions
Mast cells and carcinoid

References

Author Index

Subject Index

List of Tables

Section One: Mastocytosis
Table I. Classification of mastocytosis
Table II. Sex and age ratios in mastocytosis
Table III. 145 cases of mastocytosis with proved or possible systemic involvement
Table IV. Organ and tissue involvement in mastocytosis
Table V. Hematologic disturbances in systemic mastocytosis
Table VI. Incidence of diffuse- and circumscribed-types of roentgenographic bone lesions in 145 cases of systemic mastocytosis
Table VII. The association of diffuse- and circumscribed-types of roentgenographic bone lesions with other evidence of systemic involvement
Table VIII. Relation of roentgenographic bone changes in mastocytosis to age of the
Table IX. Relation of roentgenographic bone changes in mastocytosis to sex of the patient

Table X. The incidence of symptoms and findings associated with mastocytosis . . 149

Table XI. Differential diagnosis of urticaria pigmentosa and secondary maculopapular syphilis167

Table XII. Bullous urticaria pigmentosa—clinical differential diagnosis.168

Table XIII. Differentiation of flushing attacks of mastocytosis and of the carcinoid syndrome169

Table XIV. Clinical differential diagnosis of telangiectasia macularis eruptiva perstans 170

Table XV. Histologic differential diagnosis of bullous urticaria pigmentosa ... 180

Table XVI. Histologic differential diagnosis of telangiectasia macularis eruptiva perstans 181

Table XVII. Fatal cases of mastocytosis190

Table XVIII. The course of the cutaneous eruption of urticaria pigmentosa in 59 children followed to age of 10 years or beyond241

Table XIX. Duration of disease in 25 cases of mastocytosis with fatal termination . 242

Section Two: The Tissue Mast Cell

Table XX. Average mast cell counts in normal human skin249

Table XXI. Main morphologic differences between tissue mast cells and blood basophils 254

Table XXII. Biologically potent substances present or possibly present in mast cells 279

Table XXIII. Factors accelerating or decelerating the mast cell-histamine chain 297

Diagrams

Diagram I. Origin and interrelationships of the tissue mast cell 252

Diagram II. The ‘mast cell cycle’ in the connective tissue294

Diagram III. The ‘mast cell-histamine chain’296

Diagram IV. The action of calcifiers and challengers in the induction of the calciphylactic response304

Diagram V. The mechanism of sideromastocalciphylaxis304

Diagram VI. The influence of hormones on tissue mast cells316

Diagram VII. The tissue mast cell in the pathogenesis of myxedema 317

Diagram VIII. The mucosal mast cell as a mediator of gastric secretory stimulation 318

Diagram IX. The role of the mast cell in the acute allergic reaction321