

Clues in the Diagnosis of Non-tumoral Testicular Pathology

Manuel Nistal
Pilar González-Peramato
Álvaro Serrano

Clues in the Diagnosis of Non-tumoral Testicular Pathology

Manuel Nistal
Pilar González-Peramato
Álvaro Serrano

Clues in the Diagnosis of Non-tumoral Testicular Pathology

 Springer

Manuel Nistal
Universidad Autónoma de
Madrid (UAM)
School of Medicine
Madrid
Spain

Álvaro Serrano
University Hospital Clinico San Carlos
Department of Urology
Madrid
Spain

Pilar González-Peramato
School of Medicine, Universidad
Autónoma de Madrid (UAM)
University Hospital La Paz
Department of Pathology
Madrid
Spain

ISBN 978-3-319-49363-3 ISBN 978-3-319-49364-0 (eBook)
DOI 10.1007/978-3-319-49364-0

Library of Congress Control Number: 2016963215

© Springer International Publishing AG 2017

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made.

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

*To my wife, Piedad
To my children Rodrigo, Gonzalo, Beatriz, and Natalia
In memoriam, to my father Manuel*

Manuel Nistal

*To my husband, Alvaro
To my children Álvaro, Teresa, and Javier
In memoriam, to my parents Antonio and Pilar*

Pilar González-Peramato

*To my wife, Pilar
To my children Álvaro, Teresa, and Javier
In memoriam, to my father Lope*

Alvaro Serrano

Preface

This book is a work based on the study and reflection of the authors about hundreds and hundreds of biopsies, surgical specimens, and autopsy material reported during more than 40 years in a university hospital, which treated testicular pathology – and precisely non-tumoral testicular and epididymal pathology – as a hobby. Therefore, this book does not pretend to be a compendium on this pathology, but a presentation of diagnostic problems that to be solved need knowledge on urology, andrology, pediatric gynecological endocrinology, and genetics apart from the usual pathological armamentarium. The success that the book *Testicular and Epididymal Pathology* by Nistal M and Paniagua R, editors, had in the 1980s has encouraged us to continue being specially interested in the non-tumoral testicular and epididymal pathology that has not raised a special interest in other pathology books.

What is the difference of this book from other books of pathology? In the majority of the treatises, the non-tumoral testicular pathology is reduced to a few items where the pathologist does not seem to play an important role. Our purpose is to present the diagnostic problems from the morphology of the lesions and build the diseases and their differential diagnosis under this perspective. Although the book is written in a schematic form, details necessary to get a deeper knowledge of this pathology and its differential diagnosis are included.

The chapters have been selected considering three reasons: first, that the different fields of non-tumoral testicular pathology – genetic, malformative, developmental, functional, vascular, or inflammatory – would be represented; second, that the topics should present problems on their differential diagnosis; and, third, that the pathologies included in this book should be uncommon enough to make this book a highly consultable text to solve certain problems in non-tumoral testicular pathology.

The chapters have been divided in eight parts: genetic and developmental pathology of the testes, infertility, vascular pathology of the testes, inflammatory pathology, pathology of the rete testis, pathology of the epididymis, pathology of the vaginal tunica and paratesticular structures, and miscellanea.

Bearing in mind that in pathology images are as important as – or even more important than – text, figures have been carefully selected in each chapter. Furthermore, in many chapters, to stand out the main characteristics of the lesions or to ease the diagnostic process, a variety of diagrams or algorithms have been included. In addition, legends are straightforward.

The authors have to thank the important contribution along many years of many pathologists in the study of the cases presented in this book, either as pathologist in training or sending cases in consultation that have been kindly and enthusiastically given up. We also have to emphasize the unconditional support of our clinicians and surgeons without whose collaboration this book of clues on non-testicular and epididymal pathology couldn't have been written.

Madrid, Spain
Madrid, Spain
Madrid, Spain

Manuel Nistal
Pilar González-Peramato
Álvaro Serrano

Acknowledgments

First, our thanks are due to our publishers, the Springer-Verlag team, in particular, our associate editor, Inga von Behrens, for giving us the opportunity of publishing this book and our project coordinator, Palanisamy Dhanapal, for his support.

The authors would like to heartily thank the University Hospital La Paz, one of the first big hospitals in Spain, in which two of the authors have developed their professional activity for many years. Special thanks go to all staff members and residents of the Department of Pathology at University Hospital La Paz for their support and for bringing to our attention items and cases of special diagnostic and descriptive interest. We also express our appreciation and gratitude to technical staff of the Department of Pathology at University Hospital La Paz for their careful preparation of the slides shown in this book. We would also like to recognize with thanks the Universidad Autonoma de Madrid where we have carried out our teaching and research activity.

We would also like to express our deepest thanks and appreciation to a large number of colleagues, co-workers, and friends who throughout the years have generously contributed cases in consultation, many of which are very rare and hence precious materials.

Finally, we wish to acknowledge Ana Weyland for her invaluable help to improve the English grammar and syntax of our manuscripts to transform them into readable documents.

Manuel Nistal
Pilar González-Peramato
Álvaro Serrano

Contents

1	What Does the Presence of Seminiferous Tubules Inside the Tunica Albuginea Mean?	1
1.1	Structure of the Normal Tunica Albuginea	1
1.2	Persistence of Testicular Blastema	2
1.3	Persistence of Seminiferous Tubules in Normal Tunica Albuginea	4
1.4	Ectopia of Testicular Parenchyma in the Normal Tunica Albuginea	6
1.5	Ectopia of Seminiferous Tubules in an Ovarian-Like Stroma	7
	References	8
2	Disorders of Sexual Development from the Pathologist's Perspective	9
2.1	Introduction	9
2.2	Histological Classification	10
2.3	Types of Gonads	11
2.4	True Agonadism	13
2.5	Gonadal Dysgenesis with Classical Streak Gonad	14
2.5.1	Turner's Syndrome	14
2.5.2	46,XX Pure Gonadal Dysgenesis	14
	References	15
3	Clinical Syndromes Associated with Streak Gonads with Epithelial Cords	17
3.1	46,XY Gonadal Dysgenesis	17
3.2	Syndromes Associated with 46,XY Gonadal Dysgenesis	21
3.2.1	Denys-Drash Syndrome	21
3.2.2	Frasier Syndrome	21
3.2.3	WARG Syndrome	21
3.2.4	Campomelic Dysplasia	22
	References	22
4	Clinical Syndromes Associated with Dysgenetic Testis	25
4.1	Introduction	25
4.2	Mixed Gonadal Dysgenesis	25
4.3	Dysgenetic Male Pseudohermaphroditism	27
4.4	Persistent Müllerian Duct Syndrome (PMDS)	27
	References	30

5 True Hermaphroditism (Ovotesticular DSD)	33
5.1 Introduction	33
5.2 Karyotype.....	33
5.3 Pathogenetic Theories	33
5.4 Phenotype.....	34
5.5 Gonadal Types	34
5.6 Types of True Hermaphroditism	38
5.7 Biological Behaviour of the Gonads	38
5.8 Patient Management.....	38
References.....	38
6 Usefulness of Histological Studies in Patients with the Androgen Insensitivity Syndrome	41
6.1 Introduction	41
6.2 CAIS in Fetal Age	41
6.3 CAIS in Prepubertal Patients.....	42
6.3.1 Histological Findings.....	42
6.3.2 Differential Diagnosis	43
6.3.3 Associated Pathology.....	43
6.4 CAIS in Pubertal and Adult Patients	45
6.4.1 Histological Findings.....	45
6.4.2 Associated Pathology.....	45
6.5 PAIS.....	47
6.6 MAIS.....	47
6.7 Tumors in AIS	48
References.....	48
7 Differential Diagnosis of Tumors in the Adrenogenital Syndrome	51
7.1 Introduction	51
7.2 Development of Tumors of the Adrenogenital Syndrome	51
7.3 Clinical and Laboratory Diagnostic Clues.....	52
7.4 Diagnostic Imaging	53
7.5 Histological and Immunohistochemical Clues	53
References.....	56
8 Fetal Gonadoblastoid Testicular Dysplasia: An Early Defect in Testicular Tubulogenesis	59
8.1 Introduction	59
8.2 Histology	59
8.3 Differential Diagnosis	60
8.4 Etiopathogenesis	62
References.....	64
9 Differential Diagnosis of Sertoli Cell Nodules	67
9.1 Introduction	67
9.2 Histology	67
9.3 Variability of Sertoli Cell Nodules.....	67

9.4	Differential Diagnosis	69
9.4.1	Sertoli Cell Nodules Versus Intratubular Large Cell Hyalinizing Sertoli Cell Neoplasia	70
9.4.2	Sertoli Cell Nodules with GCNIS Versus Gonadoblastoma	70
9.4.3	Sertoli Cell Nodules Versus Sex Cord Tumor with Annular Tubules (SCTAT)	73
9.4.4	Macroscopic Sertoli Cell Nodules Versus Sertoli Cell Tumors “Not Otherwise Specified”	74
	References.	74
10	Meaning of the Finding of Testicular and Paratesticular Calcifications	75
10.1	Testicular Calcifications.	75
10.1.1	Testicular Microlithiasis.	75
10.1.2	Macrolithiasis Separated from Any Intratubular Mass	78
10.1.3	Tumor-Associated Calcifications.	79
10.2	Paratesticular Calcifications.	80
10.2.1	Calcifications of the Epididymis	80
10.2.2	Epididymal Stones.	81
	References.	81
11	Helpful Data for Evaluating an Undescended Testis in Childhood	83
11.1	Hypothalamic-Pituitary-Testicular Axis	83
11.2	Basic Data to Evaluate an Undescended Testis	84
11.2.1	Clinical Data	84
11.2.2	Histological Data	85
11.3	Classification of Undescended Testis.	89
	References.	90
12	The Most Frequent Histological Findings in the Adult Testis When Testicular Descent Was Performed in Childhood	93
12.1	Most Frequent Testicular Lesions Observed in Adulthood	93
12.2	Correlation Between Pre- and Postpubertal Biopsies	97
12.3	Associated Secondary Testicular Lesions in Adult Testes	98
12.3.1	Obstruction.	98
12.3.2	Varicocele.	99
12.4	Summary of the Nature of Testicular Lesions	99
	References.	100
13	Testicular Dysgenesis Syndrome (TDS)	101
13.1	Concept of Testicular Dysgenesis Syndrome.	101
13.1.1	Testicular Germ Cell Tumors.	101
13.1.2	Cryptorchidism	101
13.1.3	Hypospadias.	102
13.1.4	Infertility	102

13.2	Etiology of TDS	102
13.3	Histological Findings in TDS	103
	References	108
14	Differential Diagnosis of Macroorchidism	111
14.1	Asymmetric Testicular Size: Compensating Hypertrophy	111
14.2	Non-tumoral Macroorchidism	111
14.2.1	Early Harmonious Development of the Testis: Gonadotropin-Dependent Precocious Puberty – Central Precocious Puberty (CPP)	111
14.2.2	Dissociation of Tubular and Interstitial Development	112
	References	119
15	Macroorchidisms Secondary to Functioning Tumors during Childhood	123
15.1	Introduction	123
15.2	Leydig Cell Tumors	123
15.3	Sex Cord Tumors	126
15.4	Adrenocortical Tumors	127
15.5	Extratesticular HCG-Secreting Tumors	128
15.6	Other Tumors	128
	References	129
16	Value of Testicular Biopsy in Nonobstructive Azoospermia	131
16.1	Tubular Hyalinization	131
16.2	Sertoli Cell-Only Syndrome (SCOS)	132
16.3	Mixed Atrophy	134
16.4	Lesions of Basal and Adluminal Compartment	135
16.4.1	Hyospermatogenesis	135
16.4.2	Maturation Arrest	136
16.5	Potentially Predictive Factors	139
	References	139
17	Obstructive Mechanism Lesions Simulating Primary Testicular Lesions	143
17.1	Histological Characteristics of the Obstructive Mechanism Lesions	143
17.1.1	Qualitative Data	143
17.1.2	Quantitative Data	143
17.2	Mechanism of the Testicular Lesions	147
17.3	Factors Affecting the Development of Testicular Lesions	147
17.4	Differential Diagnosis Between Obstructive Mechanism Lesions and Primary Testicular Lesions	149
	References	149
18	Fertility in Patients with Chromosome Abnormalities	151
18.1	Numerical Chromosome Aberrations	151
18.1.1	Klinefelter’s Syndrome	151
18.1.2	The XX Male Syndrome	153

18.1.3	The XYY Syndrome	154
18.2	Structural Chromosome Aberrations	155
18.2.1	Structural Aberrations of the Autosomes	155
18.2.2	Structural Aberrations of the Sex Chromosomes	155
18.3	Y-Chromosome Microdeletions	156
	References	159
19	Fertility Potential of Patients with Hypogonadotropic Hypogonadism	163
19.1	The Male Reproductive Axis	163
19.2	Classification of Hypogonadotropic Hypogonadism	163
19.2.1	Congenital Hypogonadotropic Hypogonadism (CHH)	164
19.2.2	Acquired Hypogonadotropic Hypogonadism (AHH)	166
19.3	Fertility Predictor Data	167
19.4	Treatment Methods	169
	References	169
20	Ultrastructural Pathology of the Spermatozoa with Genetic Basis	171
20.1	Introduction	171
20.2	Microcephalic Spermatozoa	171
20.2.1	Globozoospermia: Round-Headed Spermatozoa Syndrome	171
20.2.2	Microcephalic Spermatozoa with Acrosome Hypoplasia	173
20.3	Macrocephalic Head Spermatozoa Syndrome: Large-Headed Spermatozoa	173
20.3.1	Spermatozoa with Multiple Flagella	173
20.3.2	Macrocephalic Spermatozoa Without Flagella	174
20.4	Abnormal Head-Tail Attachment	174
20.4.1	Decapitated Spermatozoa/Acephalic Spermatozoa	175
20.4.2	Defects of the Connecting Piece	176
20.4.3	Separated Head and Flagellum: Decapitated and Decaudated Spermatozoa	176
20.5	Fibrous Sheath Dysplasia	176
20.6	Primary Ciliary Dyskinesia (PCD): Immotile Cilia Syndrome	177
	References	179
21	Spermatic Cord Torsion and Infertility	183
21.1	Introduction	183
21.2	Physiopathology	184
21.3	Indicators of Testicular Salvage Ability	184
21.4	Causes of Infertility	187
21.5	Potential Protective Agents	187
	References	189

22	Clues to the Analysis of Testicular Lesions in Infertile Patients with Varicocele	191
	22.1 Varicocele and Infertility	191
	22.2 Pathogenetic Mechanism	191
	22.3 Clues to Interpret Testicular Lesions	194
	References	198
23	Surgical Treatment of Varicocele	201
	23.1 Indications for Varicocele Surgical Repair	201
	23.2 Treatment Options	201
	23.2.1 Open Surgery	202
	23.2.2 Laparoscopic Surgery	204
	23.2.3 Retrograde and Antegrade Embolization or Sclerotherapy of the Spermatic Veins	205
	23.3 Results of Surgical Techniques	206
	References	207
24	Testicular Involvement in Noninfectious Vasculitis	209
	24.1 Polyarteritis Nodosa (PAN)	209
	24.2 Henoch-Schönlein Purpura	210
	24.3 Wegener's Granulomatosis	211
	24.4 Giant Cell Arteritis	213
	24.5 Thromboangiitis Obliterans (TAO)	213
	24.6 Kogan's Disease	215
	24.7 Behçet's Disease	215
	24.8 Vasculitis Associated with Other Processes	215
	References	215
25	Vascular Pathology Related to Extracellular Material Accumulation	219
	25.1 Arteriolar Hyalinosis	219
	25.2 Disseminated Intravascular Coagulation (DIC)	221
	25.3 Amyloidosis	222
	References	227
26	Interpretation of Testicular Non-granulomatous Lymphoid Infiltrates	229
	26.1 Infiltrates Rich in Polymorphonuclear Leukocytes	229
	26.1.1 Acute Orchiepididymitis	229
	26.2 Infiltrates Rich in Lymphocytes	230
	26.2.1 Primary Autoimmune Orchitis (Focal Orchitis)	230
	26.2.2 Chronic Nonspecific Orchitis	231
	26.2.3 Testicular Pseudolymphoma	231
	26.3 Infiltrates Rich in Macrophages	232
	26.3.1 Macrophages with Granular and Eosinophilic Cytoplasm	232
	26.3.2 Macrophages with Clear Cytoplasm	234
	26.4 Infiltrates Rich in Plasma Cells	236
	26.5 Mast Cells and Infertility	237
	References	237

27	Histological Basis for the Interpretation of Granulomatous Orchitis	241
27.1	Granulomatous Orchitis Destroying Testicular Architecture	241
27.1.1	Granulomatous Orchitis with Necrotizing Granulomas	241
27.1.2	Granulomatous Orchitis with Non-necrotizing Granulomas	244
27.1.3	Granulomatous Orchitis by Foreign Bodies	245
27.2	Granulomatous Orchitis Preserving Testicular Architecture	247
27.2.1	Idiopathic Granulomatous Orchitis (IGO)	247
27.2.2	Peritumoral Granulomatous Orchitis. Granulomatous Tubulitis	248
	References	250
28	Rete Testis Dysgenesis as a Marker of Undescended Testis	253
28.1	Normal Rete Testis	253
28.2	Rete Testis Dysgenesis	254
28.2.1	Definition	254
28.2.2	Histological Patterns of Dysgenesis of the Rete Testis	254
28.2.3	Relationship Between Dysgenesis of the Rete Testis and Other Primary Anomalies of the Undescended Testis	257
28.2.4	Differential Diagnosis	258
28.2.5	Situations in Which Dysgenesis of the Rete Testis Can Be Observed	259
	References	259
29	Congenital Cystic Pathology of the Rete Testis	261
29.1	Cysts of the Rete Testis	261
29.2	Cystic Dysplasia of the Rete Testis	261
29.2.1	Definition	261
29.2.2	Histological Features	263
29.2.3	Differential Diagnosis	265
29.2.4	Associated Pathology	266
29.2.5	Treatment	267
	References	267
30	Acquired Cystic Transformation of the Rete Testis (Cystic Ectasia of the Rete Testis)	269
30.1	Defense Mechanisms of the Testis Against Testicular Fluid Obstruction	269
30.2	Concept of Acquired Cystic Transformation of the Rete Testis (ACTRT)	270
30.2.1	Definition	270
30.2.2	Diagnosis	270
30.2.3	Differential Diagnosis of the Cystic Transformation of the Rete Testis	271