PEDIATRIC SURGICAL PATHOLOGY

LOUIS P. DEHNER

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with a foreword by

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with 823 *illustrations*

THE C. V. MOSBY COMPANY

SAINT LOUIS 1975

Printed in the United States of America

Distributed in Great Britain by Henry Kimpton, London

Library of Congress Cataloging in Publication Data

Dehner, Louis P 1940-
Pediatric surgical pathology.

Includes bibliographies and indexes.
1. Children, Surgery. 2. Diagnosis, Surgical. I. Title. [DNLM: 1. Pathology, Surgical—In infancy and childhood. WO142 D322p]
RD137.D44 617'.98'07 75-9758
ISBN 0-8016-1218-7

CB/CB/B 9 8 7 6 5 4 3 2

To that most important individual who influenced the writing of this book:

the sick child.

To those people who most influenced my personal life:

Sara and Pick.

To those men who most influenced my professional life:

Lauren V. Ackerman, M.D., and John M. Kissane, M.D.

Foreword

It was less than 25 years ago that, at a slide seminar devoted to pediatric lesions, a pathologist in the audience asked if there were a book on the subject. One of the distinguished panelists replied that there was then no book in English devoted to pediatric pathology. Now, less than a generation later, there are not only several books devoted to pediatric pathology generally, but particularization within that area is already well advanced. There are now complete works devoted to pediatric hematology and pediatric oncology as well as substantial sections dealing with pathology in books on pediatric dermatology, pediatric endocrinology, pediatric gynecology, pediatric neurology—I hesitate to go on too specifically lest I offend, by omission, devotees of one or another subsubspecialty.

Louis P. Dehner's book represents the first staking out of the specific boundaries of the surgical pathology of infancy and childhood. I have been privileged to observe the sequential refining of this interest in Louis first as a student, then as a trainee and colleague, and always as a friend. He learned early how to answer the question *Why pediatric pathology?* and has translated those skills to answering the next question *Why pediatric surgical pathology?*

Infants and children are not merely small adults, and the pathologist who examines tissue surgically excised from infants and children develops different sets of differential diagnoses, of correlations, of questions to ask and answers to give than does the general surgical pathologist. The histologic diagnosis of aganglionosis, participation by the pathologist in characterization of an immune-deficiency syndrome, the differential diagnosis of lesions characterized by proliferations of histiocytes are all problems that, if not unique to early life, have at least different answers in young patients. Louis's broad and firm grounding in general pathology shines out, and his infectious enthusiasm carries the reader along in this exciting, even apostolic work. It deserves to be widely read by physicians concerned with diseases of young patients.

John M. Kissane

Preface

This book was conceived, much of it written, and most of it based upon the rich reservoir of pathologic material made available to me while a member of the resident and full-time staff in the Division of Surgical Pathology, Barnes and St. Louis Children's Hospitals, Washington University School of Medicine. Most of the specimens were from the patients of Drs. Teresa Vietti and Jesse Ternberg and their staffs. The excellence of care provided to each child was unsurpassed by virtually any parameter applied. An extremely important factor in the cycle of excellence was that of the pediatric radiologist, Dr. William McAlister. A special note of gratitude is extended to Dr. McAlister for his assistance in the review and selection of the roentgenographs used in this book. A volume on surgical pathology regardless of its emphasis has limited value without quality illustrations. Mr. Cramer Lewis, head of the Department of Medical Illustration, Washington University School of Medicine, has once again, as so often in the past, added the artist's touch to all of the photomicrographs and most of the gross illustrations in this volume. I thank Mr. Lewis for his help.

The idea of compiling a volume on the surgical pathology problems of children was a natural outgrowth of my association with Dr. Lauren V. Ackerman, former Professor of Pathology and Surgical Pathology, and Dr. John M. Kissane, Professor of Pathology, Washington University School of Medicine. Their respective influences upon the direction of my interest in surgical pathology and general pediatric pathology permitted me to crystallize my thoughts and ultimate goals in the writing of this book. One of the major purposes of this volume is an attempt to bridge the interface between the problems of general pediatric pathology and surgical pathology.

Throughout this book, the entire emphasis is upon clinicopathologic correlation. For this reason I have chosen to include clinical information that some may find unconventional for a text in pathology. It is my opinion that pathologists are quite capable of utilizing it and should find it helpful when approaching a surgical problem in a child. Similarly, it is felt that surgeons, pediatricians, radiologists, radiotherapists, and oncologists who use this volume will be able to orient themselves somewhat better to the pathologic anatomy if the features of disease as they see them are readily available. Illustrations are generously used in all chapters, and when considered appropriate, clinical photographs and roentgenographs are included to provide a balanced presentation. Both the common pediatric disorders and in some cases the exotic have been illustrated. Some chapters may seem quite lengthy; however, in such areas as pediatric skin and liver diseases, there are very few reference sources to which the pathologist can turn for assistance in a diagnostic problem. The spectrum of renal diseases in children, both medical and surgical, are also discussed at some length. At the end of each chapter are numerous bibliographic citations that aided and directed me. I hope that I have accurately interpreted various authors' data when used in the text.

There are three contributing authors in this book, each of whom brought an element of expertise that I could not approach. I wish to recognize and thank Dr. Frederic B. Askin, Assistant Professor of Pathology, Washington University School of Medicine, for his section on the developmental anomalies of

the respiratory tract in Chapter 5; Dr. Robert McKenna, Assistant Professor of Laboratory Medicine and Pathology, Department of Laboratory Medicine and Pathology, University of Minnesota School of Medicine, for his section on bone marrow biopsies in children in Chapter 13; and Dr. Karl R. Meyers, Assistant Professor of Pathology, University of Pennsylvania School of Medicine, for his section on neuromuscular disorders in Chapter 16.

In order for any author to finally complete a book, he must surround himself with the necessary moral and logistic support. The former category includes the many colleagues who patiently listened to the seemingly inexhaustible prose and then leveled the needed criticism and advice. Drs. Juan Rosai and Walter C. Bauer, one a present chief and the other a former chief, have served as wise advisors while I was writing this book. The excellence of the histopathologic sections from which the photomicrographs were taken is the product of Mr. Julio Happa, Chief Histotechnician, Division of Surgical Pathology, Barnes Hospital, and his staff. The translation of my barely legible handwriting to a finished typed page must be recognized as a major accomplishment by Ms. Phyllis Christensen and Ms. Karen Wallace.

The final paragraph of this preface is reserved for the most important people in a man's life—his family. It is the author's family who sacrifices the most in terms of inconvenience and the time taken away from them. The understanding of my family, Helen, Louis, Jr., Carl, Christopher, and Elizabeth, was an all-important factor in the completion of this book.

Louis P. Dehner

Contents

1 Skin and supporting adnexae

GENERAL CONSIDERATIONS

This chapter attempts to focus the pathologist's and surgical pathologist's attention on a variety of dermatopathologic conditions in the child, many of which are unique to the pediatric age group and some of which are exclusively limited to various periods in childhood (Table 1-1). Though not emphasized to any great extent in the past, the skin biopsy occupies an important position in the diagnosis of many pediatric skin disorders. All skin biopsies submitted during a one year period to the surgical pathology laboratory, Barnes Hospital and Washington University School of Medicine, were reviewed. A total of 150 cases from individuals 15 years old or younger was found (Table 1-2). This figure represents 1.3% of all surgical specimens and approximately 10% of all skin biopsies during this interval.

The presentation in this chapter includes not only the histopathologic features but also some of the more important clinical aspects of the lesions. Most pathologists lack an appreciation for gross morphology. On occasion, it can be extremely helpful with the microscopic diagnosis.

EPIDERMIS AND DERMIS: CONGENITAL AND HEREDITARY DISORDERS

Congenital aplasia of the skin (aplasia cutis) is an uncommon condition whose relation to the other heredofamilial disorders, such as the genodermatoses and ectodermal and mesodermal dysplasias, remains a point of discussion (Croce et al., 1973). A circumscribed midline defect in the occipital region of the scalp is the commonest form (60% to 80% of the cases). The extremities, particularly the patellar regions bilaterally, are the other sites of involvement. A defect in the skull or more severe malformations of the central nervous system may be associated with aplasia cutis (Fowler and Dumars, 1973). Most lesions are recognized in the newborn period, and there is a predilection for females (Pullon, 1972). A relationship with epidermolysis bullosa has been suggested and is a major point in the differential diagnosis. A skin biopsy from the central portion of the defect shows an absence of the epidermis and supporting adnexae. Some hypoplastic appendages are occasionally identified. Elastic tissue is also markedly reduced. An inflammatory reaction is generally not prominent. A subepidermal bullous lesion may be the precursor process in utero.

Congenital constricting band (amniotic band syndrome) is a rare malformation (1 per 5,000 to 10,000 births) associated not only with epidermal changes but also with soft tissue defects, including intrauterine amputations (Chemke et al., 1973; Field and Krag, 1973). Rupture of the amniotic sac in utero with the formation of fine fibrous bands at the base of the umbilical cord is the basic process responsible for the defects (Fig. 1-1). Distal syndactylism, circular or transverse clefts in the soft tissues with or without lymphedema, clubfoot, and autoamputations are some of the more important gross abnormalities. Plastic or orthopedic intervention or both is often necessary. Microscopically, the epidermis in the affected area is normal or slightly atrophic. There is a striking reduction in the thickness of the dermis, which is largely replaced by dense fibrous tissue.

Ectodermal dysplasia is not a single inherited abnormality of the ectodermally derived structures but is represented by a number of clinical variants (Reed et al.,

Table 1-1. Classification of pediatric dermatologic entities according to cause and age of onset*

Cause	Infancy	Childhood	Adolescence
Inflammation			
Microorganisms	Ritter's disease Candidiasis Toxic epidermal necrolysis Skin infections due to *Hemophilus influenzae*	Impetigo, ecthyma Tinea of scalp and body Molluscum contagiosum Warts Herpes simplex Varicella, herpes zoster Exanthems Infestations: lice, scabies Kaposi's varicelliform eruption Tuberculosis verrucosa cutis	Tinea pedis and cruris
Physical agents	Diaper rash Miliaria	Insect bites Keloids Porphyria	Intertrigo
Chemical agents			Acid, alkali, solvents
Hypersensitivity	Drug reactions	Reactions to poison ivy, other plants	Erythema multiforme bullosum
	Food reactions	Reactions to shoe linings, elastic, adhesive tape Photosensitivity eruptions	Erythema nodosum Anaphylactoid purpura
Developmental defects			
Accidental	Angioma: capillary, strawberry, cavernous Lymphangioma Pigmented nevi Linear nevi Urticaria pigmentosa		
Inherited	Atopic dermatitis Seborrheic dermatitis Leiner's disease Ectodermal dysplasia Epidermolysis bullosa Acrodermatitis enteropathica	Neurofibromatosis Adenoma sebaceum, tuberous sclerosis Keratosis palmaris et plantaris Cutis hyperelastica Ichthyosiform dermatoses Keratosis pilaris Xeroderma pigmentosum	Psoriasis Darier's disease Pseudoxanthoma elasticum
Metabolic defects	Sclerema neonatorum		Eruptive xanthomas Necrobiosis lipoidica diabeticorum
Neoplasia	Histiocytosis syndrome	Leukemia Lymphoma	Melanoma
Emotional stress, fatigue		Nummular eczema Traumatic maceration dermatitis of hand and feet Hyperhidrosis Trichotillomania Alopecia areata Neurotic excoriations	Acne vulgaris Factitia Lichen planus
Unknown mechanisms	Toxic erythema of the newborn Subcutaneous fat necrosis of the newborn Incontinentia pigmenti	Urticaria Granuloma annulare Vitiligo Pityriasis lichenoides et varioliformis acuta	Pityriasis rosea Morphea, scleroderma Dermatomyositis Systemic lupus erythematosus Lichen nitidus

*From Lorincz, A. E.: Pediatric dermatology. In Fitzpatrick, T. B., Arndt, K. A., Clark, W. H., Eisen, A. Z., Van Scott, E. J., and Vaughan, J. H., editors: Dermatology in general medicine, New York, 1971, McGraw-Hill Book Company.

Table 1-2. Distribution and histopathologic types of skin lesions in children (Barnes and St. Louis Children's Hospitals, 1970)

Category	Number	Percent	Histologic type	Number
Pigmented lesions	41	27	Compound nevus	24
			Intradermal nevus	8
			Spindle-epithelioid nevus	3
			Junctional nevus	2
			Cellular blue nevus	1
			Malignant melanoma	3
Vascular lesions	17	11	Hemangioma, capillary and cavernous	9
			Pyogenic granuloma	8
Epithelial cysts	14	9	Keratinous cyst	10
			Dermoid cyst (periorbital)	4
Inflammations	12	8	Chronic dermatitis, NOS	5
			Eczema	4
			Foreign body inflammation	3
Epidermal-adnexal tumors	10	6	Pilomatrixoma	4
			Basal cell carcinoma	2
			Trichofolliculoma	1
			Trichoepithelioma	1
			Nevus sebaceous of Jadassohn	1
			Seborrheic keratosis	1
Fibrous proliferation	9	6	Keloid	6
			Connective tissue nevus (including Shagreen patch)	2
			Subepidermal nodular fibrosis	1
Viral disorders	8	5	Verruca vulgaris	5
			Molluscum contagiosum	2
			Varicella	1
Vasculitis and purpura	7	5	Vasculitis, allergic	3
			Pityriasis lichenoides et varioliformis acuta (Mucha-Habermann disease)	1
			Vasculitis (c/w Henoch-Schönlein purpura)	1
			Vasculitis, NOS	1
			Purpura, NOS	1
Papulosquamous diseases	6	4	Psoriasis	4
			Seborrheic dermatitis	1
			Lichen planus	1
Neural tumors	6	4	Neurofibroma	6
Miscellaneous	6	4	Urticaria pigmentosa	1
			Accessory tragus	1
			Achrochordon	1
			Congenital absence of pain	1
			Lichen sclerosus et atrophicus	1
			Panniculitis	1
Palisading granuloma	4	3	Granuloma annulare	4
Ichthyosis, linear	3	2	Ichthyosis vulgaris	2
			Linear epidermal nevus	1
Connective tissue disorder, calcinosis	3	2	Calcinosis cutis	2
			Tumoral calcinosis	1
Histiocytic lesions	3	2	Juvenile xanthogranuloma	2
			Histiocytosis X	1
Bullous disorder	2	1	Subcorneal pustular dermatosis	1
			Erythema multiforme	1

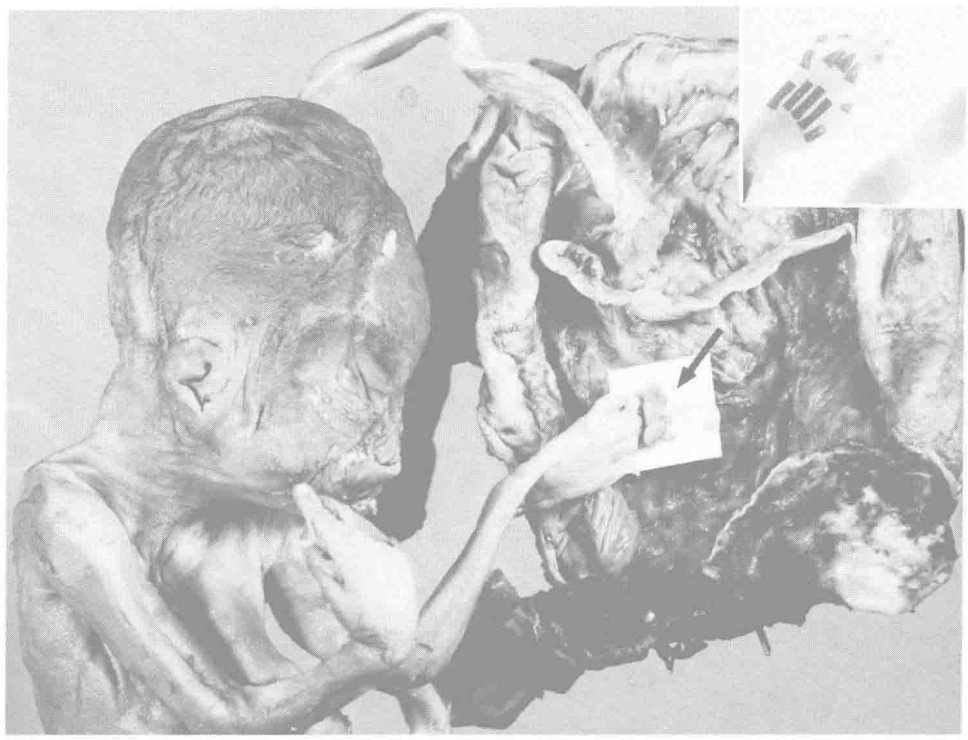

Fig. 1-1. Congenital constricting band, with partial fusion of the fingers secondary to the fibrous strands (arrow) and resulting in distal syndactyly (inset). (W.U. Ill. 73-8188.)

1970; Witkop et al., 1975). Anhidrotic ectodermal dysplasia (sex-linked recessive) and hidrotic ectodermal dysplasia (autosomal dominant) are the two principal types of this uncommon abnormality.

Hidrotic ectodermal dysplasia is the more frequent form. In it the structural defects are much less severe, except for the nails, which are quite dystrophic. Some reduction in body hair may be noted. Dental abnormalities vary from one patient to another. Hyperkeratosis of the palmar and plantar skin without other major changes in the cutaneous morphology is present in childhood. Epidermoid carcinoma developing in these sites has been reported in adults. A skin biopsy shows no appreciable alterations in the quality and quantity of the sweat gland apparatus.

Hypotrichosis, anodontia, and anhidrosis are the classic features of *anhidrotic (hypohidrotic) ectodermal dysplasia,* which because of its mode of inheritance occurs overwhelmingly in males. The facies also present a peculiar and distinctive appearance (Verbov, 1970). A number of ocular abnormalities (corneal dystrophy, cataracts) are noted (Beckerman, 1973). Soft, shiny, dry skin without nail changes is the characteristic clinical picture. X-linked ichthyosis associated with anhidrotic ectodermal dysplasia alters the typical appearance (Esterly et al., 1973). Grossly, the sweat pores are virtually nonexistent (Crump and Danks, 1971). The epidermis is essentially unremarkable in the biopsy, but the eccrine sweat glands are completely absent. In rare cases deep sweat glands may be found, but only after exhaustive examination. The other adnexal structures are variably affected and are less important in the histologic diagnosis. A reduction in the number of submucosal glands of the upper respiratory tract is another finding.

Other forms of hereditary ectodermal dysplasia are Rothmund-Thomson syndrome, pachyonychia congenita, and dyskeratosis congenita (Zinsser-Engman-Cole syndrome). Many of the cutaneous manifestations of the

latter disorder are similar to the hidrotic form of ectodermal dysplasia (Ortega et al., 1972; Inoue et al., 1973). An aplastic anemia or pancytopenia and diminished gamma globulins are integral features of Zinsser-Engman-Cole syndrome. Pachyonychia congenita (Jadassohn-Lewandowsky syndrome) is an autosomal dominant keratoderma whose earliest sign is subungal thickening noted in the infancy period. Later, focal areas of hyperkeratosis develop at pressure points. Follicular plugs and lesions that are identical to cutaneous horns are among the principal histologic findings.

Focal dermal hypoplasia (Goltz's syndrome) is a rare ectodermal and mesodermal disorder with a variety of cutaneous, osseous, soft tissue, ocular, and dental manifestations (Goltz et al., 1970). Aplasia cutis, linear foci of hypopigmentation, telangiectasias, palmar and plantar hyperkeratosis, hypohidrosis, and dystrophic nails are some of the more important dermatologic features. The areas of dermal hypoplasia are very often linearly distributed. Herniation of subcutaneous fat into these defects can simulate the nevus lipomatosus. Epidermolysis bullosa and incontinentia pigmenti are other entities considered in the differential diagnosis. Histologically, the epidermis is moderately atrophic, but the major changes are noted in the dermis. A thin band of dermal collagen is located beneath the epidermis and about the pilosebaceous units. Adipose tissue largely replaces the dermal connective tissue. Adnexal structures can be difficult to identify in the skin biopsy in spite of serial sectioning (Fattah, 1969).

Familial focal facial dermal dysplasia is unrelated to focal dermal hypoplasia but produces similar dermal alterations. Symmetrically depressed, pigmented lesions in the region of the temples characterize this autosomal dominant disorder (McGeoch and Reed, 1971, 1973). The dermis is atrophic with juxtaposition of the epidermis and underlying temporalis muscle.

Orofacial-digital syndrome (type 1), in addition to facial and skeletal abnormalities, has cutaneous manifestations that include alopecia and milia. The hair follicles and sebaceous apparatus are diminished or absent in the skin biopsy (Solomon et al., 1970). Also, keratinous cyst formation occurs early.

Keratinization defects

Ichthyosiform dermatoses is a general term encompassing four major inherited disorders, all of which are characterized in part by excessive scaling of the skin (Table 1-3). An autosomal dominant mode of inheritance is documented for at least two of these (ichthyosis vulgaris and bullous congenital ichthyosiform erythroderma), an autosomal recessive for one (nonbullous congenital ichthyosiform erythroderma), and the other is sex linked (sex-linked ichthyosis). Frost and Van Scott (1966), Esterly (1968), and Schnyder (1970) have thoroughly reviewed many of the more important aspects of the various ichthyosiform dermatoses.

In *ichthyosis vulgaris,* the commonest clinical variant, the signs begin at varying times after birth, but rarely in early infancy. Hyperkeratotic scaling on the extensor surfaces of the extremities and trunk is characteristic. A biopsy of the skin shows moderate to very marked hyperkeratosis, with the paradoxical finding of an absent or reduced granular cell layer. The overall thickness of the epidermis is not necessarily increased, and the rete ridges are flat. Follicular plugs are present in some biopsies. A nonspecific perivascular inflammatory infiltrate is often noted in the upper dermis (Wells and Kerr, 1966).

Nonbullous congenital ichthyosiform erythroderma (lamellar ichthyosis) is initially recognized in the newborn period as the so-called collodion baby (Reed et al., 1972; Vandersteen and Muller, 1972). The collodion baby is a clinical presentation not restricted to lamellar ichthyosis. A major problem for the newborn infant with this disorder is thermal regulation. Histologically, hyperkeratosis occurs with a granular cell layer that varies in thickness. Parakeratosis is a less constant feature. In contrast to ichthyosis vulgaris, acanthosis is noted here. The dermal perivascular inflammatory reaction can be quite striking. A lethal variant of nonbullous congenital ichthyosiform erythroderma is the harlequin fetus.

Bullous congenital ichthyosiform erythroderma (epidermolytic hyperkeratosis) presents

Table 1-3. Types of ichthyosis*

Condition	Inheritance	Age of onset	Distribution
Ichthyosis vulgaris	Autosomal dominant	Usually after 3 months of life	1. Forehead and cheeks involved 2. Back more severely affected than abdomen 3. Limbs variably involved 4. Flexures spared 5. Increased palmar and plantar markings
Sex-linked ichthyosis	X-linked; female to male transmission	Birth to 1 year	1. Lateral face, neck, and scalp most severely affected 2. Abdomen more severely involved than back 3. Total involvement of limbs common 4. Flexures variably affected; antecubital fossae and axilla more commonly in childhood, popliteal fossae in adulthood 5. Palms and soles normal
Nonbullous congenital ichthyosiform erythroderma (lamellar ichthyosis)	Autosomal recessive	Birth	1. Upper face more involved than lower face 2. Uniform generalized hyperkeratosis of trunk 3. Limbs show generalized involvement 4. Flexures always affected (dry) 5. Palms and soles affected
Bullous congenital ichthyosiform erythroderma (epidermolytic hyperkeratosis)	Autosomal dominant	Birth to 6 months	1. Lower face more involved than upper face 2. Trunk variably affected 3. Limbs variably affected 4. Flexures always affected (moist) 5. Palms and soles usually affected
Ichthyosis linearis circumflexa	Autosomal recessive	Birth	1. Generalized migratory polycyclic lesions 2. Flexures hyperkeratotic
Erythrokeratoderma variabilis	Autosomal dominant	Birth	1. Face, buttocks, extensor surfaces, and extremities for both hyperkeratotic plaques and erythematous areas

*From Solomon, L. M., and Esterly, N. B.: Neonatal dermatology, Philadelphia, 1973, W. B. Saunders Company.

in the newborn as either a collodion baby or, more typically, as a bullous eruption with an erythrodermatous background. It is therefore necessary to differentiate this disorder from a variety of other bullous conditions in the neonatal period. A skin biopsy is very important because of its diagnostic features. The cells of the middle and upper epidermis show vacuolation of the cytoplasm and intercellular edema that coalesces to form intraepidermal bullae (Fig. 1-2). Peculiar keratohyalin granules are noted in the stratum granulosum. There is also marked hyperkeratosis, a prominent granular layer, acanthosis, and elongation of rete ridges. The dermal changes are restricted to nonspecific chronic inflammation. Similar histologic features are also associated with congenital epithelial nevi and acquired keratoses (Ackerman, 1970).

Sex-linked ichthyosis is diagnosed before 3 months of age, and a collodion membrane may be present at birth. Hyperkeratosis and a prominent granular cell layer are some of the principal microscopic findings. The inflammatory reaction in the dermis is much more intense than that associated with the other

Associated features	Scales	Histology
1. Localized shiny hyperkeratosis of knees and elbows 2. Atopic dermatitis common 3. Family history positive for atopic diseases in a high percentage of cases 4. Keratosis pilaris common	Fine, branny, and white	1. Mild to moderate hyperkeratosis 2. Decreased to absent granular layer 3. Normal rete ridges
1. "Dirty" appearance due to character of scales 2. Only males affected 3. Occasionally have collodion membrane at birth 4. Deep corneal dystrophy on slit lamp examination 5. Normal cellular kinetics	Thick, dark brown, and large	1. Moderate hyperkeratosis 2. Increased granular layer 3. Prominent rete ridges 4. Dermal perivascular infiltrate
1. Background erythroderma 2. Prematurity common 3. Occasionally have collodion membrane at birth 4. Harlequin fetus the most rare and severe 5. Ectropion present and often progressive 6. Increased epidermal mitotic rate	Flat, dark, and large	1. Moderate hyperkeratosis with focal parakeratosis 2. Irregular increase in granular layer 3. Hypertrophic epidermis 4. Dermal perivascular infiltrate
1. Background erythroderma 2. Bullae during infancy and childhood 3. Increased epidermal mitotic rate	Small, yellow, and shotty	1. Marked hyperkeratosis 2. Prominent granular layer 3. Papillomatous, hypertrophic epidermis 4. Vacuolation of epidermal cells with abnormally large keratohyaline granules
1. Background erythroderma 2. Hair shaft abnormalities (Netherton's syndrome) 3. Hyperhidrosis of palms and soles (adults)	White, double-edged scale bordering migratory lesions	1. Hyperkeratosis with focal parakeratosis 2. Acanthosis 3. Dilatation of dermal vessels 4. Mild perivascular infiltrate
1. Areas of discrete mascular erythema, transient and migratory 2. May have thickened palms and soles	Thick, yellow-brown	1. Laminated stratum corneum 2. Focal parakeratosis 3. Prominent granular layer 4. Papillomatosis, irregular acanthosis 5. Elongated papillary capillaries

types of ichthyosis, and is a more consistent feature.

Ichthyosis is not restricted to these conditions alone, but is also found with Rud's syndrome, Sjögren-Larsson syndrome, Netherton's syndrome, and Refsum's syndrome (Rook, 1972).

Epidermal nevus syndrome is represented by three clinical variants: ichthyosis hystrix, nevus unius lateralis, and bilateral linear epidermal nevi (Solomon et al., 1968). Congenital acanthosis nigricans is thought to be a related problem, and there is some clinical and pathologic overlap with the congenital ichthyosiform erythrodermas and nevus sebaceous of Jadassohn. Nevus unius lateralis is recognized at or shortly after birth as linear, verrucous or papillary processes located along the long axis of the extremity. The same configuration and characterization of lesions occur with bilateral linear epidermal nevi. Ichthyosis hystrix, though resembling nevus unius lateralis clinically, has many histopathologic features that relate it to epidermolytic hyperkeratosis; however, a great deal about these disorders remains unanswered.

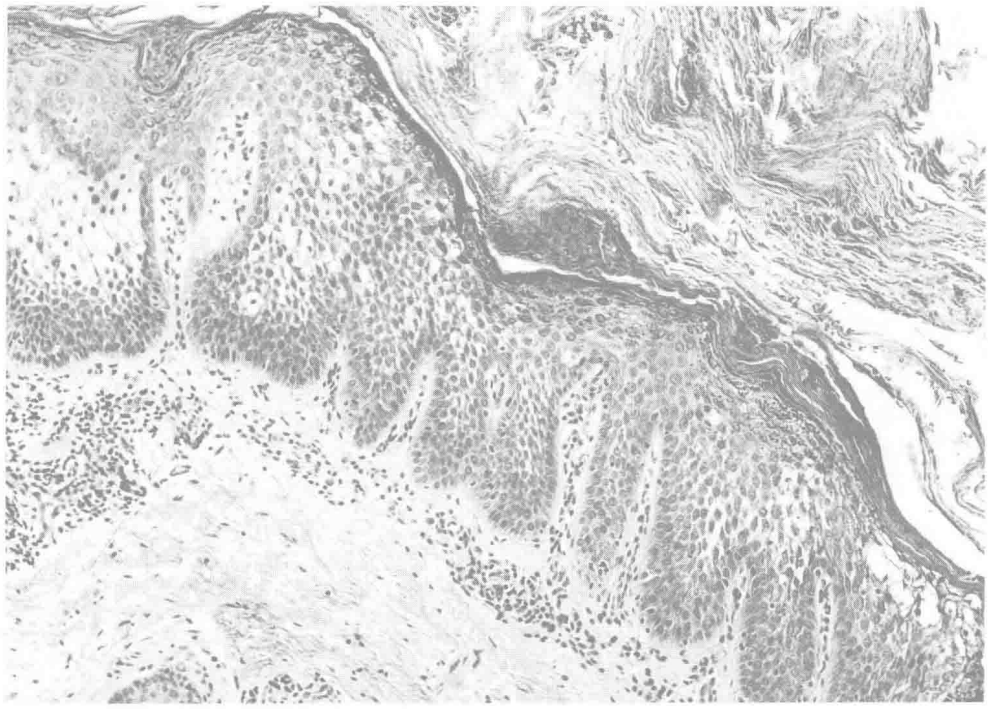

Fig. 1-2. Bullous congenital ichthyosiform erythroderma, or epidermolytic hyperkeratosis, showing hyperkeratosis and the typical vacuolation of the cells in the upper and middle epidermis. (W.U. Ill. 73-2273, ×150.)

Another important clinical feature of nevus unius lateralis is its association with major skeletal, neurologic, and vascular anomalies. Histologically, the nevus unius lateralis may show only marked hyperkeratosis, rarely parakeratosis, a granular layer, and acanthosis. In approximately one-third of the biopsies, vacuolation of the midepidermis as noted in epidermolytic hyperkeratosis can be seen (Solomon et al., 1968).

Keratotic disorders (keratodermas), in addition to those already discussed, often have their early clinical manifestations in childhood. Reed and Porter (1971) have categorized the keratoses into generalized conditions that may or may not include palmar and plantar involvement and those whose major features are limited to the palms and soles. *Palmar-plantar hyperkeratosis* and *periodontal destruction* (Papillon-Lefèvre syndrome) is one example of the latter type of disorder (Giansanti et al., 1973). Hyperkeratosis in the absence of other distinctive findings is noted histologically.

Darier's disease (keratosis follicularis) is an autosomal dominant keratotic disorder with occasional palmar-plantar involvement in addition to the more generalized crusted, hyperkeratotic, yellowish brown papules and masses. The face, neck, and trunk are the sites of predilection. Initial lesions are small follicular papules that later coalesce and are generally recognized between 8 and 16 years of age (Gottlieb and Lutzner, 1973). Suprabasilar lacunae containing acantholytic and dyskeratotic cells, corps ronds, and grains are the major histologic findings. The epidermis is both hyperkeratotic and parakeratotic.

Warty dyskeratoma (isolated keratosis follicularis, focal acantholytic dyskeratosis) has microscopic features very similar, if not identical, to those of Darier's disease. The lesions are clinically solitary and are concentrated in the head and neck region (Tanay and Mehregan, 1969). The youngest patients have been 10 and 13 years old, but most cases occur during the fifth decade of life. In spite of the morphologic likenesses, there is no known relation with Darier's disease.

Porokeratosis is a chronic, progressive