

RESIDENT ROUNDS: PART II

Ichthyosis and Ichthyosiform Dermatoses

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Ichthyosis and Ichthyosiform Dermatoses

Disorder	Inheritance and Gene Defect	Presentation
Ichthyosis Vulgaris	AD Filaggrin	Presents in infancy. Fine, white scales on extensor surfaces; sparing of flexures; hyperlinear and hyperkeratotic palms/soles. Associated with keratosis pilaris and atopy. Histology: Absent granular layer and compact orthokeratosis.
X-Linked Ichthyosis	XLR Arylsulfatase C (steroid sulfatase)	Presents in infancy. Mild erythroderma and large translucent scales that evolve into dark, large scales over extensor extremities and trunk, especially the neck, with sparing of face, scalp, and palms/soles; clearing during summer. Mother with low estrogen in urine and amniotic fluid and low placental sulfatase leading to failure to progress during labor and C-section. Comma-shaped corneal opacities on slit-lamp exam. Cryptorchidism and increased risk of testicular cancer. Histology: Hyperkeratosis or parakeratosis overlying normal or slightly thickened granular layer.
Lamellar Ichthyosis	AR TGM1 gene (transglutaminase deficiency) or ABCA12 (ATP binding cassette A12)	Presents at birth. Collodion membrane with large, thick, dark scale that is quadrilateral, free at the edges, and adherent in the center; prominent flexural involvement along with the palms and soles. Associated with ectropion, eclabium, heat intolerance, scarring alopecia. Histology: Massive orthokeratosis and acanthosis.
Nonbullous Congenital Ichthyosiform Erythroderma (CIE)	AR TGM1 gene or ALOXE3 or ALOX12B (encoding lipoxygenase)	Presents at birth. Collodion membrane with underlying erythroderma and persistent generalized scaling involving flexures, face, palms, and soles. Associated with heat intolerance, scarring alopecia, ectropion. Histology: Parakeratosis, acanthosis, and hypergranulosis.
Bullous Congenital Ichthyosiform Erythroderma (Epidermolytic Hyperkeratosis)	AD Keratin 1 and Keratin 10	Presents at birth. Erythroderma, bullae, denuded skin evolving into warty hyperkeratotic scaling most prominent over joints; variable palmoplantar involvement. Failure to thrive, recurrent skin infections, malodor. Histology: Massive orthokeratosis, hypergranulosis, cytolysis of suprabasal/granular layers, clumpled tonofilaments.

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Ichthyosis Bullosa of Siemens	AD Keratin 2e	Presents at birth. Little to no erythroderma and mild blistering that evolves into brown hyperkeratotic plaques over flexures; spares palms and soles. Histology: Orthokeratosis, acanthosis, and vacuolization of granular cell layer.
Harlequin Ichthyosis	AR ABCA12	Presents at birth. Encasement of hard, thickened, yellow-brown plates of scale with bright red fissures; severe ectropion, eclabium, mitten-like hands and feet; death within a few days of birth due to respiratory difficulties and sepsis. Histology: Thickened and compact orthokeratosis; sweat ducts and hair follicles with hyperkeratotic plug.
Sjögren-Larsson Syndrome	AR FALDH (encoding fatty aldehyde dehydrogenase)	Presents at birth. Erythema and ichthyosis that evolves into dark scales on lower abdomen, flexures, and neck. Spastic ditetraplegia by age 2, mental retardation, perifoveal glistening white dots in ocular fundus. Histology: Orthokeratosis, papillomatosis, and moderate acanthosis.
Netherton Syndrome	AR SPINK5 gene (encodes serine protease inhibitor LEKT1)	Presents at birth. Generalized erythroderma and scaling and +/- collodion membrane; can have either ichthyosis linearis circumflexa (migratory polycyclic patches) or look like CIE. Trichorrhexis invaginata and trichorrhexis nodosa. Atopy; high serum IgE, food allergies, recurrent infections. Increased drug absorption, so avoid topical tacrolimus. Histology: Significant parakeratosis with absent granular layer.
CHILD Syndrome	XLD NSDHL gene (encodes NADPH steroid dehydrogenase-like protein)	Presents at birth. Unilateral erythema with waxy adherent scale that later becomes verrucous. Ipsilateral alopecia, ipsilateral organ hypoplasia, ipsilateral skeletal defects, and stippled epiphyses that resolves during childhood. Histology: Acanthosis and papillomatosis overlying mild superficial perivascular infiltrate.
Chondrodysplasia Punctata	XLD (Conradi Hünermann Happle Syndrome) EBP gene (encoding emopamil binding protein → accumulation of 8(9) cholesterol and 8-dehydrocholesterol)	Presents at birth. Ichthyosiform erythroderma (whorled or linear eggshell-like ichthyosis) leading to hyperkeratosis that is replaced by linear or patchy follicular atrophoderma and ice pick-like scars along Blaschko's lines. Stippled epiphyses that is detected during infancy; cataracts; unilateral cataracts; deafness; scarring alopecia; frontal bossing with flat nasal bridge. Histology: Hyperkeratosis with focal parakeratosis in follicular ostia.
	XR Arylsulfatase E defect	
	AR [Rhizomelic] PEX 7 gene	Presents at birth. Erythroderma and ichthyosis leading to follicular atrophoderma, scarring alopecia, and absent eyebrows or eyelashes. Punctate chondrodysplasia, cleft vertebrate, other skeletal abnormalities, psychomotor retardation with death by 2 years.

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KID Syndrome (Keratitis, Ichthyosis, Deafness)	AD GJB2 gene (encoding connexin 26)	Presents at birth. Symmetric erythematous hyperkeratotic plaques on knees, elbows, and face; perioral leathery plaques. Stippled palmoplantar keratoderma. Congenital sensorineural deafness; vascularizing keratitis; nail and teeth dystrophy; increased risk of oral and cutaneous squamous cell carcinoma. Histology: Acanthosis and papillomatosis with basket-weave hyperkeratosis; follicular plugging.
Refsum Disease	AR PHYH gene (phytanoyl-CoA hydroxylase) or PEX7 gene (peroxisome biogenesis factor 7) → accumulation of phytanic acid	Presents at childhood/adolescence. Mild ichthyosis, cerebellar ataxia, peripheral neuropathy, salt and pepper retinitis pigmentosa, deafness. Treat with dietary restriction of phytanic acid. Histology: Orthokeratosis and lipid-containing vacuoles in basal keratinocytes.
Neutral Lipid Storage Disease	AR ABHD5 (Regulatory defect that alters the synthesis and degradation of phospholipids)	Presents at birth. Generalized fine, white scales with erythema. Myopathy, hepatomegaly, hearing impairment, vacuolated leukocytes. Histology: Several lipid-containing vacuoles in circulating granulocytes, eosinophils, and monocytes.
Trichothiodystrophy (Tay Syndrome, PIBIDS)	AR ERCC2, ERCC3	Presents at birth. Generalized scaling with minimal to no erythema. Photosensitivity, brittle hair/nails, intellectual impairment, decreased fertility, short stature. Histology (polarized light): Light and dark bands in "tiger-tail" pattern.
Erythrokeratoderma variabilis (Mendes da Costa)	AD GJB3 and GJB4 (Connexin 31 and 30.3)	Presents shortly after birth. Bizarrely configured, sharply demarcated erythematous patches that can change shape or size over time + fixed, polycyclic, hyperkeratotic plaques on knees, elbows, extremities, buttocks. Associated with palmoplantar keratoderma. Histology: Orthokeratosis, basket-weave hyperkeratosis, acanthosis with prominent granular layer.

AD, autosomal dominant;
AR, autosomal recessive;
CIE, congenital ichthyosiform erythrodema;
XLD, X-linked dominant;
XLR, X-linked recessive.

DISCLOSURES

The authors have no conflicts of interest to declare.

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