Incontinentia Pigmenti

Dr. L. Y. Chan

Date:	13 October, 1999
Venue:	Yaumatei Skin Centre
Organizer:	Social Hygiene Service, DH; Clinico-pathological Seminar

CASE SUMMARY

History and physical examination

A female baby was delivered by normal spontaneous delivery at 39 weeks gestation. Her birth weight was 3.2 kg and Apgar score was 8 at both 1 and 5 minutes. She was found to have multiple vesicles at birth. The lesions were arranged in lines over all four limbs. This was the second pregnancy of her mother. The first pregnancy resulted in a male miscarriage. Antenatal history was uneventful. There was no history of genital herpes.

Patient's mother, all two maternal aunts, and maternal grandmother also had pigmented lines over the back of their legs. One 18-month-old daughter of her aunt had similar rash as patient. The pedigree is shown in Figure 1. All family members have normal intelligence. There was no history of mental retardation or epilepsy.

Physical examination at day 3 revealed an afebrile, non-toxic looking infant. There was an erythematous papulo-vesicular eruption over her limbs, arranged in linear pattern. Generalised erythematous streaks and whorls were present (Figures 2 and 3). No verrucous

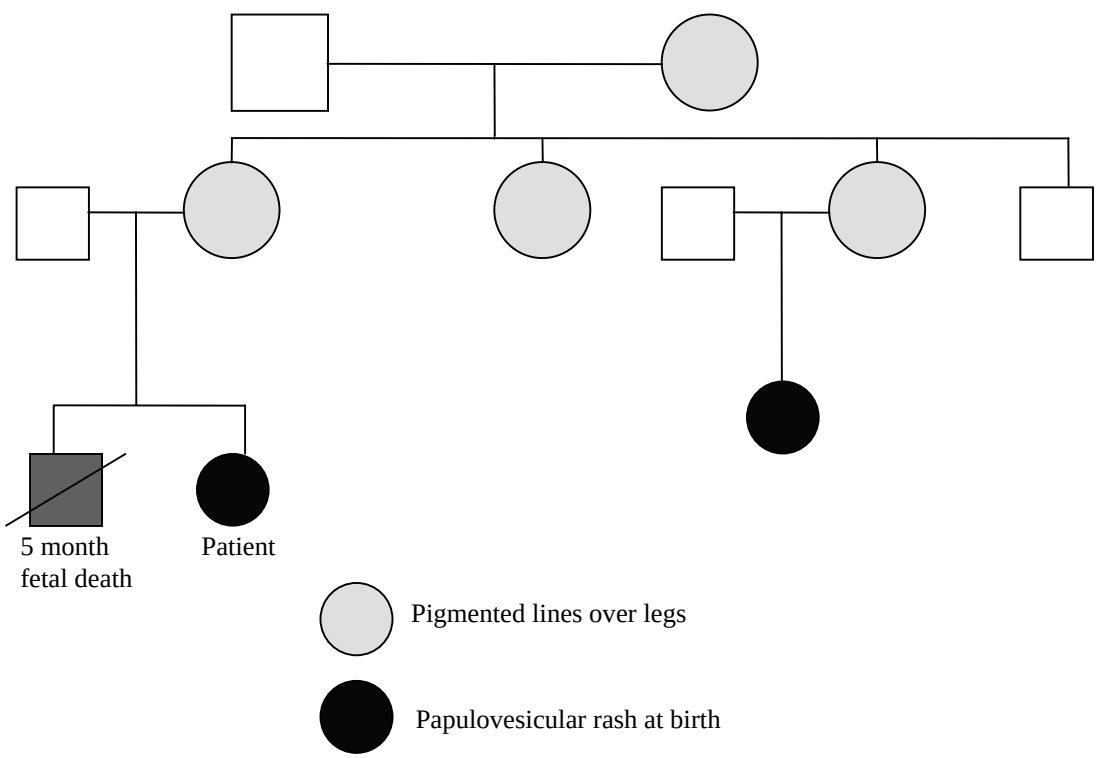

Figure 1: Pedigree of patient's family with features compatible with different stages of incontinentia pigmenti

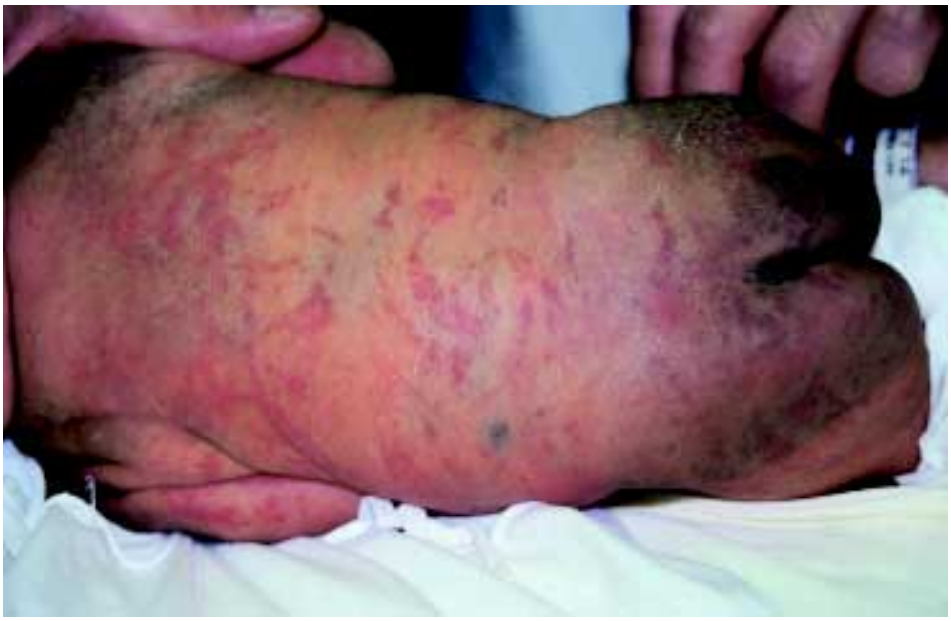

Figure 2: Erythematous streaks and whorls at the back of the 3-day-old infant

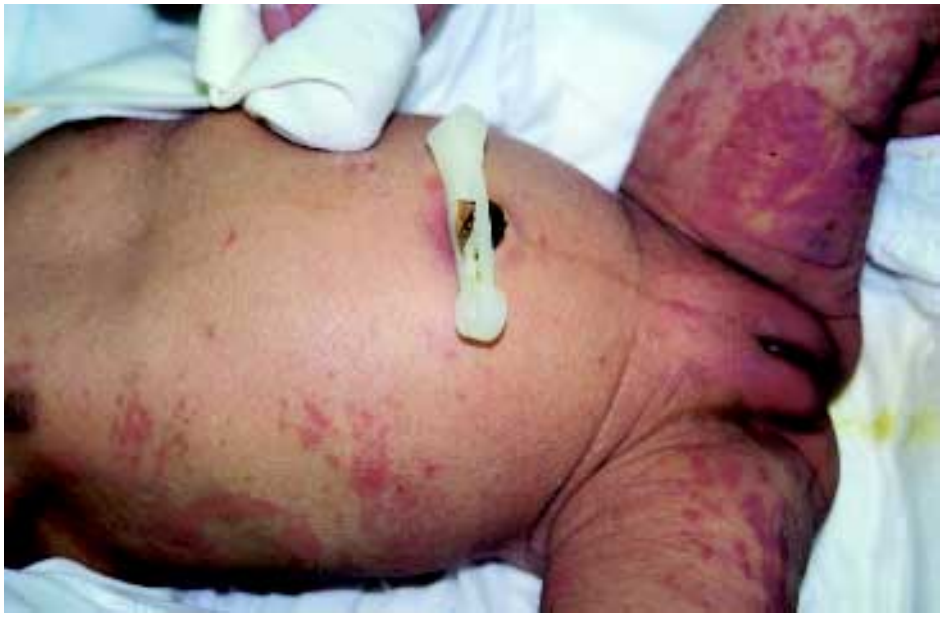

Figure 3: Streaks and whorls were also noted at the legs

lesion was seen. The hair and nail were normal. Examination of patient's mother revealed brownish streaks over back of both legs.

Differential diagnosis included incontinentia pigmenti, epidermolysis bullosa and herpes simplex infection.

Investigation and diagnosis

The complete blood picture was normal. There was no eosinophilia. Blood for viral titre was normal. Skin swab yielded no growth.

Skin biopsy revealed spongiotic vesicles with numerous eosinophils in the epidermis, where there were many dyskeratotic cells. There was a mild superficial perivascular infiltrate of many eosinophils and some lymphocytes in the dermis. No significant acanthosis, hyperkeratosis or papillomatosis was seen.

The final diagnosis was incontinentia pigmenti.

Management and progress

The vesicles and pustules were more prominent at week 2 and topical antibiotic cream was prescribed. Most skin lesions subsided gradually. Only pigmented lines and whorls were seen at 2 months of age.

She was also being followed up by paediatrician and ophthalmologist. There was no extracutaneous involvement. Skull X-Ray and MRI of brain were refused by parents. She was also referred to clinical genetic unit.

REVIEW ON INCONTINENTIA PIGMENTI

Incontinentia pigmenti (IP) is a rare X-linked dominant genodermatosis. The condition is usually lethal in male. The female to male ratio is 35:1. However, only 55% of patients have a positive family history. The other cases may be due to spontaneous mutation.

There are two genotypes. IP-1 represents sporadic cases with translocation between chromosomes X and 5. The affected gene resides on chromosome Xp11. IP-2 represents the familial cases with the gene locus linked to Xq28. However, the IP gene has not yet been isolated and cloned.

Cutaneous features and histological findings of incontinentia pigmenti

Cutaneous manifestations affect about 96% of patients. The striking pattern of normal and abnormal skin is presumed to reflect the clonal proliferation of two genetically different cell types during embryogenesis of the skin. Cellular mosaicism occurs in 46, XX females because of the random inactivation of one X chromosome (lyonization). The four different stages of IP are shown in Table 1.[1]

Overlap of stages 1, 2 and 3 can occur. Although the verrucous lesions usually occur in the same location as the vesicles, the subsequent hyperpigmentation does not necessarily correspond to the site of earlier lesions. Stage 3 lesions usually follow the lines of Blaschko.

Systemic manifestation of incontinentia pigmenti

Apart from skin, other tissues arising from neuro-ectoderm may also be affected and they are summarised in Table 2.[1,2]

Table 1. Clinical morphology and pathologic changes in different stages of incontinentia pigmenti

Stages	Clinical morphology	Pathologic changes
1. Vesicular (birth to 1-2 wks)	Linear vesicles, pustules, and bullae with underlying erythema	Eosinophilic spongiosis, intra-epidermal vesicles, and dermal infiltrate
2. Verrucous (2-6 weeks)	Warty, keratotic papules and plaques	Eosinophilic dyskeratosis of keratinocytes, hyperkeratosis, acanthosis, and papillomatosis
3. Hyperpigmented (3-6 months)	Macular hyperpigmentation in a whorled pattern	Dermal melanophages and vacuolar alteration of the epidermal basal layer
4. Hypopigmented (2nd - 3rd decade)	Hypopigmented streaks and / or patches; cutaneous atrophy may be present	Absence of skin appendages, mild epidermal atrophy, and decreased, normal, or small melanocytes

Table 2. Neuro-ectodermal derived tissues apart from skin that are affected in incontinentia pigmenti

Organ	Frequency (%)	Common manifestations
Dental	65->80	partial anodontia, delayed dentition, conical or pegged teeth, impactions
Hair	38-50	vertex alopecia, wooly hair nevus, eyelash and eyebrow hypogenesis
Eyes	35-40	strabismus, cataracts, optic atrophy, micropthalmos, retinal pigmentation and detachment
Nails	7-40	onychogryphosis, pitting, ridging
Central nervous system	10-31	seizures, spastic paralysis, microcephaly, mental and motor retardation
Skeletal	14	scoliosis, skull deformities, spina bifida, congenital hip dislocation, dwarfism
Malignancy		retinoblastoma, Wilm's tumour, acute myeloid leukaemia, rhabdomyosarcoma

Differential diagnosis

The differential diagnoses depend on the stages. These are listed in Table 3.

Table 3. Differential diagnoses of different stages of incontinentia pigmenti

Stages of IP	Differential diagnosis
Vesicular stage	· Epidermolysis bullosa · Bullous impertigo · Congenital varicella, herpes simplex infection · Congenital syphilis
Verrucous stage	· Epidermal naevus
Hyperpigmented stage	· Linear and whorled nevoid hypermelanosis · Focal dermal hypoplasia
Hypopigmented stage	· Hypomelanosis of Ito · Focal dermal hypoplasia · Segmental vitiligo

Treatment

The patient should be jointly managed by dermatologist, paediatrician, ophthalmologist and dentist (once dentition begins).The main role of dermatologist is to confirm the diagnosis and to manage the skin condition. Genetic counseling and prenatal diagnosis in subsequent pregnancy is also important. However, the gene remains unidentified yet. DNA analysis may be available in future.[2] Fetal skin biopsy is not advisable at the moment because the gestational age at which diagnostic changes become apparent are not well defined. Also, the localised expression of the disease may lead to a false negative result.

Male with incontinentia pigmenti

There are several possible explanations of IP in male.[3,4] The patients may have Klinefelter syndrome (47, XXY karotype) or 46, XY/47, XXY mosaicism. For the normal 46, XY male, it may be due to either half chromatid mutation or genetic heterogeneity. Half chromatid mutation is mutation of the IP gene on one of the two X chromatids after X chromosome has replicated, but before segregation. Theoretically, these male would have a mosaic of two different populations of cells: one group with a normal X chromosome and a second population with a mutated IP gene. Genetic heterogeneity is the gene mutation presenting as IP but not inherited in an X-linked dominant fashion.

Learning points:
Incontinentia pigmenti is a rare X-linked dominant genodermatosis affecting female infants usually. Extracutaneous manifestation may be present. Genetic counseling is important.

References

1. Cohen PR. Incontinentia pigmenti. Clinicopathologic characteristics and differential diagnosis. Cutis 1994;54:161-6.
2. Basarab T, Dunnill MG, Munn SE, et al. Incontinentia pigmenti: variable disease expression within an affected family. J Eur Acad Dermatol Venereol 1998;11:73-6.
3. Emery MM, Siegfried EC, Stone MS, et al. Incontinentia pigmentia: transmission from father to daughter. J Am Acad Dermatol 1993;29:368-72.
4. Prendiville JS, Gorski JL, Stein CK, et al. Incontinentia pigmenti in a male infant with Klinefelter syndrome. J Am Acad Dermatol 1989;20:937-40.