

# Incontinentia Pigmenti Associated with Congenital Heart Diseases

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Incontinentia pigmenti(IP) is an X-linked dominantly inherited disorder with female predominance. Skin lesions are characterized by three or four stages ; vesicobullous, verrucous, hyperpigmented and hypopigmented lesions. About 80% of patients with incontinentia pigmenti have one or more associated ectodermal or mesodermal anomalies involving teeth, nail, hair, eye, breast, bones and nervous system.

A newborn girl had erythematous based vesicles and bullae on her trunk and extremities with peripheral eosinophilia. Within several days, she showed linear verrucous plaques. A skin biopsy specimen showed eosinophilic spongiosis in the epidermis and numerous eosinophils in the dermis. The diagnosis of IP was made. She was revealed to have some congenital heart anomalies ; atrial septal defect (ASD) and patent ductus arteriosus(PDA).

Cases of IP with congenital heart disease have been reported very rarely. Therefore, we report this unique case of IP associated with ASD and PDA.

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*Key Words* : Incontinentia pigmenti, Congenital heart disease.

Incontinentia pigmenti(IP) is an unusual genodermatosis occurring almost exclusively in female patients<sup>1-7</sup>. IP is characterized by swirling hyperpigmented skin lesions and is associated with a high incidence of systemic defects. Skin lesions may have three (vesicles and pustules, verrucous and warty lesions, and hyperpigmented lesions) or four (hypopigmented lesions) stages<sup>1-6</sup>. Extracutaneous manifestations occur in 70 to 80 percent of patients. Most commonly involved are the central nervous system, the eyes, the bones, and the teeth<sup>1-7</sup>. Other structural defects such as cardiac abnormalities may occur at a frequency of less than 2 percent. Herein, we report a case of IP with congenital heart diseases. We review the cutaneous features and their pathological changes, and the disease-associated systemic manifestations of IP

## CASE REPORT

A 3-day-old female was evaluated for erythematous patches and vesicobullous lesions on the trunk and extremities that developed at birth. The patient had multiple, erythematous based, vesicobullous lesions on the trunk and extremities. They showed linear distribution on the upper extremities and whorled pattern on the trunk. A few days later, some of the vesicobullous lesions changed into pustules(Fig. 1). Several days later, most of the skin lesions changed into linear verrucous plaques(Fig. 2).

The patient was a full term baby and weighed twenty-nine hundred gram. Her Apgar scores at 1 and 5 minutes were 9 and 10, respectively. A physical examination revealed a systolic murmur at the left sternal border, but her general appearance was healthy and alert. A skin biopsy specimen was taken from the right abdomen on the 7th day after birth. It showed eosinophilic spongiosis in the epidermis and numerous eosinophils in the dermis(Fig. 3). Laboratory studies, including a complete blood count, urine analysis, CRP, VDRL, blood culture, urine culture, and TORCH test were within normal

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**Fig. 1.** At 7 days of age, she had erythematous based, vesicles and pustules on the trunk and upper extremities. They showed linear distribution on the upper extremities and whorled patterns on the trunk.

**Fig. 2.** On the 13th day after birth, most of the skin lesions changed into linear verrucous plaques.

**Fig. 3.** The epidermis showed eosinophilic spongiosis and the dermis showed marked eosinophilic infiltration.

**Fig. 4.** At 1 year of age, the vesicular and verrucous skin lesions had completely disappeared and she had hyperpigmented lesions on the trunk and extremities.

**Fig. 5.** At 1 year of age, a follow-up color doppler echocardiogram showed PDA but ASD had spontaneously closed.

limits or negative except for peripheral eosinophilia (WBC count : 16,400/mm<sup>3</sup>, eosinophil : 16%). A chest roentgenogram was insignificant. An electrocardiogram showed right atrial enlargement and right ventricular hypertrophy. A doppler echocardiogram showed a patent ductus arteriosus(PDA) and an atrial septal defect(ASD). According to clinical, histopathological and laboratory findings, we made the diagnosis of IP and congenital heart diseases. There was no familial history of similar skin le-

**Table 1.** Clinical and pathological features of incontinentia pigmenti<sup>4</sup>

Stage	Clinical morphology	Pathological changes
Vesicular	Linear vesicles, pustules, and bullae with underline erythema	Eosinophilic spongiosis, intraepidermal vesicles, and dermal infiltration
Verrucous	Warty, keratotic papules and plaques	Eosinophilic dyskeratosis of keratinocytes, hyperkeratosis, acanthosis, and papillomatosis
Hyperpigmented	Macular hyperpigmentation in a swirled pattern	Dermal melanophages, and vacuolar alteration of the epidermal basal layer
Hypopigmented	Hypopigmented streaks and /or patches; cutaneous atrophy may be present	Absence of skin appendage, mild epidermal atrophy, and decreased, normal or small melanocytes

**Table 2.** Systemic manifestations of incontinentia pigmenti<sup>4</sup>

Organ system	Frequency of involvement(%)	Common manifestations
Dental	65~80	Anodontia, delayed eruption of teeth, hypodontia, impaction, and malformation of the crowns
Hair	38~50	Thin or sparse hair, and alopecia (especially at the vertex)
Eyes	35~40	Amblyopia, avascularity in the peripheral temporal retina, cataract, retinal detachment, strabismus, and optic nerve atrophy
Nails	7~40	Onychogryphosis, pitting, ridging, and subungual keratotic tumors
Central nervous system	10~31	Convulsive disorders, mental retardation, microcephaly, motor retardation, nystagmus, and spastic paralysis
Breast*	1	Aplasia, hypoplasia, hypoplasia of nipple, and supernumerary
Skeletal and structural	14	Chondrodysplasia, cleft palate or cleft lip or both, club foot, congenital hip dislocation, dwarfism, ear anomalies, hemiatrophy, skull deformities, spina bifida, and congenital cardiac anomalies

\*The incidence of breast anomalies was at least ten times greater than the incidence in the general population<sup>6</sup>.

sions or congenital heart anomalies. She was a first baby of her parents and examination of the infant's mother did not reveal any IP-associated stigmata.

We gave her conservative management for the skin lesions and recommended a regular observation for congenital heart disease by a pediatrician. At a follow-up examination 1 year later, the vesicular

and verrucous skin lesions had disappeared and the patient had only linear hyperpigmented patches on the trunk and extremities (Fig. 4) and her dentition was within the normal range and other congenital anomalies were not detected. A follow-up color doppler echocardiogram revealed spontaneous closure of ASD but PDA had still persisted (Fig. 5).

## DISCUSSION

Skin lesions of IP are characterized by three stages: vesicular, verrucous, and swirled hyperpigmentation. In some patients with IP, a fourth stage occurs as the pigmented lesions fade: hypopigmented streaks and/or patches that appear with or without cutaneous atrophy<sup>2,4,6</sup>. At birth, lesions of any one of these stages (or more than one stage) may be observed in a newborn<sup>4,6</sup>. Each of the clinical stages of IP may be characterized by specific histological findings (Table 1)<sup>4,5</sup>. The skin lesions of the first stage develop within the first few weeks of life and clear completely by four months. They occur anywhere on the body but usually spare the face. The hyperkeratotic lesions of stage 2 usually appear on the distal limbs. Sometimes these lesions may not occur. They clear completely by six months in over 80% of cases. Stage 3 is, classically, the hallmark of IP but its presence, timing and extent are variable. This hyperpigmentation, in general, gradually appears sometime after the blisters have disappeared and fades by the end of second decade<sup>4,6</sup>. Although the hyperkeratotic lesions usually occur in the same location as the vesicles, the subsequent hyperpigmentation often appears in a random distribution that does not necessarily correspond to the site of earlier lesions<sup>4,6</sup>. These hyperpigmented lesions are more often apparent on the trunk than the limbs and occur in streaks or whorls which respect Blaschko's lines<sup>6</sup>. In our case, the skin lesions of stage 1, 2, and 3 appeared on her trunk and extremities and occurred in the same location. The typical lesions of the fourth stage seen in adults and adolescents with IP are pale, hairless patches or streaks best seen on the lower leg<sup>2,4,6</sup>. In our case, vesicular and pustular lesions had appeared since birth, and verrucous lesions began to appear at two weeks of age. At 1 year of age, the skin lesions of stage 1 and stage 2 had completely disappeared and she had hyperpigmented lesions on the trunk and extremities. A common laboratory finding in newborns with IP is peripheral eosinophilia<sup>4,7</sup>. Our patient's eosinophil count increased to 2624/mm<sup>3</sup> 7 days after birth.

About 80% of all patients with IP have one or more associated ectodermal or mesodermal anomalies (Table 2)<sup>4,7</sup>. Disease-associated systemic manifestations may be presented at birth, or occur subsequently, in patients with IP<sup>4,5</sup>. Among these, the

teeth, the hair, the eyes, the nails, and the central nervous system are most commonly involved<sup>4,7</sup>. Other skeletal and structural anomalies, such as skull deformities, dwarfism, ear anomalies, congenital heart diseases, have been reported in about 13.7% of IP patients<sup>5</sup>. Carney<sup>1</sup> had reported a case of IP with congenital heart disease in 1951. A recent review showed that congenital heart diseases occur at a frequency of less than 2% of patients with IP<sup>7</sup>. Some claimed that congenital heart diseases and other structural anomalies have been too variable and too infrequent to be regarded as more than chance associations with IP<sup>8</sup>. We think that congenital heart diseases in patients with IP may go undetected. This is because many cases of congenital heart diseases may be asymptomatic when IP is diagnosed.

On the other hand, similar to ataxia-telangiectasia and Fanconi's anemia, IP has recently been classified as a chromosomal instability syndrome<sup>9</sup>. Therefore, the patients with this genodermatosis may be at an increased risk of cancer<sup>10</sup>. As of 1988, eight malignancies have been reported in six young children (each less than three years of age) with IP: acute myelogenous leukemia, bilateral Wilms' tumor, malignant rhabdoid tumor of the kidney, and retinoblastoma (two patients). The sixth patient had a paratesticular rhabdomyosarcoma, acute myelogenous leukemia, and Wilms' tumor in a horseshoe-shaped kidney<sup>9</sup>.

Up until now, many cases of IP and its associated abnormalities has been reported. However, IP with congenital heart disease has been reported very rarely<sup>1,7</sup> and to date, not in the Korean literature. Therefore, we report this unique case of IP with congenital heart diseases (ASD and PDA).

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