

CASE REPORT

Incontinentia Pigmenti in a Malaysian child

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ABSTRACT

Incontinentia pigmenti (IP) is a rare genodermatological disorder, that is X-linked dominant and almost always invariably lethal in males. The condition is often missed and overlooked. We present the case of an 18-month-old female with IP

Keywords: Incontinentia pigmenti, Ventricular septal defect, Genodermatosis

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INTRODUCTION

Incontinentia pigmenti, also known as Bloch-Sulzberger syndrome, was first described by Bardach, Siemens, Bloch, and Sulzberger (1) although the latter two names are featured in the syndrome. It is a rare disorder with an estimated prevalence at birth of 0.7 per 100 000 (2). IP is X-linked dominant with lethality in males, although, there are case reports of males with IP usually because of mosaicism, hypomorphic alleles, and also those with Klinefelter syndrome (1, 2, 3). It is a neuroectodermal disorder, with characteristic skin lesions. It is thought to be due to a mutation of NEMO (NF-kappa-B essential modulator) also known as IKK- γ /IKBKG (inhibitor of nuclear factor appa-B kinase subunit gamma) gene which is located on chromosome Xq28 (2, 3, 4). Diagnostic criteria had been suggested for this genodermatosis based on Landy and Donnai (1) (Table I).

The skin manifestations are usually present in 100% of the cases and hence become the hallmark of this disorder, forming a major criteria, and undergoes various evolution stages: Stage 1 being the presence of vesiculo-bullous lesions that follow along the lines of Blaschko (usually seen in the neonatal period), in stage 2 which appears after a variable period of time ranging from months to years from Stage 1, these vesicobullous lesions change to become verrucous and then hyperpigmentation in Stage 3, and finally in adolescence, these hyperpigmented lesions become atrophic and pale (stage 4).

This genodermatosis is known to affect multiple organ systems. These are used to form its minor criteria. Teeth

Table I: Diagnostic criteria for incontinentia pigmenti (adapted from 1, 5)

Major criteria	Minor criteria
Typical IP skin stages distribute along Blaschko's lines:	Dental involvement
Vesiculo-bullous stage	Multiple male miscarriages
Verrucous stage	Central nervous system involvement
Hyperpigmented stage	Alopecia
Atrophic/hypopigmented stage	Woolly hair/abnormal nails
	Retinal disease
	Palate anomalies
	Nipple and breast anomalies

Conditions for establishing IP diagnosis

If no evidence of IP in a first-degree female relative:
If lacking genetic IKBKG mutation data, at least two or more major criteria or one major and one or more minor criteria are necessary to make a diagnosis of sporadic IP
In the case of confirmed IKBKG mutation typical for IP any single major or minor criterion is satisfactory for IP diagnosis

Evidence of IP in a first-degree female relative:
Any single major or at least two minor criteria
In all cases eosinophilia and skewed X-chromosome inactivation supports diagnosis

and central nervous system (CNS) defects are the next most common associations that are seen with IP, with CNS defects ranging from developmental delays and seizures to more complex ones with brain malformations (2, 5). Other case reports reveal that there may be involvement of the heart (4), and immunologic systems (2, 5) although these appear less often.

CASE REPORT

We would like to report a case of IP that was not diagnosed till she came to our attention at the age of eighteen months because of a second episode of febrile seizures that brought her to a hospital that we visited. She had been seen in two major hospitals at least, because of her associated problems of having congenital heart disease, namely a ventricular septal

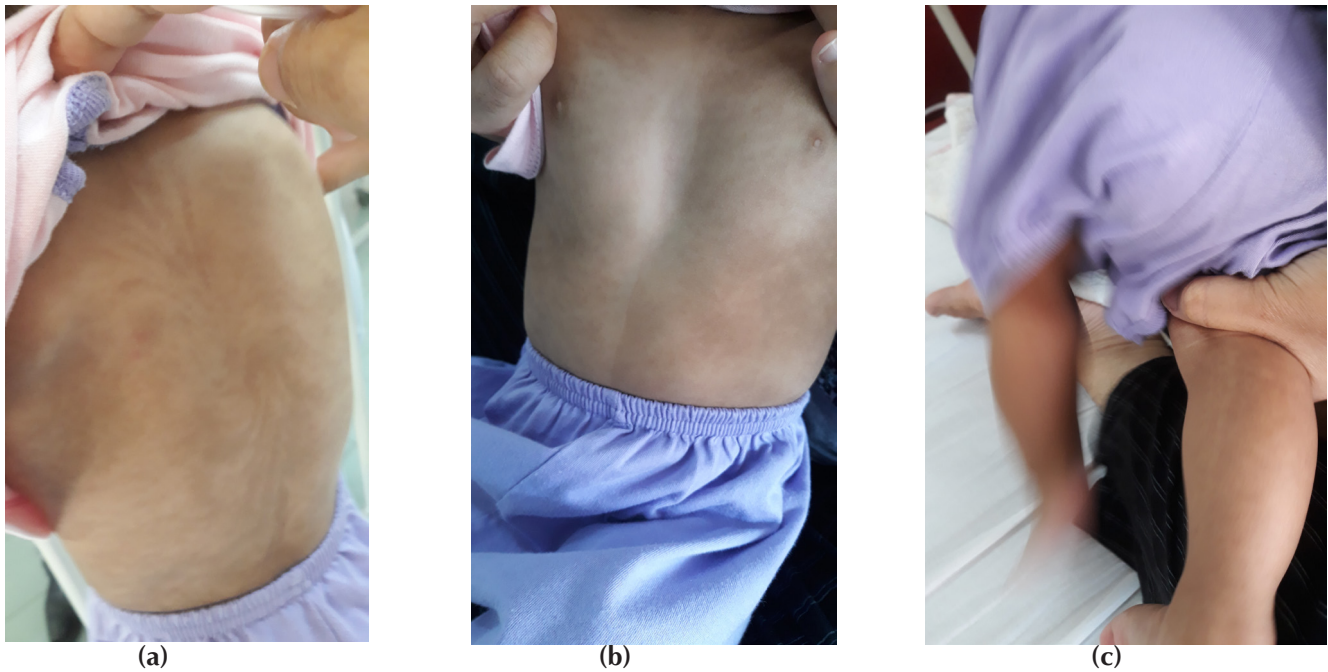


Figure 1: (a). Whorled hyperpigmentation along the lines of Blaschko on the back of the child. (b) Verrucous lesions and hyperpigmentation lines seen on the chest. (c) Leg of patient showing stage 4 IP skin lesion – hypopigmented linear streaks

defect (VSD) which was perimembranous in position, and also developmental delay with peg-shaped teeth.

When we managed to examine her, besides her pansystolic murmur that could be heard all over her praecordium, she had skin lesions that were noted as in Figures 1(a-c). Consent was obtained from her parents to document these via photographs. At the time, her skin lesions were mainly stage 3, with some at stage 2 (mainly a few verrucous lesions still present on her chest). Her mother had been previously told that these were normal scarring lesions from the vesicobullous eruptions noted at birth. Despite not having a proper explanation nor a proper diagnosis, her parents had accepted her condition as having scarring. Her mother also notes that she is slower in terms of neurodevelopment compared to her siblings, specifically speech and walking.

Although we would have liked to perform investigations to proof our diagnosis, this was not possible at the district hospital, so she was referred back to one of the major hospitals that saw her for congenital heart disease, with the diagnosis and plan written for the child.

DISCUSSION

IP is a rare genodermatosis, and for which there is 1 previous case report (5) originating from Sarawak of this disorder, and there were cases seen by one of the authors previously. Because this case and others similar to her that had been missed, this genetic disorder may be underreported. We highlight this case as a case example so that such cases may be brought to the attention of doctors who may care for such children. As mentioned previously, the hallmark of this disorder

are the skin lesions which go through various stages and may be falsely diagnosed as other conditions. In the case mentioned, her parents related that they were told at birth, that it could represent an infection or a skin condition, that blistered upon pressure. Because there was no recourse to her medical notes at the two different hospitals where she was previously seen, we could not confirm nor deny what was actually told to her parents, but they were never told of it being a genetic disorder that was X-linked. Incidentally, the discharge letters from these major hospitals, mentioned that she was treated for bullous impetigo and possibly staphylococcal scalded skin syndrome, without any reference to this being IP.

Because IP is a multisystem disorder, it becomes important to recognise this condition, so that optimal care can be provided for the patient. In this case, the patient suffers from seizures, which at this time occurs with fevers, she also has abnormal dentition, delayed development (4) and congenital heart disease that had been previously reported as being associated with IP (4). Retinal involvement may be present and should actively be searched for in these cases. It has been reported as occurring in about 35 to 77% of cases, with it being mainly unilateral, and the most devastating of which is a retrolental mass with retinal detachment (5). Hence, it is vital to recognize IP so that optimal multidisciplinary care can be afforded to these individual patients.

CONCLUSION

This child illustrates the need for a proper diagnosis and care for this rare genodermatosis (IP) that should be seen by a multidisciplinary team in a tertiary hospital, because

of the possible problems that may present in such cases, hence recognition of this rare disorder is important and crucial for the proper care of such patients.

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REFERENCES

1. Landy S J, Donnai D. Incontinentia pigmenti (Bloch-Sulzberger syndrome). *J Med Genet* 1993; 30: 53 – 59.
2. Shastry B S. Mini review: Recent progress in the genetics of Incontinentia Pigmenti (Bloch-Sulzberger syndrome). *J Hum Genet* 2000; 45: 323 – 326.
3. Chung W K, Lee D W, Chang S E, Lee M W, Choi J H, Moon K C. A case of Incontinentia Pigmenti associated with multi-organ abnormalities. *Ann Dermatol (Seoul)* 2009; 21 (1): 56 – 59.
3. Minic´ S, Trpinac D, Obradovic´ M. Incontinentia pigmenti diagnostic criteria update. *Clin Genet* 2014; 85: 536–542
5. Wahiduzzaman MD. Incontinentia Pigmenti involving only the skin. *J Medicine* 2009; 10: 25 - 27.