A 7-year-old female child of incontinentia pigmenti presenting with vitreous hemorrhage

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Incontinentia pigmenti (IP) is a rare disease with multisystemic anomalies, which commonly presents just after birth. Here, we report a rare case of IP patient with vitreous hemorrhage in school-age children. Therefore, physicians have to be alert and evaluate IP patients at all ages. Regular ophthalmic follow-up is necessary, and fluorescein angiography should be performed if peripheral ischemia or neovascularization is suspected. The effect of peripheral laser ablation on peripheral retinal nonperfusion is not clear and merits further study.

Key words: Incontinentia pigmenti, retinal avascularity, vitreous hemorrhage

Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_560_16

Incontinentia pigmenti (IP), also known as Bloch-Sulzberger syndrome, is a rare genodermatosis with an estimated prevalence at birth of 0.7/100,000. IP is an X-linked dominant disorder and is usually lethal in males. IP is caused by a mutation of the nuclear factor-κB essential modulator (NEMO) gene, and a deletion of exons 4–10 is found in nearly 80% of IP patients. This multisystemic disease affects the skin and other tissues. Skin manifestations, which follow Blaschko lines, are considered the main diagnostic criteria for IP according to Landy and Donnai.[1] Minic *et al*. presented the updated IP diagnostic criteria,[2] with major ones being the stages of IP

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Manuscript received: 15.07.16; Revision accepted: 02.05.17

Cite this article as: Huang SY, Chen LJ, Chiu SC. A 7-year-old female child of incontinentia pigmenti presenting with vitreous hemorrhage. Indian J Ophthalmol 2017;65:533-5.

skin lesions and minor ones including dental, ocular, and other tissues anomalies [Table 1].[2]

Case Report

A 7-year-old female child presented with blurred vision of the left eye suddenly happening 2 days before the visit. Her visual acuity with correction was normal on the right eye (20/25) but only light perception on the left eye. Anterior segments were normal. Vitreous hemorrhage of the left eye was found with blurred fundus, and ultrasound did not show retinal detachment (RD). She denied trauma, and there was no sign of ocular injury. Fundus examination of the right eye found some peripheral avascular areas of retina.

Tracing her history, IP was diagnosed when she was a baby. She was born at 37 weeks' gestational age, via cesarean delivery, without specific pre- or peri-natal history. At the time of birth, she presented with diffuse skin rash and vesicles on axillary area, inguinal area, and upper and lower limbs. Blood examination showed leukocytosis (white blood cell [WBC]: 25,050/μl) with eosinophilia (10%). Skin biopsy from trunk showed the features consistent with those of early-stage IP. Gene analysis presented exons 4–10 deletion of the NEMO gene. Her mother also had the same mutation. Ophthalmic examination was not performed at that time. Cranial ultrasound showed subdural effusion at 4 months old, but subsequent brain computed tomography at 2.5 years old was normal. No seizure had ever happened. While she was getting older, hyperopia and amblyopia were diagnosed. She never had fundus examination until this time.

According to her IP history and the findings of right fundus, IP-related vitreous hemorrhage of the left eye was highly suspected. Vitreous hemorrhage decreased 3 days later. Fluorescein angiography presented obvious peripheral nonperfusion and neovascularization of both eyes [Fig. 1a-d]. After further reduction in vitreous hemorrhage, fibroproliferation with focal tractional RD (TRD) of the left eye was noted [Fig. 1e]. Therefore, retinal laser photocoagulation was advocated for both eyes. Finally, her visual acuity with correction of the left eye improved to 20/40. Spectacle with correction of hyperopia was administered and therapy for amblyopia continued. After follow-up for 15 months, the vision remained stable without new vitreous hemorrhage, progression of RD, or other complications.

Discussion

Etiology of IP in this case is familial. Her mother has the same NEMO gene defect. This 7-year-old female child had typical IP skin changes of the vesiculobullous stage when she was a newborn baby. IP diagnosis was established on the basis of typical skin manifestations with NEMO mutation. Moreover, she had eosinophilia (10% of WBCs) initially. Few years later, amblyopia and retinopathy were noted. According to the updated IP diagnostic criteria,[2] she met one major and one minor criteria with NEMO mutation. Clinical expressions of IP vary from person to person. Her mother had the same NEMO mutation without ocular problems.

Ophthalmologic abnormalities including retinopathy are present in approximately one-third of IP patients (range: 20%–77%),[3-5] which could result in severe visual loss. Ocular findings previously reported include nystagmus, amblyopia, strabismus, microphthalmos, corneal changes, pigmentation of the conjunctiva, cataract, optic atrophy, vitreous hemorrhage, retinal avascularity, and RD. Retinopathy is an important cause which results in vision loss of IP patients. Retinal avascularity or neovascularization is a common retinal finding. Based on the similarities to retinopathy of prematurity, familial exudative vitreoretinopathy, sickle cell disease, and Eales disease, laser ablation has been advocated for peripheral ischemic retina or neovascularization.[4] RD is the most severe ocular manifestation of IP. A bimodal distribution of RDs was observed.[5] TRDs were seen in younger patients (age 2 weeks to 2.5 years) and more severe with poor surgical prognosis. Rhegmatogenous RDs (RRDs), with all cases occurring at 14 years or older, were successfully treated with either surgery

Table 1: Incontinentia pigmenti diagnostic criteria update

Major criteria	Minor criteria
Typical skin manifestations distributed along Blaschko's lines	Ocular abnormalities
Stage 1: Vesiculobullous stage	Central nervous system abnormalities
Stage 2: Verrucous stage	Dental abnormalities
Stage 3: Hyperpigmented stage	Alopecia
Stage 4: Atrophic/ hypopigmented stage	Abnormal hair (sparse hair, wooly hair, anomalies of eyebrows and eyelashes)
	Abnormal nails
	Palate anomalies
	Nipple and breast anomalies
	Multiple male miscarriages
	Typical skin pathohistological findings

*Conditions for establishing IP diagnosis: (1) Family history (−), NEMO gene mutation (−): At least 2 or more major criteria or one major and one or more minor criteria (sporadic IP). (2) Family history (−), NEMO gene mutation (+): Any single major or minor criterion. (3) Family history (+): Any single major or at least two minor criteria (4) In all cases, eosinophilia and skewed X-chromosome inactivationsupport diagnosis.[2] IP: Incontinentia pigmenti, NEMO: Nuclear factor-κB essential modulator

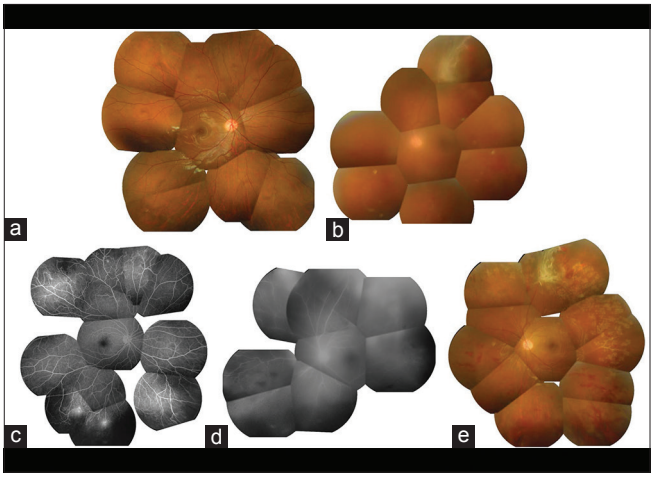

Figure 1: Color fundus and fluorescein angiography. Color fundus: right (a) and left (b) eye. Fluorescein angiography: right (c) and left (d) eye. Fluorescein angiography showed nonperfusion and neovascularization of both eyes. (e) Fibroproliferation with focal tractional retinal detachment of the left eye was noted

or laser. It remains uncertain whether peripheral laser ablation prevents RD later. Several reports have described the efficiency of laser ablation in halting the fibrovascular proliferation and reducing the risk of RD, but in some cases, laser ablation failed to prevent RD.[4,6] This 7-year-old child had TRD, not RRD, with good result after laser photocoagulation. Pediatric vitreous hemorrhage may have multiple etiologies, but manifest and occult trauma is most common. If a child has vitreous hemorrhage without trauma, physicians should take history and examine both eyes carefully.

Owing to the early onset of retinopathy and the potential for quick progression to TRD, all babies suspected of having IP should be screened as soon as possible to detect peripheral retinal vascular changes.[3,4,6] The extent of peripheral nonperfusion or neovascularization may be difficult to recognize clinically; therefore, the ophthalmologic examination for infants should preferably be performed under general anesthesia. Early fluorescein angiography provides the angiographic evidence of peripheral retinal ischemia and thus predicts the severity of retinopathy. Previous reports suggested that retinal examination should be every 2 weeks to 1 month for 3 months and then every 1–3 months until 1 year old. Follow-up interval may be biannually until 2–3 years old and increased to every 6–12 months after 2 years. Given the lifelong risk for RD, patients should be monitored throughout adulthood and be warned of the symptoms of retinal tear or detachment.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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