Piebaldism with a Variant Gene

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Piebaldism is patchy areas of depigmentation on the skin, most frequently on the forehead (producing a white forelock), ventral trunk, elbows, and knees. It is a rare autosomal dominant condition, caused by mutations in the cell-surface receptor tyrosine kinase gene (KIT). Piebaldism must be differentiated from other pigmentation disorders, such as vitiligo, nevus depigmentosus, and Waardenburg syndrome.

We present a preterm baby boy born at 32^{+} weeks due to antepartum hemorrhage. The birth weight was 1.85 kg. The baby was found to have a white forelock (Piebaldism) and gray eyebrows and eyelashes. His neonatal course was complicated by mild respiratory distress syndrome which was managed by one-day intubation and assisted ventilation (on PTV mode). The gene panel revealed that the baby carries in exon 16 of KIT the variant of uncertain significance c.2318C>T p.(Ser773Phe) in heterozygous state.

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The term "piebaldism" originated from magpie (pie) which is a bird with black and white feathers and bald eagle (bald), a USA national bird that has white feathers[1]. It is a rare autosomal dominant condition of pigmentation that is characterized by complete lack of melanocytes in certain areas of the skin and hair. The precise prevalence of piebaldism is not well known, but approximately less than 1 in 20,000 children are born with this condition[2]. It is characterized by a wedge-shaped or a diamond-like depigmented macule in the midline of the forehead and a white forelock found in about 90% of the affected. There is generally an equal involvement of the ventral skin of the trunk and middle part of the limbs. The lesions are constant and have an unvarying progression[3]. Piebaldism is due to mutations in the KIT and SNAI2 genes, the receptor KIT is a member of the type III group of transmembrane receptor tyrosine kinase[4]. The marked or total absence of melanocytes in the affected regions is due to the inappropriate migration of melanoblasts in the embryo. Therefore, a severe phenotype showing a larger depigmented area is associated with severely damaged migration in the embryo[5].

The aim of this report is to present a unique case of piebaldism, its diagnosis and management.

THE CASE

A preterm baby boy was born at 32^{+} weeks due to antepartum hemorrhage. The Apgar score was 1, 4 and 7 at minutes 1, 5 and 10, respectively. The birth weight was 1.85 kg.

The baby was found to have a white forelock (piebaldism) and gray eyebrows and eyelashes, see figures 1 and 2. No family history of similar condition among the parents or their first child. His neonatal course was complicated by mild respiratory distress syndrome which was managed by one-day intubation and assisted ventilation (on PTV mode). The baby stayed in the NICU for 16 days for feeding and weight gain. The gene panel revealed that the baby carries in exon 16 of KIT the variant of uncertain significance c.2318C>T p.(Ser773Phe) in heterozygous state which could be causative for the piebaldism phenotype.

Figure 1: The Baby Shows the Distinct White Forelock

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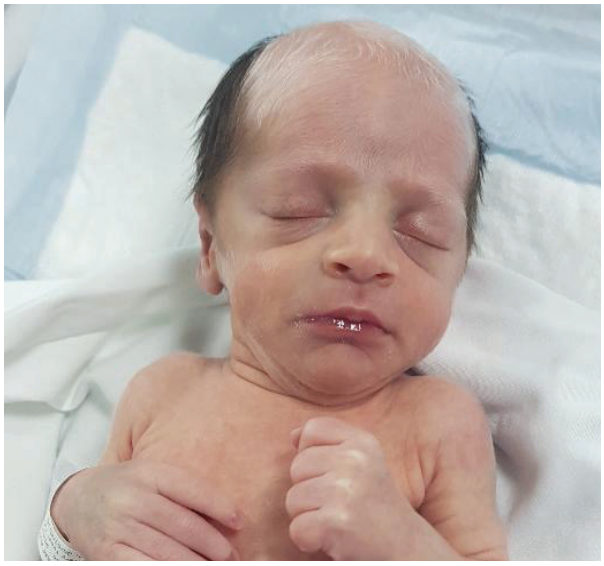

(Consent was obtained)
Figure 2: Hypopigmented (Gray) Eyebrows

The baby was examined by a pediatric ophthalmologist who confirmed the gray eyebrows and eyelashes; however, the baby did not have heterochromia irides, blue eyes or dystopia canthorum.

Initial hearing screening using Otoacoustic Emissions (OAE) was normal. The baby was discharged after 16 days in NICU with weight of 2.05 kg.

DISCUSSION

The genetic testing for piebaldism found that the KIT gene is situated on the long arm of chromosome number 4 (4q12), there are approximately 69 mutations in the KIT gene in the affected individuals with piebaldism; these mutations will produce multifunctional proteins which interfere with the growth, proliferation and migration of melanocytes leading to the depigmentation[6]. The differential diagnosis of piebaldism includes vitiligo, albinism, tuberous sclerosis, chediak-Higashi syndrome, nevus depigmentosus and Waardenburg syndrome[7].

Vitiligo is an acquired depigmentation, generally in an acral and periorificial distribution. Piebaldism is uniquely distinguished by the existence of the depigmented lesions from birth, the presence of hyperpigmented macules within and at the margin of the depigmented areas, and its stationary development. Furthermore, piebaldism usually spares the dorsal midline, hands, feet, and periorificial areas[8].

Other differential diagnosis of piebaldism is Waardenburg syndrome which is an auditory-pigmentary condition including congenital sensorineural hearing loss and pigmentary disruption of the hair, skin and iris with dystopia canthorum (which is a lateral dislocation of the inner canthi)[9]. Waardenburg syndrome has four main types, which have been differentiated on genotypic and phenotypic differences according to the Waardenburg Syndrome Consortium Criteria for diagnosis. Types 1 and 2 are more common compared to types 3 and 4.

The minor criteria for diagnosis of piebaldism are congenital hypopigmentation, synophrys (eyebrows), broad high nasal root, hypoplasia of alae nasi and premature greying of the hair[3]. The major criteria for diagnosis are: congenital sensorineural hearing loss, pigmentary disturbance of iris, pigmentary disturbance of hair (white forelock), dystopia canthorum and first degree relative affection [3].

Treatment of piebaldism is difficult with variable outcomes. Sunscreens are recommended to prevent the affected areas from sunburn[3]. Topical treatments with makeup or artificial pigmenting agents, such as dihydroxyacetone which is used for tanning are useful but as short-term solution. Numerous surgical methods have been reported for treatment of the depigmented lesions but with variable outcome[2].

CONCLUSION

Piebaldism is a rare autosomal dominant disorder of pigmentation causing white forelock and leukoderma. It results from mutations in the KIT proto-oncogene. Among the most important associations is Waardenburg syndrome which must be investigated and ruled out.

Follow-up of piebaldism patients with hearing tests and eye examination is advised. Genetic counselling and further gene study should be done for the parents. It is socially challenging for the patient to have normal interactions with the community which requires the psychological support for the family and the affected child to overcome these difficulties.

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