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Case Report Open Access

Piebaldism and Neurofibromatosis type -1: Family Report Familial Case of Piebaldism with Regression of the Depigmentation over the Trunk

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Abstract

Piebaldism is a rare disorder present at birth and inherited as an autosomal dominant trait. It results from a mutation in the *c-kit* proto-oncogene and is associated with a defect in the migration and differentiation of melanoblasts from the neural crest. Clinical manifestations and phenotypic severity strongly correlates with the site of mutation within the *KIT* gene. The white hair and patches of such patients are completely formed at birth and do not usually progress or regress thereafter.

Here I report a family (one year and seven months old daughter, nine year old boy and their father) with piebaldism associated with clinical criteria for Neurofibromatosis type -1. There are rare reports of piebaldism associated with neurofibromatosis -1. I also report a case of piebaldism with regression of the depigmentation over the trunk. Regression of the white foreloke was rarely reported but regression over the depigmentation over the trunk has not been reported.

Case 1

A 36 years old man presented to dermatology department, ALERT hospital for a consultation of his skin problem. He states that he has a congenital pigment disorder. He was worried if it were leprosy. He had no symptoms of leprosy such as numbness of the extremities or contact history either. The patient claimed the pigment disorder, mainly on his trunk, improved a lot over the years. He also brought two of his children (9yr old boy and 1yr and7/12 daughter) to the hospital, for they had similar congenital disorder. The children had no other medical problems.

Physical examinations reveals poliosis (loss of pigment of the hair) over the scalp (fronto-temporal), medial part of the eye brow of the left side and the chin area. The skin over the anterior trunk has hypopigmented patches with areas of repigmentations and leukotrichia. There are also numerous discrete *café-au-lait* spots of different size (>15mm the largest one) located over the back of the patient. There were also axillary frecklings. No neurofibromas were observed (Figures1-3).

Figure 1: The family with pibaldism (father and children).

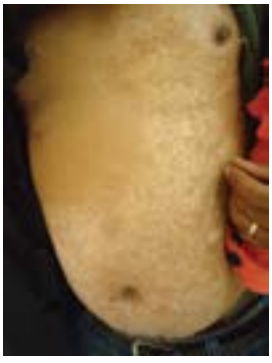

Figure 2: Depigmented patch showing regression. Note also the leukotrichia.

Figure 3: *café-au-lait* spots (case 1).

Case 2

Physical examination of the skin of the boy reveals patches of hypopigmentation and depigmentations over mid-forehead, chest, abdomen, upper and lower extremities. A white forelock and pigment loss of the medial eye brows were noted. Within the depigmented patches, islands of hyperpigmented macules are seen. Multiple hyperpigmented macules(*café-au-lait* spots of size >5 mm) were also seen over the back of this child .There were also axillary freckling. No neurofibromas were observed [Figures 4-7].

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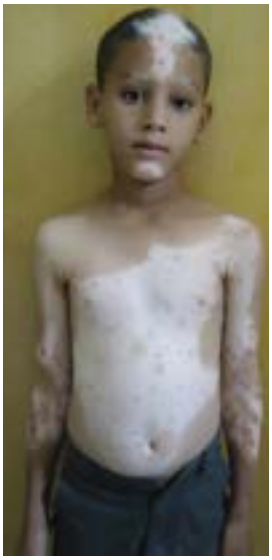

Figure 4: white foreloke ,symmetric depigmented patch with hyperpigmented macules within(Case2).

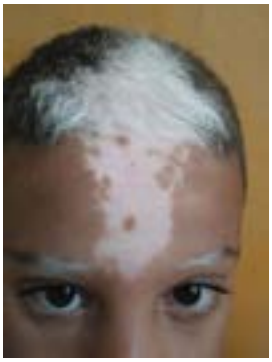

Figure 5: white foreloke ,depigmentation on mid forehead ,medial eyebrow (Case2).

Case 3

Physical examination of the skin of the daughter reveals mild forelock, depigmented patch over the abdomen , multiple *café-au-lait* spots (>5 mm) on her back with axillary frecklings [Figures 8-10].

Introduction to Piebaldism

Piebaldism is a rare inherited autosomal dominant disorder that is associated with defect in migration and differentiations of melanoblasts from neural crest. Piebaldism results from a mutation in the c-kit proto-oncogene, which is located on chromosome 4q12. The c-kit proto-oncogene encodes for the cell-surface tyrosinekinase receptor, whose ligand is a stem cell and mast cell growth factor [1]. This gene is important for pigment cell development.

Piebaldism is due to absence of melanocytes on the affected skin and hair follicle [1]. Multiple mutations have been described by Richards et al .The severity of the phenotypic presentation correlates with the site of mutation [2].

Piebaldism is stable disease i.e. the white hair and patches of such patients are completely formed at birth and do not usually expand thereafter. But there are two case reports which described progressive depigmentation [3,4]. Rare case reports have showed that Piebaldism could be sometimes be a cutaneous sign of Waardenburg syndrome which is a constellation of lateral displacement of the inner acanthi, sensorineural deafness, heterochromia of the iridis [11].

Piebaldism presents at birth with depigmented patches on the mid-forehead, central eyebrows, neck, and anterior trunk, mid extremities (in a bilateral distribution sparing the hands), feet, back, shoulders, and hips. Islands of hyperpigmented to normally pigmented patches within and at the borders of hypopigmentation are often seen

The white forelock is evident in 80-90% of those affected [5]. Both hair and skin in the central frontal scalp are permanently white from

Figure 6: Note the *café-au-lait* spots (Case 2).

Figure 7: Note the *café-au-lait* spots (Case 2).

Figure 8: Mild poliosis (case 3).

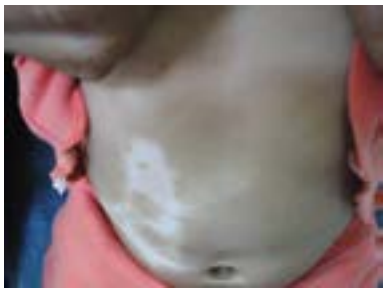

Figure 9: Depigmented patch with islands of normal skin. (Case 3).

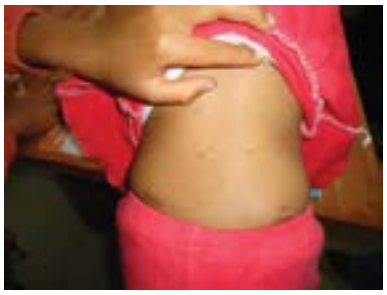

Figure 10: Note the *café-au-lait* spots (Case 3).

birth or when hair color first becomes apparent. Regression of the white forelock has been described [6].The forelock and white skin may have a triangular shape. The only pigmentation change of skin or hair may be a white forelock in some patients.

Neurofibromatosis type 1 (*NF1*) is an autosomal dominant neurocutaneous disorder. The *NF1* gene belongs to the family of tumor suppressor genes and encodes a widely expressed protein called neurofibromin, which is a major negative regulator of the *Ras* oncogene pathway, participating in the control of cell growth and differentiation [7]. Despite progress in understanding the molecular basis, the diagnosis of *NF1* is based on clinical criteria established by the National Institute of Health (NIH) Consensus Conference in 1987 [8]. According to these criteria, two or more of the following findings establish the diagnosis of *NF1*: a) six or more *café-au-lait* spots greater than 5 mm in diameter in prepubertal individuals and more than 15 mm after puberty, b) two or more neurofibromas or one plexiform neurofibroma, c) freckling in the axilary or inguinal regions, d) optic pathway tumor, e) two or more Lisch nodules (iris hamartomas), f) distinctive bone lesions such as sphenoid wing dysplasia and g) a first-degree relative with *NF1* [7-9].

Depigmented skin in piebaldism is generally considered unresponsive to medical or light treatment. Several surgical techniques have been proposed for the treatment of piebaldism. These procedures are usually poorly suited for the treatment of large, hypopigmented patches because they can result in scars and require multiple donor sites.

In some studies dermabrasion and split-skin grafting followed by minigrafting may be a good option for selected patients. Autologous punch grafting for repigmentation in piebaldism may be considered in selected individuals [12].

Piebaldism is a benign disorder. However, patients are at risk for actinic complications related to absence of cutaneous melanocytes. Therefore sun protection is advised to all patients with piebaldism. Camouflage using dermablend could also be recommended as alternative treatment.

Discussion

Piebaldism is usually a benign isolated skin condition, but there are rare reports of piebaldism association with Hirschprung disease, mental retardation, *NF1*, congenital dyserythropoietic anemia type II, Diamond-Blackfan anemia, Grover disease, deafness, and cerebellar ataxia [5].

At least four cases of piebaldism associated with neurofibromatosis have been reported and none of them developed neurofibromas, although at their young age (3-17 years of age) it is not possible to exclude the possibility of subsequent development of those lesions [8]. Whether, the simultaneous occurrence of these two dominantly inherited diseases is significantly higher than by chance remains to be established [13]. **However, the diagnosis of the suspicion of neurofibromatosis, which requires adequate follow-up and genetic counseling**

The pigment alterations in piebaldism usually remain stable, are permanent, and are unresponsive to medical treatments and phototherapy. However, in a small number of patients, repigmentation may occur spontaneously [5 14].

Patients generally have a normal life span but some experience social disabilities requiring psychological support [5].

These case reports strengthen the fact that the association of Pibaldism with NF-1 is more than a chance. Therefore I recommend screening of all patients with piebaldism for NF-1 and genetic counseling should be offered.

Repigmentation of the white foreloke has been reported rarely but to my knowledge repigmentaion of the trunk pigment loss has not been reported.

These case report could also be used to demonstrate the different clinical manifestation and phenotypic severity of Piebaldsim .

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