

PIEBALDISM - REPORT OF THREE CASES AND REVIEW OF THE LITERATURE

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Abstract:

In this text we present three Qatari patients with the clinical diagnosis of piebaldism. The first two cases are a daughter and her father showing typical lesions of piebaldism. The third is an unrelated infant girl three months old who had since birth wide spread hypopigmentation. The three cases have no hearing loss.

Introduction:

Piebaldism is an autosomal dominant disorder of melanocyte development characterized by congenital white patches of skin and hair from which melanocytes are completely absent⁽¹⁾. The white forelock is the most specific feature observed in up to 90% of cases and is represented by a triangular or diamond shaped hypopigmentation on the forehead⁽²⁾. Other white macules are distributed on anterior abdomen, chest, back, upper arm, forearm, thighs and legs. The size and shape of these depigmented areas are variable and usually does not change with age⁽²⁾. Islands of normal or hypermelanotic skin usually less than one centimeter in diameter occur in the white areas⁽³⁾. Deafness is not typical in piebaldism but sensory neural deafness was reported in one case⁽⁴⁾ thus increasing the similarity of piebaldism to Waardenburg syndrome.

There is strong evidence for the role of proto-oncogene c-KIT in the embryonic development of human melanocytes and in pathogenesis of piebald trait⁽⁵⁾. A c-KIT proto-oncogene mutation was identified in a proband with classic autosomal dominant piebaldism. This mutation results in gly-Arg substitution at Codon 664 within the tyrosine kinase domain⁽⁶⁾.

Case Reports:

1- First patient is a Qatari girl 6 months old. She has white forelock with triangular hypopigmentation of the forehead. She has white patches on front of both knees spotted with hyperpigmented macules since birth [Fig.1, 2]. All other organs and systems are normal.

2- Second patient is the father of the first case. He is a 31 years old Qatari male showing white forelock and white patches in front of both knees since birth [Fig.3, 4].

3- The third case is a Qatari girl seen at age of 3 months. She had white macule of forehead and white hairs of medial thick of both eye brows. She also had hypopigmented skin of front of chest, upper limbs, abdomen and both knees [Fig. 5 to 11].

Discussion:

Piebaldism is an autosomal dominantly inherited disorder of pigmentation characterized since birth by white forelock and the medial eye brows and may be the eye lashes. Triangular or diamond shaped symmetric white macule of the forehead and in 10-20% of cases white macules occur symmetrically elsewhere in the body could be the only expression of piebaldism⁽⁷⁾. The sites reported to be affected are the anterior abdomen extending to the chest; the back when affected usually spare midline, mid upper arm, mid calf, sometimes the face in addition to the white forelock and sometimes mucosal membrane.

Islands of pigmented macules usually less than one centimeter in diameter are seen in areas of hypomelanotic skin. General health is usually not affected. Multiple family members



Fig. 1: White forelock - case # 1



Fig. 2: White patches in front of both knees showing hyper pigmented macules - case # 1

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Fig. 3: White forelock case # 2



Fig. 4: White patches of knee region case # 2



Fig. 5: White patch of forehead with white hairs of medial eye brows - case # 3

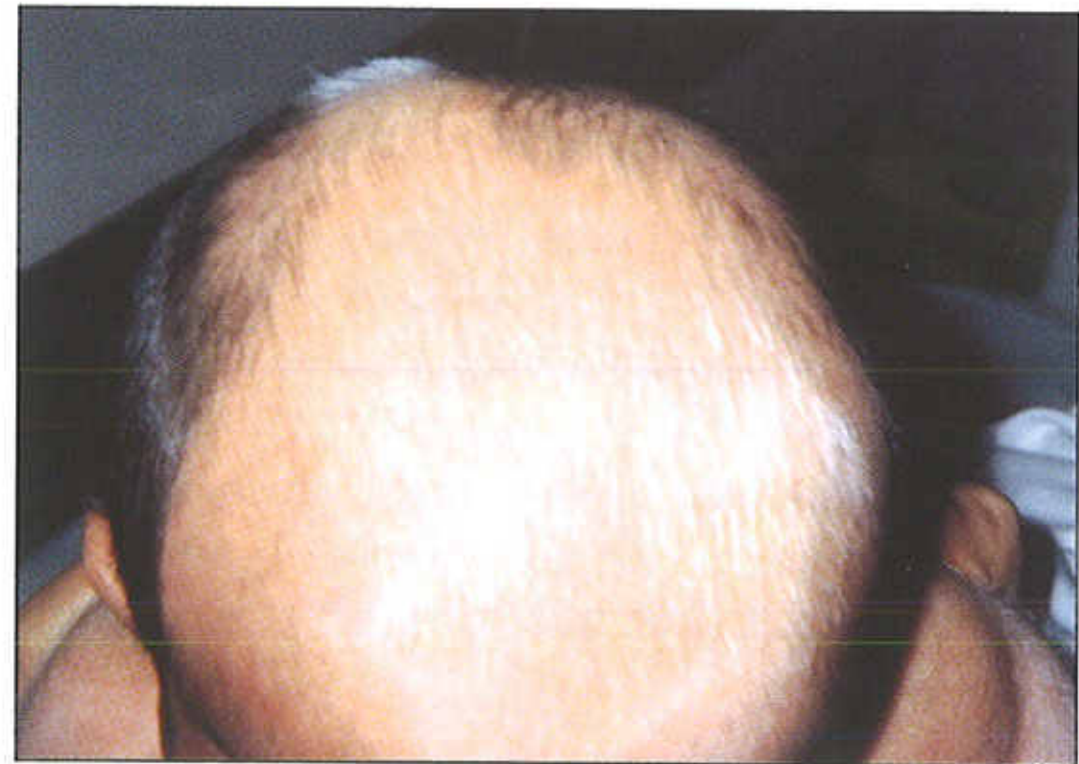


Fig. 6: White patches of scalp and white hair of vertex - case # 3



Fig. 7: White patches of front of upper limb and chest - case # 3.



Fig. 8: White patche of front of abdomen case # 3.



Fig. 9: White patches of upperarm - case # 3

may be affected with variable expression. Our first and second patients are daughter and father showing similar lesions. The third case shows white hairs of medial eye brows and wide spread symmetric hypopigmentation since birth. These hypopigmented patches lack melanocytes as a result of defective melanoblast differentiation, migration, proliferation or survival during embryonic development^(8,9).

Piebaldism results from mutation of the Kit proto-oncogene which encodes the cell surface receptor transmembrane tyrosine kinase from embryonic growth factor variously termed steel factor (SLF); stem cell factor; or kit ligand^(9,10,11,12). When KIT dependant signal transduction is inhibited aberrant melanocyte proliferation or migration during embryonic development results⁽¹³⁾ and the KIT gene is mapped to chromosome 4q11-4q12^(14,15).

It is reported that a mentally retarded girl with piebaldism had deletion of the long arm of chromosome 4⁽¹⁴⁾. The white skin in piebaldism showed evidence that it is immunologically different from normal skin when a graft versus host reaction occurred only in an area of piebaldism in a patient who was treated with allogenic bone marrow transplant⁽¹⁶⁾.

Melanogenesis occurs in steps. The starting step is migration of melanocytes from the dorsal neural crest to specific target sites. The second step is melanin synthesis and transfer of pigment to the neighbouring cells. The steps of melanogenesis also include the response of melanocytes to exogenous agents. All these steps of melanogenesis are controlled by encoded genes⁽¹⁷⁾.

Mutations of these genes can disturb melanogenesis and result in hypopigmentation⁽¹⁷⁾ as in piebaldism or hyperpigmentation as in type-2 neurofibromatosis⁽¹⁸⁾. Interacting genes regulate embryonic development of melanocytes and

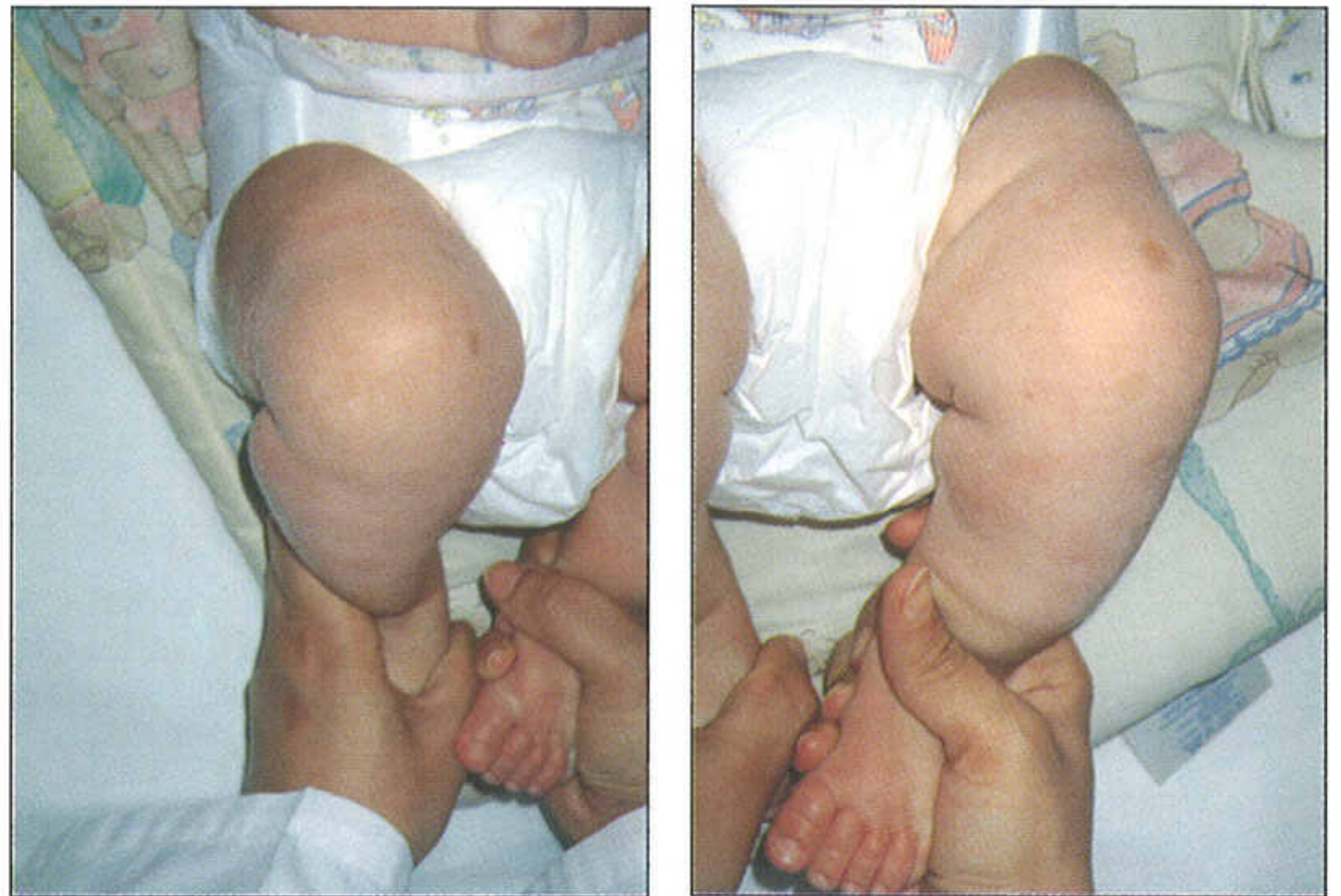


Fig. 10 & 11: White patches in front of both knees - case # 3.

abnormalities of these regulatory genes result in different genetic disorders of melanocyte development⁽¹⁹⁾. The specific transcription factor PAX 3 and microphthalmia transcription factor (MITF) appear to play a regulatory role in early embryonic development of the pigment system and the associated Waardenburg⁽¹⁷⁾. Continued survival of the migrating melanoblasts depends on the steel factor (SLF), c-KIT. The lack or dysfunction of this receptor results in piebaldism⁽¹⁷⁾.

Mutations in the genes encoding formation of melanosomes and conversion of tyrosine to melanin results in hypopigmentation disease called oculocutaneous albinism⁽¹⁵⁾. The melanocyte function must be maintained in the target tissue for life. White hairs result from absence of repopulation of germinative hair follicle by melanocytes in subsequent anagen phases. Vitiligo results from removal of melanocytes from affected skin or mucous membrane⁽¹⁷⁾. Disorders of melanocyte development are characterized by heterogenous distribution of pigmentation, typified by piebaldism and Waardenburg syndrome.

These disorders of pigment cell development represent a subgroup of the neurocrestopathies involving defects of various neural crest cell lineages that include not only melanocytes but also other tissues derived from neural crest⁽¹⁹⁾. Piebaldism overlaps phenotypically with Waardenburg syndrome⁽²⁰⁾. The Waardenburg syndrome is an autosomal dominant disorder with variable penetrance and its gene is in locus 2q37⁽¹⁸⁾ and is characterized by⁽²¹⁾ dystopia canthorum (99%), synophrys (17-69%), broad nasal root (78%), depigmentation of hair or skin or both (17-58%), with white forelock, heterochromia iridis (7-20%) and congenital deafness (9-38%). So Waardenburg

syndrome can be present with or without deafness. Piebaldism does not show dystopia canthorum, broad nasal root and synophrys⁽²¹⁾ and no hearing disturbance⁽¹⁸⁾.

The white skin in peibaldism does not respond to medical or phototherapy⁽²²⁾. Dermabrasion and split skin grafting followed by minigrafting is recommended to treat the white skin in piebaldism and is reported to cause 95%-100% repigmentation of the leukodermic defect⁽²²⁾. Epidermal sheets obtained by a high speed air driven dermatome were used to repigment white areas in one boy with piebaldism⁽²³⁾.

The surgical management of refractory and stable defects of vitiligo and piebaldism includes melanocyte transplantation, suction epidermal grafts and cultured epidermal autografts followed by additional mini grafting in areas of residual achromia⁽²⁴⁾.

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