

# Piebaldism: A Case Report and a Concise Review of the Literature

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## GOAL

To understand piebaldism to better manage patients with the condition

## OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Describe the clinical presentation of piebaldism.
2. Discuss the differential diagnosis of piebaldism.
3. Identify treatment options for piebaldism.

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*Piebaldism is a rare autosomal dominant disorder characterized by congenital poliosis and leukoderma. We present a case of a 10-year-old girl with a typical clinical presentation, followed by a concise review of the literature discussing the etiology, clinical features, diagnosis, and management of the condition.*

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## Case Report

A 10-year-old girl presented for evaluation of a white forelock and multiple white patches of skin on the trunk and extremities (Figure). The white forelock was present at birth and a few white patches appeared on the chest at 3 months of age. During the subsequent 4 years, the white patches gradually progressed to involve the central forehead, abdomen, and extremities. Multiple frecklelike macules also appeared within the patches and the surrounding healthy skin.

Physical examination revealed a healthy girl with a prominent, large, diamond-shaped, depigmented patch on the central forehead that was associated with a white forelock. The hairs of the medial eyebrows and the eyelashes also were depigmented. Large, irregularly shaped, depigmented patches were

A prominent, large, diamond-shaped, depigmented patch on the central forehead associated with a white forelock and depigmentation of the hairs of the medial eyebrows and the eyelashes.



present on the trunk and anterior extremities. There were multiple hyperpigmented macules overlying both the depigmented patches and the adjacent normally pigmented skin. The rest of the physical examination and the results of routine blood tests and urinalysis were unremarkable.

The patient's mother and 4 siblings also were born with a white forelock. Similar depigmented patches on the trunk and extremities with a similar pattern and distribution were noted in all of them. Neither the patient nor her mother and siblings had midfacial anomalies, deafness, or heterochromia irides.

### Comment

Piebaldism is a rare autosomal dominant disorder of melanocyte development resulting from mutations of the *c-kit* protooncogene.<sup>1,2</sup> The disorder is characterized clinically by congenital poliosis and leukoderma. A white forelock is present at birth and may be the only manifestation in most affected individuals.<sup>3</sup> The white forelock may have a triangular or diamond shape, and the underlying skin of the scalp also is amelanotic. Typical piebald lesions are typified by well-circumscribed, irregular, chalk white patches, often with hyperpigmented freckle-like macules noted on both depigmented and unaffected adjacent skin.<sup>4</sup> The lesions often exhibit a classic distribution, involving the central forehead

and anterior trunk, with extension to the flanks and anterior midarms, midknees, and midlegs. The medial third of the eyebrows and eyelashes also may be affected in severe cases.<sup>4</sup> Characteristically, there is sparing of the dorsal midline, hands, feet, and periorificial areas.

Piebaldism generally is a static disorder of pigmentation, though contraction of the affected areas with time or the appearance of new hyperpigmented macular lesions has been described.<sup>5</sup> Progression of the depigmented patches has been reported in isolated cases with a novel Val620Ala mutation in Kit.<sup>6</sup> Piebaldism rarely is associated with other disorders such as Hirschsprung disease, neurofibromatosis type 1, congenital dyserythropoietic anemia type II, Diamond-Blackfan anemia, and Grover disease.<sup>7-11</sup> Individual case reports with associated deafness also have been described.<sup>12</sup>

Histopathologic evaluation of the depigmented lesions reveals absent or considerably reduced melanocytes. The hyperpigmented macules have a normal number of melanocytes and an increased number of melanosomes in the melanocytes and keratinocytes.<sup>4</sup>

The molecular basis of piebaldism was traced by Giebel and Spritz<sup>1</sup> and Fleischman et al<sup>13</sup> to mutations of the *c-kit* protooncogene. To date, 14 point mutations, 9 deletion mutations, 2 nucleotide splicing mutations, and 3 insertions of Kit have been described.<sup>6,14</sup> *c-kit* Mutations are found in about

75% of patients with piebaldism.<sup>14</sup> Mutations in the *slug* gene, which is a zinc-finger neural crest transcription factor, have been reported in piebaldism that lacked mutations in *Kit*.<sup>15</sup>

The human *kit* gene encodes the tyrosine kinase transmembrane cellular receptor for mast/stem cell growth factor, which is a critical factor for melanoblast migration, proliferation, differentiation, and survival.<sup>6</sup> It would be pertinent to note here that the severity of the phenotype in piebaldism correlates with the site of the mutation within the *kit* gene. The most severe phenotypes are caused by mutations involving the intracellular tyrosine kinase domain, whereas the mildest phenotypes result from mutations involving the amino-terminal extracellular ligand-binding domain.<sup>6</sup>

The differential diagnosis of piebaldism includes any condition that may present with a depigmented lesion. Vitiligo is characterized by acquired depigmentation, typically in an acral and periorificial distribution. Piebaldism generally is distinguished from vitiligo by the presence of lesions from birth, hyperpigmented macules within and at the border of depigmented areas, and its static course. Moreover, piebaldism spares the dorsal midline, hands, feet, and periorificial areas.

Waardenburg syndrome is an autosomal dominant disorder characterized by a congenital white forelock, lateral displacement of the medial canthi, a hypertrophic nasal root, heterochromia irides, and sensorineural hearing loss.<sup>16</sup> At least 4 types of Waardenburg syndrome have been described based on the clinical and genetic criteria. The presence of hyperpigmented patches within the islands of depigmentation and on healthy skin; the absence of midfacial lesions, heterochromia irides, and deafness; and the location of depigmented patches on the trunk and extremities help to distinguish piebaldism from the various forms of Waardenburg syndrome.<sup>16</sup>

Ziprkowski-Margolis syndrome is a rare X-linked recessive syndrome characterized by deaf-mutism, heterochromic irides, piebaldlike hypomelanosis, and hyperpigmented macules, with a geographic appearance developing mainly on the trunk and extremities.<sup>17</sup>

Woolf syndrome is an autosomal recessive disorder consisting of piebaldism and deafness. Audiometry is crucial to exclude this diagnosis.<sup>18</sup> Depending on its presentation, other conditions to consider include Addison disease, albinism, and systemic sclerosis, as well as use of depigmenting agents.

Piebaldism is considered a relatively benign disorder, but it may have psychological impact because it is socially disabling, which presents a therapeutic challenge. Depigmented skin in piebaldism

generally is considered unresponsive to medical or light therapy. Of note, the diagnosis of piebaldism should alert the clinician to the possibility of Waardenburg syndrome as determined by the results of ocular and auditory examinations. Sunscreens are recommended to avoid sunburns and to reduce the carcinogenic potential. To camouflage the exposed areas, makeup or temporary pigmenting agents such as the tanning product dihydroxyacetone may be used.<sup>19</sup>

The lesions of piebaldism do not respond to the topical agents used to treat vitiligo. Different surgical techniques have been tried, with variable success, including thin split-thickness grafts, minigrafting, transplant of autologous cultured melanocytes, and a combination of dermabrasion and grafting of the pigmented skin into the depigmented areas.<sup>20,21</sup> Guerra et al<sup>22</sup> reported achromic epidermis removed with the erbium:YAG laser and autologous cultured epidermal grafts were applied to the recipient bed in 6 patients. Autologous cultured epidermis, bearing a controlled number of melanocytes, induced repigmentation of all piebald lesions. The mean percentage repigmentation was 95.45%.<sup>22</sup>

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