

# Case Report: A Case of Full Expressivity Piebaldism

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**Abstract:** Piebaldism is a rare inherited disease with a specific clinical manifestation. Here with, we reported a case of piebaldism in a 17-year-old boy with the feature of a severe phenotype (full expressivity). White forelock, poliosis, and depigmented patch observed on midline forehead and neck along with ventral and lateral trunk, mid-arms, thighs, knees, and the lower leg area were found. Hyperpigmented macule between depigmented lesions were found in all the lesions. The patient was a new mutant since his both parents were normal. The diagnosis was established based on clinical appearance, histopathological examination, and immunohistochemistry staining with S100, HMB45, and Fontana-Masson.

## 1 INTRODUCTION

Piebaldism (OMIM #172800) is an rare autosomal dominantly inherited pigment anomaly characterized by a congenital white forelock and leukoderma on the frontal scalp, forehead, ventral trunk and extremities (Oiso,2012). Its first descriptions date back to early Egyptian, Greek and Roman writings an it has been observed throughout history in families with a distinctive, predictable congenital white forelock (Spritz,1994). Although piebaldism is a skin condition which occurs in limited and fixed areas, it remains a social problem in patients so that piebaldism therapy becomes a challenge to date (Thomas,2004). The absence of melanocyte in affected areas of the skin and hair is due to mutation of the KIT protooncogenes, which affects the differentiation and migration of melanoblast. Piebaldism can also be caused by heterozygous mutation in the gene encoding the zinc finger transcription factor SNAI2 (Sanchez,2003) (Taieb,2016).

The incidence of piebaldism is estimated to be less than 1 among 20,000 people. Piebaldism reported in all races with equally number between women and men. The incidence of such cases is estimated to be less than 1 among 20,000 people

(Agarwal,2012). Medical record data of Dr. Sardjito General Hospital showed that no case of piebaldism were recorded for last 5 years and this is the first case report of full expressivity piebaldism in Indonesia.

Here with, we reported a case of piebaldism in a 17-year-old boy with the feature of a severe phenotype. Piebaldism is a rare case, so this paper may add some knowledge in giving a differential diagnosis of skin disorders in the form of patch depigmentation. Piebaldism become a challenge for the dermatologist in diagnosis and therapy.

## 2 CASE

A 17-year-old boy from Purbalingga, Central Java, came to the Dermatology and Venereology Outpatient Clinic of Dr. Sardjito General Hospital Yogyakarta, with the chief complaint of white patches on his face and almost the entire body. He had a white patches on the forehead and neck along with white hair on the frontal part of the head. Leukoderma appearance was also found in the chest, abdomen, mid-arms, thighs, knees, and the lower leg area. There were no complaints of visual impairment, hearing loss, or expansion of the skin

lesion areas of the patient. He never had any therapy for the complaints before and no history of atopy and drug allergy. Both of his parents were reported without pigmentary disorders. The patient denied any previous similar history of complaints, atopy, drug allergy nor diabetes in the family members.

The general condition was good and dermatology status showed a white forelock and poliosis on the hair and medial eyebrow (Figure 1). There was depigmented patch along the forehead until the nose with hyperpigmented macule on the border area. There were similar lesions on the neck, chest, abdomen, the extensor sides of upper extremities, thighs, knees, and up to the lower limbs in the form of depigmented patches with edges and those of which are hyperpigmented and normal pigmentation macules (Figure 2). There was white hair on the depigmented lesion. On the upper right and left back showed ill-defined border of hypopigmented patches and multiple hyperpigmented macules spread among them. No skin lesions were found in the vertebral area, hands, and feet. The differential diagnosis presented for the patient was piebaldism, vitiligo and Waardenburg syndrome.

Skin biopsy of depigmented area in the chest was performed. Histopathologic examination revealed basket weave type orthokeratosis, focal spongiosis, and basal epidermal cell vacuolization. Melanocyte and melanin were not found in the basal layer. There was mild infiltration of inflammatory cells in the perivascular and peri-appendicular area of the dermis (Figure 3A). We also performed immunohistochemistry staining with s100 and Human Melanona Black 45 showed no positive expression on melanocyte (Figure 3B&C). No epidermal melanin were observe in Fontana-Masson staining (Figure 3D).



Figure 1. White forelock and poliosis on the hair and medial eyebrows.



Figure 2. Depigmented patch on neck, chest, abdomen, and extremities in simetrically distribution.

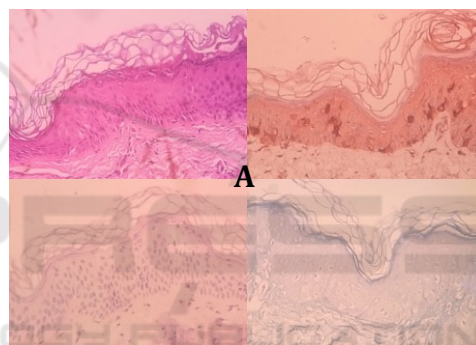


Figure 3. Hematoxylin Eosin (A), S100 (B), HMB 45 (C), and Fontana-Masson (D) staining (x40)

The diagnosis of piebaldism was established by clinical appearance, histopathological examination, and immunohistochemistry staining with S100, HMB45, and Fontana-Masson. The therapy was not given to the patient due to family consideration of the possibility for healing, the extent of the area of the body involved, and also the transportation problem.

### 3 DISCUSSION

Piebaldism is a pigmentation disorder that is inherited by autosomal dominant means and rarely occurs. It is mainly due to mutation in the KIT gene (Xu,2016). KIT protooncogene encodes the cell-surface receptor transmembrane tyrosine kinase for the steel factor, an embryonic growth factor (Thomas,2004). The formation of color of the skin,

hair, and eyes is determined by a multistep process: (i) melanoblast migration to the skin of the embryo; (ii) proliferation and survival of the melanocytes in the basal layer of the epidermis; (iii) biogenesis of the melanosomes in the melanocytes; (iv) production of melanin granules in the melanosomes in the melanocytes; (v) translocation of melanosomes from the perinuclear region to peripheral region of the melanocytes; (vi) transfer of the melanosomes from the melanocytes to the keratinocytes; and (vii) translocation of the transferred melanin granules from peripheral region to the supranuclear region of the keratinocytes. Damage during the initial step bring migration of the melanoblast in embryo and induces most or all of the loss of the melanocytes in the ventral skin and hair after birth. This is due to melanoblasts originating from neural crest located in the dorsal area and then migrating to the ventral area (Oiso,2012).

The term piebald stems from the Latin word for “magpie” and is used to describe animals whose bodies are covered in black and white patches (Huang,2016). Piebaldism has a clinical picture of white forelock and leukoderma in the scalp of the frontal region, forehead, ventral trunk, and extremities. Patients with piebaldism have hair and skin depigmentation that is visible since birth, which is relatively stable and persistent. White forelock would often form a triangle shape and might result as the only one manifestation in 80-90% of cases, although the involvement can also be found on the hair and skin in the area of the forehead that occurs altogether (Oiso,2012). The description of poliosis is based on the presence of localized patch on the white hair. Poliosis can also affect the eyebrow and eyelashes. There is a depigmented patch on the skin with an irregular shape found on the face, trunk, and extremities with symmetrical distribution. In general, there are hyperpigmentation islands within and at the border of the depigmentation area (Thomas,2004). Patients with piebaldism may develop café-au-lait spots (Oiso,2012). Pigmentary anomalies in piebaldism are typically restricted to the hair and skin. Some patients may get spontaneous repigmentation, either partially or completely, especially after injury (Thomas,2004).

Genetic analysis revealed that there was a consistent relationship between genotype and phenotype of piebaldism. Clinical manifestations and phenotypic severity of piebaldism strongly correlate with the site of mutations within the KIT gene. Dominant negative missense mutation of the intracellular tyrosine kinase domains appear to yield the most severe phenotypes, while mutations of the

amino terminal extracellular ligand binding domain result in haploinsufficiency and are associated with the mildest forms of piebaldism. Intermediate phenotype are seen with mutation near the transmembrane region (Thomas,2004). The severe form shows a typical white forelock on the frontal scalp and relatively larger leukoderma on the chest, abdomen, arms, and legs. The mild type may only show relatively smaller leukoderma on the ventral trunk and / or an extremity without a white forelock. The moderate phenotype has an intermediate appearance between the mild and severe form (Oiso,2012)(Spritz,1994). In our patient, there was a complaint of white patches on the body and white hair on the front of the head that appeared from the moment of birth. The stable depigmentation of the patch depigmentation in the patient is suitable for the description of piebaldism. This patient was considered as severe phenotype and full expressivity based on skin involving area and location of the lesion.

Melanocytes were not found or considered to be diminished on the histopathologic examination taken from the depigmentation patch. While in the hyperpigmentation area, there is a normal number of melanocytes found (Spritz,2009) (Thomas,2004) (Treadwell,2015). Immunohistochemistry staining with s100 is expressed in neural crest-derived cell (melanocyte, Schwann cells, glial cells), chondrocytes, fat cells, macrophages, Langerhans cells, dendritic cells, some breast epithelial cells and sweat glands. Another staining used in this case is Human Melanoma Black 45 which expressed in melanocyte that are synthesizing melanin. To revealed melanin pigment in the basal layer that usually not discernible in Hematoxylin-Eosin-stain section, requires a Fontana-Masson Stain for confirmation (High,2012). We performed routine histopathological examination and immunohistochemistry staining with S100, HMB45, and Fontana-Masson thus proving that no melanocytes nor melanin pigment in the basal layer.

Piebaldism therapy is still a challenge. Sunscreen treatment is recommended to prevent burns and to reduce carcinogenic potential (Thomas,2004)(Milankov,2014). Facial makeup application or pigmentation agents might be used to disguise the area involved, even though it may only be temporary. Various surgical techniques have been performed, such as a combination of dermabrasion and skin grafting with normal pigmentation to the area of depigmentation, with or without phototherapy, of which it may be of benefit to some patients (Oiso,2012) (Thomas,2004)(Maderal,2017).

In our patient, we planned a skin grafting for treatment but the patient and family considerate to not given the therapy regarding the healing possibility, the extent of the body area involved, including also the transportation problems.

#### 4 CONCLUSION

A case of piebaldism in a 17-year-old boy with full/complete phenotype expressivity was reported. Routine histopathological examination with hematoxylin-eosin staining cannot distinguish the depiction of piebaldism, vitiligo, and Waardenburg syndrome. The diagnosis of piebaldism in this patients is based on anamnesis and physical examination in accordance with the severe phenotype, of which a typical white forelock appearance was found on the scalp of the frontal region and broad leukoderma on the chest, abdomen, both arms, and legs. There are various alternative therapies in the case of piebaldism, but the patient rejected any therapy due to considerations of healing possibility, the extent of the body area involved, and also the patient's transportation problem.

#### REFERENCES

- Agarwal, S., Ojha, A., 2012. Piebaldism: A Brief report and review of the literature. *Indian Dermatol Online J.* 3, 144-147.
- High, W.A., Tomasini, C.F., & Argenziano, G.Z. I., 2012. Basic Principles of Dermatology. In *Dermatology* 3<sup>rd</sup> ed. London, Elsevier. 0:29-33.
- Huang, A., & Glick, S.A., 2016. Piebaldism in history- "The Zebra People". *JAMA Dermatol.* 152:1261.
- Maderal, A. D., & Kirsner, R. S., 2017. Use of Epidermal Grafting for Treatment of Depigmented Skin in Piebaldism. *Dermatologic Surgery*, 43(1), 159-160.
- Milankov, O., Savić, R., & Radulović, A., 2014. Piebaldism in a 3-month-old infant: Case report. *Medicinski pregled*, 67(3-4), 109-110.
- Oiso, N., Fukai, K., Kawada, A., & Suzuki, T., 2012. Piebaldism. *Journal of Dermatology*, 39, 1-6
- Sánchez-Martín, M., Pérez-Losada, J., Rodríguez-García, A., González-Sánchez, B., Korf, B. R., Kuster, W., ... & Sánchez-García, I., 2003. Deletion of the SLUG (SNAI2) gene results in human piebaldism. *American Journal of Medical Genetics Part A*, 122(2), pp. 125-132.
- Spritz, R. A., 1994. Molecular basis of human piebaldism. *Journal of investigative dermatology*, 103, 137-140.
- Taïeb, A., Morice-Picard, F., Ezzedine, K., 2016. Genetic disorders of pigmentation. In *Rook's Textbook of Dermatology* 9<sup>th</sup> ed.; London, Wiley Blackwell, 70, 3.
- Thomas, I., Kihiczak, G. G., Fox, M. D., Janniger, C. K., & Schwartz, R. A., 2004. Piebaldism: an update. *International journal of dermatology*, 43(10), pp. 716-719.
- Treadwell, P. A., 2015. Systemic conditions in children associated with pigmentary changes. *Clinics in dermatology*, 33(3), pp. 362-367.
- Xu, X. H., Ma, L., Weng, L., & Xing, H., 2016. A novel mutation of KIT gene results in piebaldism in a Chinese family. *Journal of the European Academy of Dermatology and Venereology*, 30(2), 336-338.