Piebaldism with multiple café-au-lait–like hyperpigmented macules and inguinal freckling caused by a novel *KIT* mutation

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INTRODUCTION

Piebaldism is a rare autosomal dominant disorder of pigmentation characterised by patches of leukoderma and white forelock. It is most often caused by mutations in the *KIT* proto-oncogene receptor tyrosine kinase (TK), which result in the defective migration and differentiation of melanoblasts and melanocytes.[1] Other mutations that have been described include a deletion and a double nucleotide variant in the gene encoding snail family zinc finger 2 (*SNAI2/SLUG*).[2,3]

The occasional coexistence of multiple café-au-lait macules (CALMs) in piebaldism and also piebaldism in association with CALMs and intertriginous freckling may lead to diagnostic confusion with neurofibromatosis type 1 (NF1). Another differential diagnosis is Legius syndrome, which is caused by loss-of-function mutations in the *SPRED1* gene. The syndrome is characterised by CALMs and intertriginous freckling with macrocephaly, lipomas, and learning disability. Unlike NF1, patients with Legius syndrome do not have cutaneous or plexiform neurofibromas, skeletal dysostosis, or optic pathway gliomas. The overlapping presentations of these related pigmentary disorders make it difficult to distinguish between them during the early stages and present a challenge for initial diagnosis.

Abbreviations used:

CALM:	café-au-lait macules
NF1:	neurofibromatosis type 1
TK:	tyrosine kinase

CASE REPORT

This 7-year-old girl was conceived via in vitro fertilization by a nonconsanguineous couple of German and Chinese descents. She was born in Germany prematurely at 33 weeks of gestation via emergency lower-segment cesarean section for in vitro fertilization dichorionic, diamniotic twins in labor. Perinatal history was uncomplicated, and she had good Apgar scores of 9 at both 1 and 5 minutes of life. At birth, she was noted to have a white forelock with patches of depigmentation and CALM-like hyperpigmented lesions. Results from head ultrasound scan and audiology test for hearing evaluation were both normal. Genetic testing for *NF1* gene mutation returned negative results.

She first presented to our clinic when she was 4 years and 5 months old after relocation to Singapore from Germany. On examination, she was noted to have whitish blonde forelock with well-demarcated, hypopigmented patch over the central forehead continuing to the glabella, rhinion,

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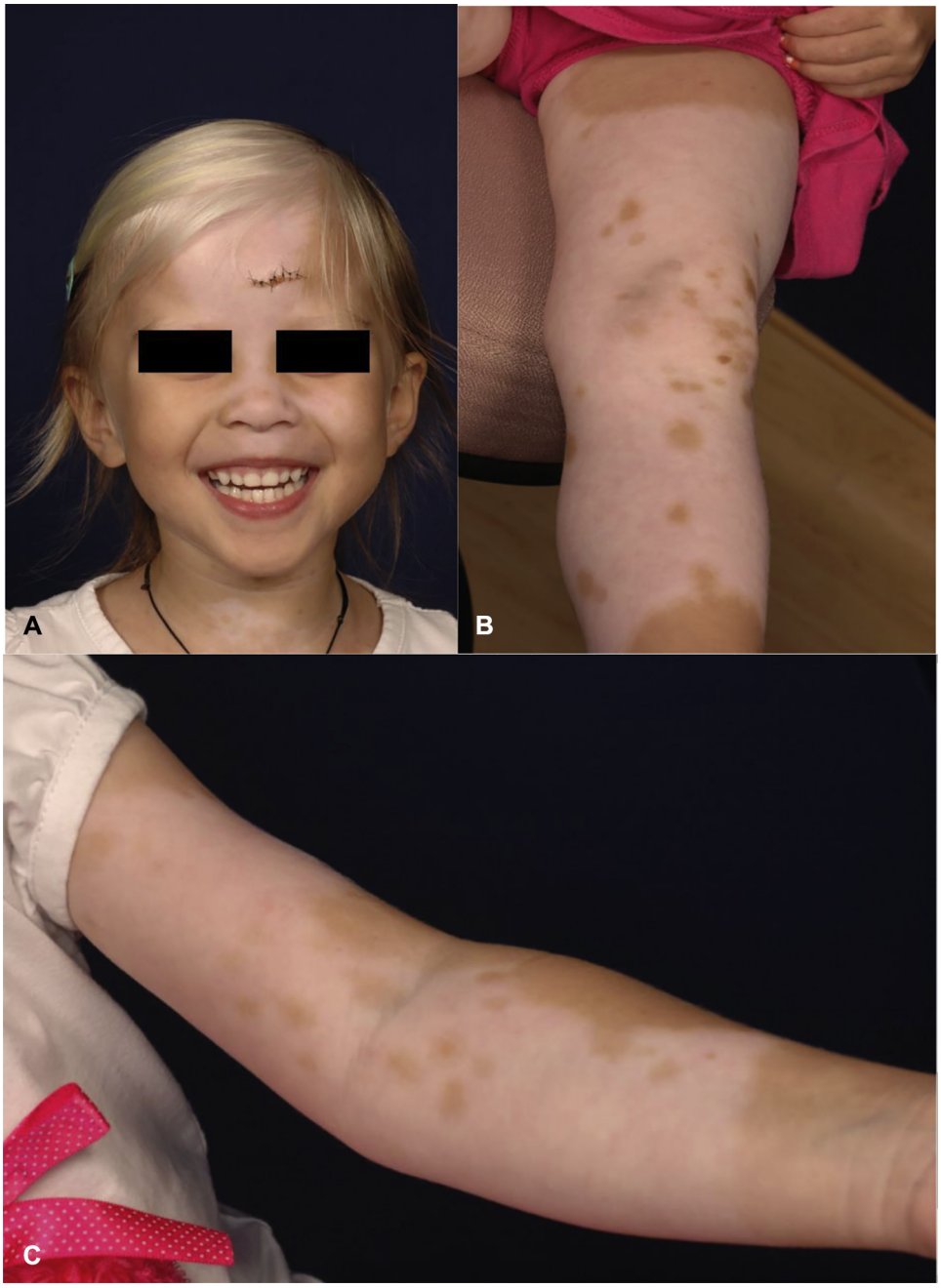

Fig 1. Depigmented patches observed (**A**) on the central forehead continuing to the glabella, rhinion, and bilateral cheeks; (**B**) on the lower limb with islands of normally pigmented skin; and (**C**) on the upper limb with islands of normally pigmented skin.

and bilateral cheeks, sparing the columella and chin (Fig 1, *A*). She also had multiple patches of hypopigmented/depigmented skin with islands of normally pigmented skin distributed across the anterior neck, ventral aspect of bilateral upper limbs (from proximal upper arms to distal forearms), and ventral aspect of bilateral lower limbs (from proximal thighs to distal lower legs) (Fig 1, *B* to *C*). Furthermore, multiple hyperpigmented lesions (some >1 cm) were also noted predominantly in the lower limbs and back. Freckling was seen in the inguinal folds, but no neurofibromas were seen. Ophthalmologic examination did not find heterochromia, Lisch nodules, or optic nerve glioma. She was otherwise developmentally appropriate for her age. There is no family history of pigmentary disorders.

Venous blood was collected with written informed consent from her mother. Sequencing was performed using the TruSight One (Illumina,