Vitiligo in a 9-year-old girl with Koolen-de Vries syndrome

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To the Editor:

Koolen-de Vries syndrome (KdVs), also known as 17q21.31 microdeletion syndrome, is a rare genetic disorder characterized by typical facial dysmorphism, congenital malformations in multiple organ systems, musculoskeletal anomalies, developmental delay, neonatal hypotonia, epilepsy, and intellectual disability [1]. Ectodermal anomalies have also frequently been reported. Koolen-de Vries syndrome is caused by either a *KANSL1* gene mutation, or a microdeletion of 17q21.31 which encompasses multiple genes, including *KANSL1*.

We report the case of a 9-year-old girl with KdVs who presented to our dermatology department for evaluation of progressive pigment loss on her upper and lower limbs, trunk, and face over the past three years. She was born at 36 weeks gestation via emergency Caesarean section owing to decreased fetal movements to a mother with Hashimoto thyroiditis and chronic plaque psoriasis. At birth, the patient weighed 2500 grams (25th percentile). The pregnancy was uneventful. Microarray-based comparative genomic hybridization performed at two years of age revealed a 0.5 megabase deletion in chromosomal region 17q21.31. As the patient grew older, she developed global developmental delay, hypotonia, epilepsy, and strabismus. Her medical history was negative for atopy or autoimmune diseases.

Clinical examination revealed subtle facial dysmorphism, including a long face, broad nasal bridge, and bulbous nasal tip. Sharply defined depigmented patches with central freckling were present over both knees, dorsal surfaces of the feet, toes and fingers, medial malleoli, elbows, flanks, and circumferentially around the lips and right eye (**Figure 1**). Dermoscopy of the lesions showed an absent pigmentary network and leukotrichia. Clinical features were in keeping with a diagnosis of vitiligo. The patient's family elected against treatment at the time of presentation.

Ectodermal anomalies appear to affect the majority of patients with KdVs; 67% in one study including a cohort of 45 individuals with KdVs [1]. Cutaneous anomalies reported in KdVs include multiple nevi, hyper/hypopigmentation, hyperkeratosis, café-au-lait macules, eczema, keratosis pilaris, ichthyosis vulgaris, acne vulgaris, piezogenic papules, and hemangiomas. Skin hyperpigmentation often

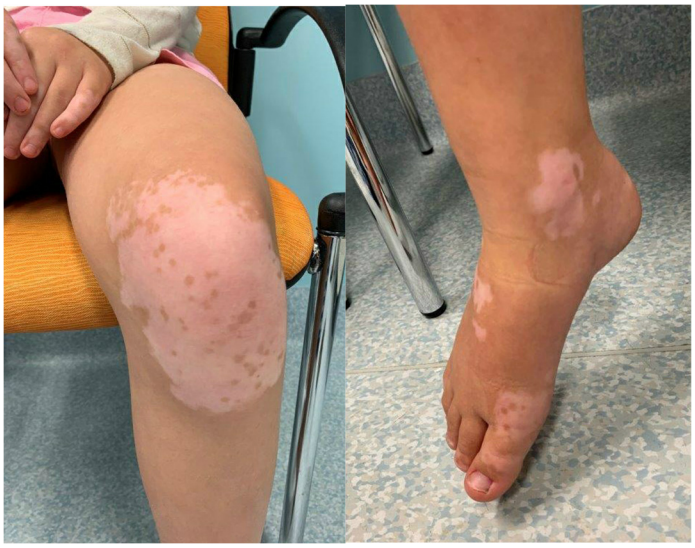

Figure 1. *Depigmented patches with well-defined borders are seen on the left knee and right foot in a patient with Koolen-de Vries syndrome.*

manifests as café-au-lait macules, generalized hyperpigmentation, or diffuse freckling [2]. Other ectodermal manifestations reported in patients with KdVs include dyspigmented hair, structural hair abnormalities, alopecia, brittle nails, and dental abnormalities [1-3].

Skin hypopigmentation has been reported in KdVs including three cases of vitiligo [1,4]. Digilio et al. hypothesized that vitiligo may be a phenotypic feature of KdVs and that one or more genes within the 17q21.31 segment may regulate the mechanisms associated with skin pigmentation or influence the expression of ectodermal features [5]. Autoimmunity has been hypothesized to play a role in some clinical manifestations of KdVs, as seen in one patient with KdVs who developed vitiligo, Addison disease and glutamic acid decarboxylase 65 autoantibodies [4]. It is unclear whether the development of vitiligo in our patient reflected a genetic predisposition given her family history of autoimmune diseases, a phenotypic feature of KdVs, or perhaps a combination of both entities.

The present case further confirms that vitiligo may be part of the clinical spectrum of KdVs. We support the current body of evidence proposing that cutaneous manifestations, including pigmentary abnormalities, should be considered among the major clinical features associated with this condition.

Potential conflicts of interest

The authors declare no conflicts of interest.

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