Dear Editors,

Incontinentia pigmenti (IP) is a rare X-linked dominant genodermatosis. While characterized by highly variable expression in females, the disease is frequently lethal in utero in males [1].

IP is caused by mutations in the IKBKG/NEMO gene [2]. Apart from neurological, ophthalmological and dental/jaw abnormalities, IP presents with skin lesions that typically occur in four successive and partly overlapping stages: vesiculobullous, verrucous, hyperpigmented, atrophic stage [1, 3]. Lesions associated with the vesiculobullous stage occur in the first weeks of life and disappear within the first 18 months. The verrucous stage begins during the first months of life and usually lasts several months. The end of the verrucous stage typically marks the beginning of the hyperpigmented stage, which may last until adolescence. This is followed by the atrophic stage which persists during life but does not occur in all patients [3]. In rare cases, such as in the context of an infection, there may be a flare-up of vesiculobullous lesions [4].

An 18-day-old girl was referred to our outpatient dermatology clinic. Clinical examination showed generalized erythematous and partly impetiginized vesicles, papules and plaques. Other findings included dirty-brown, hyperpigmented lesions arranged in a whorled pattern predominantly on the lower extremities as well as verrucous plaques on the upper extremities. The lesions were arranged along the lines of Blaschko (Figure 1). There had been no skin abnormalities at the time of birth. On the third day of life, the lesions had initially developed on the hands and subsequently spread to the extremities and trunk. The infant’s mother showed atrophic, hypopigmented lesions on her forearms. She reported that two of her three sisters have varying degrees of hypopigmentation and a niece allegedly had similar skin lesions as the patient during the first years of life.

A bacterial swab was positive for *Staphylococcus epidermidis* and *Enterococcus faecium*. Viral and fungal studies were negative. Histology of a skin biopsy showed a lamellar stratum corneum and focal parakeratosis. The most salient findings included eosinophilic spongiosis with dyskeratosis in all epidermal layers as well as numerous eosinophils (admixed with few lymphocytic cells) around the dermal papillae (Figure 2).

Molecular genetic testing of the patient and her mother provided evidence of the most common *IKBKG/NEMO* mutation: a heterozygous deletion of exons 4–10 NM_003639.3:c.400-?_*585+?del, which confirmed the diagnosis of IP.

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An unusual presentation of incontinentia pigmenti

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Figure 1 18-day-old infant showing vesicles on her right arm (a), whorled hyperpigmentation on the left thigh (b) and verrucous lesions on the fingers of the right hand along the lines of Blaschko (c).
While genetic testing is generally not mandatory for the diagnosis of IP, it is definitely indicated in clinically ambiguous cases. Genetic testing always requires the patient’s written consent or that of his/her legal representative.

The neurological and ophthalmological examination was unremarkable. In patients with IP, close follow-up is warranted in the first years of life to allow for early interventions in case of complications, e.g. retinal detachment [5, 6]. Because of the impetiginization, the patient was initially treated with IV antibiotics (amoxicillin/clavulanic acid for five days). Subsequent treatment merely consisted of basic skin care using an emollient (Excipial® Lipocream). At follow-up six months later, there were still whorled hyperpigmented lesions on the lower extremities and the chest.

Depending on disease stage, various differential diagnoses have to be considered. In stage 1 disease, it is essential to rule out infectious disorders such as a herpes simplex virus or a staphylococcal infection [1, 7, 8]. Other disorders presenting with skin lesions along the lines of Blaschko, such as Conradi-Hünermann-Happle syndrome, hypomelanosis of Ito or epidermal nevi, must also be ruled out [3].

Although our patient’s skin lesions were typical for IP our case is unusual in that three of four IP stages were already present at the 18th day of life and largely resolved within only a few months (Table 1).

There have been case reports in which stages 1 and 2 were not observed. It is believed that the early disease stages in these patients already occurred in utero [1, 9]. Unlike these cases our patient showed an accelerated evolution and resolution of the first three stages of IP which differs from the usual disease course described in the literature. Given the potential involvement of various organ systems, our patient will require multidisciplinary care, particularly during the first few years of life. More than 80 % of IKBKG/NEMO mutations in IP patients are recurrent or non-recurrent deletions that result in complete loss-of-function of NEMO/IKKgamma. Recurrent IKBKG/NEMO deletion of exons 4–10 in particular is associated with IP (78 % of cases) [10, 11].

Identification of the IKBKG/NEMO deletion in the patient and her mother not only confirmed the clinical diagnosis of IP but also enables prenatal molecular genetic testing for IP in this family.

Conflicts of interest
None.

Table 1 Clinical stages of IP (modified after [3])

| Stage       | Clinical presentation        | Onset and duration                                      |
|-------------|------------------------------|--------------------------------------------------------|
| 1) Vesiculobullous | Erythema and vesicles          | First weeks of life; regression within 18 months         |
| 2) Verrucous     | Verrucous papules and plaques  | First months of life; duration several months           |
| 3) Hyperpigmented| Hyperpigmentation              | Begins once stage 2 lesions subside; persists until adolescence |
| 4) Atrophic      | Hypopigmentation, alopecia     | Adolescence; persistent                                 |

Figure 2 Histological presentation.
Jannina Sigl¹, Julia Vodopiutz², Adrian Tanew³, Sonja Radakovic¹

¹) Department of Dermatology, Medical University of Vienna, Vienna, Austria
²) Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria

Correspondence to
Jannina Sigl, MD
Department of Dermatology
Medical University of Vienna
Währinger Gürtel 18–0
1090 Vienna, Austria
E-mail: jannina.sigl@meduniwien.ac.at

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