A case of incontinentia pigmenti reactivation after 12-month immunizations

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INTRODUCTION

Incontinentia pigmenti (IP; Bloch-Sulzberger syndrome) is an X-linked dominant genodermatosis that can have several cutaneous, dental, skeletal, neurologic, and ocular manifestations, including retinal detachment, seizures, paralysis, developmental delay, hair loss, and abnormal dentition.[1-3] Lethal for affected males in utero, IP presents overwhelmingly in females as a result of mutant X chromosome inactivation.[2] Lyonization of the X chromosome is what contributes to the reticular or whorled vesiculobullous pattern pathognomonic for IP. Eighty percent of IP patients carry mutations in the *NEMO* gene, which codes for nuclear factor κB (NFκB) essential modulator.[2] NFκB is crucial for the regulation of tumor necrosis factor (TNF)-induced apoptosis.[3] Reactivation is thought to occur when specific triggers (possibly infection, fevers, or vaccinations) reactivate pathways in residual mutant cells.[3]

CASE REPORT

We report on a 13-month old girl who presented to the Dermatology Clinic with erythematous vesicular plaques consistent with IP after receiving her 12-month immunizations (measles, mumps, and rubella; Haemophilus influenzae type B; and p*neumococcal conjugate vaccine*) on December 11, 2012. In the 2 weeks after immunization, erythematous, vesicular plaques developed on her left hand and right foot (Fig 1). The first vesiculobullous lesions to appear had, according to the mother's report, subsequently transformed into verrucous papules (Fig 2). According to the patient's mother, her previous immunizations had not resulted in similar lesions. The mother also denied that the patient had recent infections or fevers. Examination of the left thigh and flank found slightly hyperpigmented, whorled patches, with prominent vasculature. No diagnostic tests were ordered because she already carried a biopsy-supported diagnosis of IP completed at birth, and the classic appearance of the reactivation lesions was sufficient to make the diagnosis.[4] Reactivation of IP after 12-month immunizations was diagnosed.

As a neonate, her initial IP lesions involved the left thigh, extending to the groin, and her left flank. After the vesiculobullous stage, she maintained stable whorled hyperpigmented patches for months, with slightly atrophic areas interspersed with prominent vasculature. Mild ocular findings were noted, which were checked regularly by the patient's ophthalmologist. The patient's mother had a personal history of IP and currently presents with both hyper- and hypopigmented patches on her torso and left thigh.

Abbreviations used:

IP:	incontinentia pigmenti
NFκB:	nuclear factor κB
TNF:	tumor necrosis factor

DISCUSSION

Although paucity of evidence supports a vaccination-induced reactivation of IP, there is one reported case of a young child having a similar response after both her 12- and 18-month immunizations.[3] This patient, like ours, was the child of a mother with IP. Similar to our patient, this patient did not have IP recurrence after her 2-, 4-, and 6-month immunizations. There may be a link between the

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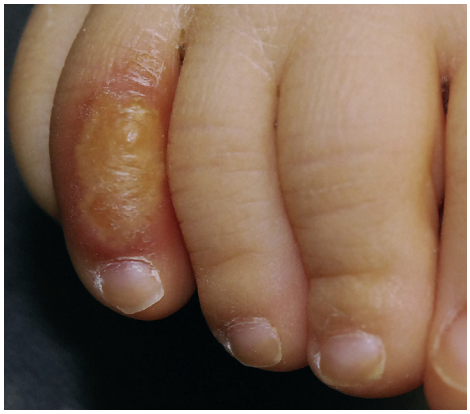

Fig 1. Vesicular plaque on the patient's right foot.

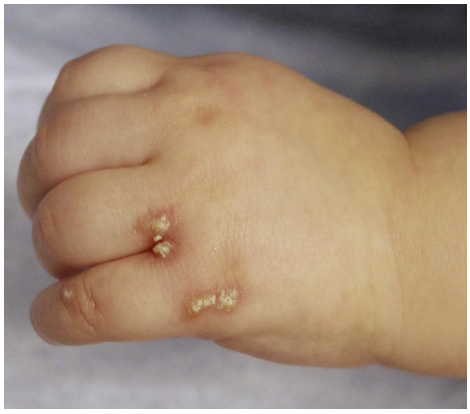

Fig 2. Verrucous papules on patient's left hand.

administration of the measles, mumps, and rubella vaccine, the first live vaccine introduced to children, and the reactivation of IP. Clinicians in the reported case confirmed the IP diagnosis with biopsy and confirmed a *NEMO* mutation via genetic analysis.[3] The patient did not report fevers or any other systemic complaints in addition to the 12- and 18-month immunizations.[3] Notably, previous upper respiratory infections and fevers had not induced IP-associated lesions.

Previous instances of late recurrences were most often associated with fevers and systemic infections.[5,6] Other instances of IP reactivation have been associated with the supplementation of estrogen to young children with incompletely formed external genitalia and with the use of laser therapy to reverse hyperpigmentation in old IP lesions.[7,8] Recurrence is not always associated with a specific trigger. Literature on the topic suggests that some recurrent IP manifestations are entirely unprovoked.[9]

Mutations in the *NEMO* gene, which is normally responsible for regulating immune responses and protection from TNF-induced apoptosis, lead to abnormal functioning of mutant cells when certain stresses are induced on the body.[10] The *NEMO* gene specifically forms the IκB kinase complex responsible for activating the NFκB pathway, which, in turn, protects cells from TNF-induced apoptosis. As a consequence of the mutation, residual mutant cells undergo unregulated apoptosis, which produces clinical manifestations consistent with IP. Interestingly, some females with these *NEMO* mutations do not exhibit the clinical symptoms. It has been hypothesized that some of these clinically unaffected women may have had favorable selection against mutation-activated cells early during prenatal development. Further genetic research is necessary to determine why some women with the genetic predisposition do not exhibit symptoms, whereas others have classical clinical manifestations.[2]

We report an additional case of IP reactivation after 12-month immunizations. The pathogenesis of IP, its triggers, and methods of prevention continue to raise countless questions. Although additional evidence is necessary to further elucidate the relationship between vaccinations and the reactivation of IP, it is evident that further investigation is warranted.

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