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CASE REPORT

Phacomatosis pigmentokeratotica or the Schimmelpenning-Feuerstein-Mims syndrome?

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Key Clinical Message

Cutaneous symptoms in some patients with clinical picture of Schimmelpenning-Feuerstein-Mims syndrome can include a speckled lentiginous nevus, also known as nevus spilus. Recent investigations show that somatic heterozygous HRAS mutations are present in the sebaceous and speckled lentiginous nevus tissues of patients with combination of two nevi.

Keywords

Congenital melanocytic nevus syndrome, nevus sebaceous, nevus spilus, phacomatosis pigmentokeratotica, Schimmelpenning-Feuerstein-Mims syndrome.

Introduction

Phacomatosis pigmentokeratotica was first identified in 1996 as a distinct type of the epidermal nevus syndrome [1]. On the skin, it is manifested as a combination of the linear nevus sebaceous and the speckled lentiginous nevus, also known as nevus spilus. Other associated features reported in patients with phacomatosis pigmentokeratotica most commonly included skeletal or neurological abnormalities [2, 3].

In turn, the linear nevus sebaceous is commonly observed as a part of the Schimmelpenning-Feuerstein-Mims syndrome (OMIM #163200), and the speckled lentiginous nevus – as the congenital melanocytic nevus syndrome (OMIM # 137550).

Molecular basis of these syndromes is presented by mutations in different genes, but HRAS mutations have been recorded in both. Moreover, Groesser et al. [4] identified heterozygous HRAS mutations present both in the sebaceous nevus and in the speckled lentiginous nevus tissues of patients with phacomatosis pigmentokeratotica. The analysis of various nonlesional tissues showed a wild-type sequence of HRAS, consistent with mosaicism [4]. Thus, phacomatosis pigmentokeratotica can now be categorized as one of the phenotypes of Schimmelpenning-Feuerstein-Mims syndrome as well as a variation in the congenital melanocytic nevus syndrome [5].

There have been described cutaneous abnormalities and extracutaneous defects in patients with the Schimmelpenning-Feuerstein-Mims syndrome. Mehregan and Pinkus [6] were first to outline the natural history of organoid nevi. The first stage is characterized by alopecia with absent or primitive hair follicles and numerous small hypoplastic sebaceous glands. At puberty, lesions become verrucous with hyperplastic sebaceous glands. Benign or malignant tumors develop at later stages. Schimmelpenning-Feuerstein-Mims syndrome is associated with variable abnormalities of the central nervous system, including mental retardation, as well as ocular anomalies and skeletal defects. Apparently, the extracutaneous defects noted in the congenital melanocytic nevus syndrome may differ noticeably

from those typical of the Schimmelpenning-Feuerstein-Mims syndrome.

Case Presentation

We report a 9-year-old boy admitted to our hospital for the laser treatment of extensive epidermal nevus. An advice of a dermatologist was required because of unusual cutaneous abnormalities (Fig. 1).

The patient born after the first pregnancy weighed 3.2 kg. The newborn had a neonatal jaundice that required a phototherapy. At birth, he was noted for some yellow smooth lesions on the scalp and face. Lesions were mostly confined to the left side of the head and only one of them on the upper lip had papilloma-like surface. At the age of 6 months, the infant had a clinical picture of multiple epidermal nevus with sebaceous features arranged along Blaschko lines and involved left side of the scalp and face, both sides of the neck, the chest, and the upper back. Lesions of the epidermal nevus on the scalp were hairless. Lesions were also localized on the eyelids and extended to their conjunctiva. The cornea of the left eye was cloudy, possibly due to the contact with lesions on the palpebral conjunctiva. In addition, a giant café-au-lait spot appeared on the right side of the boy's chest, abdomen, and hip extending across his back to the left side of the neck and left shoulder. Along with that, there were some small pigmented lesions around the large one. During the subsequent years, spots and papules of pigmentation have been developing within the giant café-au-lait lesion. They were not seemingly related to the sun exposure (Fig. 2).

By the age of 9, the patient had a giant congenital nevus-like nevus on the chest, abdomen, left hip, back, neck, and left arm composed of speckled lentiginous nevus and satellite melanocytic lesions. The congenital nevus-like nevus coexisted with epidermal nevus on the neck and the upper back. At the same time, pigmented lesions and the epidermal nevus expanded beyond the midline. Lentiginous and papular melanocytic lesions were noticed not only in the area of the café-au-lait spot but also in the area of epidermal nevus on the scalp and face (Fig. 3).

The boy had a severe scoliosis in the left thoracic curve pattern. The curve progression required an operation which was performed at the age of 8. A transpedicular system was used to correct and stabilize spinal segments. A speech delay and a mild mental retardation were also observed. Speech therapist worked with the patient until recently.

Investigations and Treatment

It is interesting that the patient was first diagnosed as a neurofibromatosis coexisting with a linear nevus sebaceous. Although the patient had hyperpigmented spots, no axillary or inguinal freckles, nor neurofibromas, optic nerve glioma, iris hamartomas, and typical long-bone anomalies have been found. Neither he had any first-

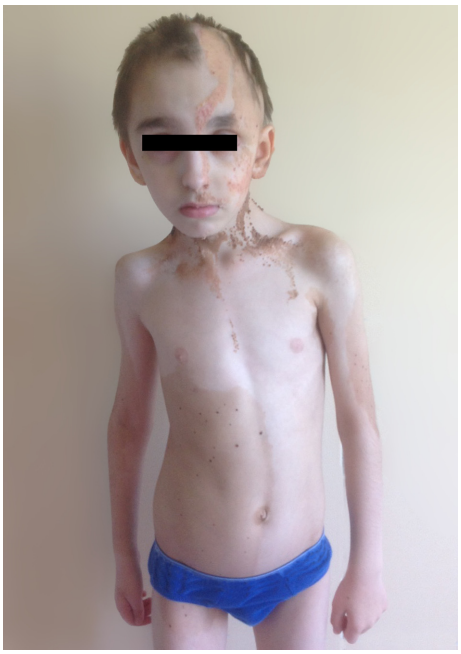

Figure 1. The patient with combination of two nevi: front view.

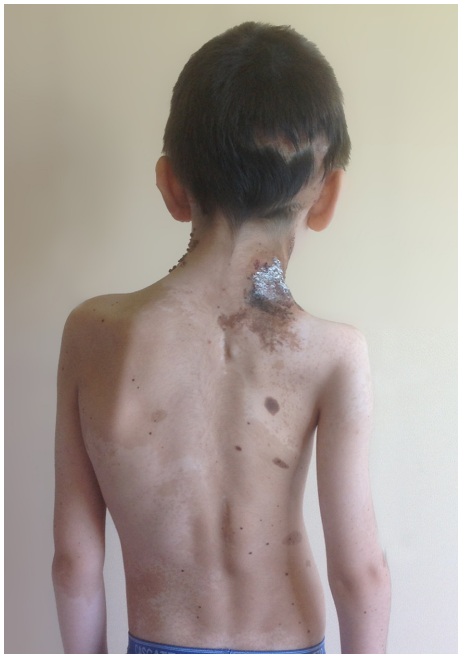

Figure 2. The patient with combination of two nevi: back view.

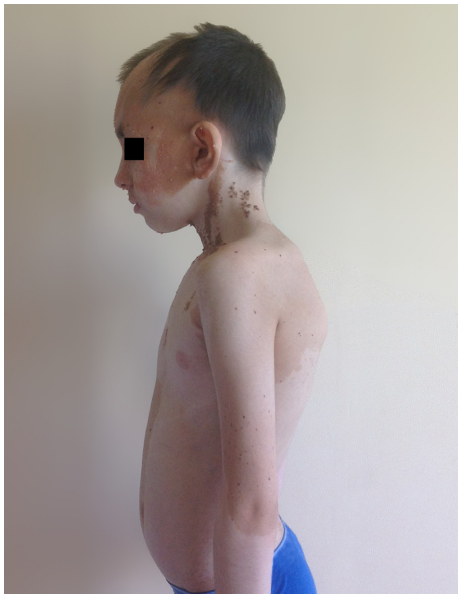

Figure 3. The patient with combination of two nevi: left side view.

degree relatives with neurofibromatosis type 1. MRI did not reveal any lesions indicative of neurofibromatosis type 2. All the results of investigations, including hematology panel, biochemistry panel, sonography, electrocardiogram, electroencephalogram, were normal. The patient was observed by the oncologist, and surgical excision of pigmented lesions was not needed. Two laser treatments of epidermal nevus located on the face and neck, as well as a radio-excision of lesions on eyelids, have already been undertaken under general anesthesia. Further laser treatment and plastic surgery of lesions on scalp are considered. An excision of some pigmented lesions might be needed before puberty, due to the possible risk of malignant transformation.

Comment

Phacomatosis pigmentokeratotica is caused by a postzygotic HRAS mutation in a multipotent progenitor cell. In light of a new hypothesis, the respective mutation in the multipotent progenitor cell gives rise to both cutaneous and extracutaneous abnormalities noted in phacomatosis pigmentokeratotica. The timing of the mutation during embryogenesis and differentiation potential of the cell in which it occurs are believed to be crucial determinants for the resulting phenotype [4]. Similarly, the hypothesis may explain clinical manifestations of the Schimmelpenning-Feuerstein-Mims syndrome which differs from phacomatosis pigmentokeratotica only in that the progenitor cell has lost ability to differentiate in the melanocytes at the time of a mutation. It is equally interesting to look at the congenital melanocytic nevus and the neurocutaneous melanosis. It is known that they are based on some mutations in the NRAS. Kinsler et al. [7] concluded that multiple congenital melanocytic nevi and neuromelanosis, as well as nonmelanocytic central nervous system lesions, result from somatic mosaicism and that the mutation in NRAS probably occurs in the progenitor cell during the development of the neural crest or neuroectoderm. The nevus spilus (HRAS mutations) and the congenital melanocytic nevus (NRAS mutations) are now considered as the congenital melanocytic nevus syndrome (NRAS, HRAS mutations), but at the same time the congenital melanocytic nevus is a part of neurocutaneous melanosis. As the congenital melanocytic nevus is a part of neurocutaneous melanosis, the nevus spilus could also be a part of the Schimmelpenning-Feuerstein-Mims syndrome (HRAS, NRAS, KRAS mutations).

In the presented clinical case report, all cutaneous and extracutaneous symptoms of phacomatosis pigmentokeratotica except nevus spilus are found in the clinical synopsis of the Schimmelpenning-Feuerstein-Mims syndrome. The nevus spilus used to be considered as the congenital nevus-like nevus, because of its onset and clinical picture which are distinct from the congenital melanocytic nevus. Therefore, in our opinion, cutaneous and extracutaneous symptoms of phacomatosis pigmentokeratotica match the Schimmelpenning-Feuerstein-Mims syndrome. Accordingly, the nevus spilus may be included in the clinical synopsis of the Schimmelpenning-Feuerstein-Mims syndrome that has been diagnosed in our patient.

Conflict of Interest

None declared.

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