Phacomatosis Cesioflammea with Cutis Marmorata-like Lesions and Unusual Extracutaneous Abnormalities: Is It a Distinct disorder?

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Introduction

Phacomatosis pigmentovascularis (PPV) is an umbrella term including several different skin disorders being characterized by the coexistence of a large vascular nevus and an extensive pigmented nevus. All of these types reflect postzygotic mosaicism and occur sporadically. In the past, they were taken as possible examples of nonallelic twin spotting,[1] but this hypothesis has recently been withdrawn by Happle[2] because both nevus flammeus and Sturge–Weber syndrome were found to originate from a postzygotic heterozygous \( GNAQ \) mutation,[3] thus excluding loss of heterozygosity as a mechanism explaining phacomatosis cesioflammaea. Recently, phacomatosis cesioflammea was found to be caused by postzygotic activating mutations in \( GNA11 \) and \( GNAQ \) genes.[4]

Within the group of PPV, the most frequently encountered form is phacomatosis cesioflammaea. Other distinct types include phacomatosis cesiromarmorata, phacomatosis spilorosea, and phacomatosis melanorosea [Table 1]. We here present a male infant with an extremely unusual combination of skin lesions in the form of nevus cesius, nevus flammeus, and cutis marmorata telangiectatica congenita (CMTC)-like lesions. Moreover, the boy had serious venous malformations, hepatosplenomegaly, and various other extracutaneous defects. Remarkably, a similar case has recently been published in this journal,[9] which is why we wonder if such unclassifiable cases may later qualify to be taken as a distinct disorder within the group of PPV.

Case Report

A 2-month-old boy, a product of nonconsanguineous parents, was admitted for increased head size, high-grade fever, and dark yellow discoloration of sclera and urine for the past week. There was no significant neonatal history. The mother reported a history of fever with a blisters eruption during the 2nd month of gestation. The rash had spontaneously resolved leaving hyperpigmentations that lasted for 2 months. His weight was 2.7 kg (<3rd centile). His head was large with open sutures of the anterior fontanelle. He had a coarse face...
with depressed nasal bridge. His skin was icteric, and the abdomen was distended. There were no petechiae or other signs of bleeding. He had a moderately enlarged palpable liver and spleen. A large bluish-gray macule covered the back, the buttocks, and the anterolateral part of the abdominal wall, compatible with a diagnosis of segmental dermal melanocytosis (nevus cesius). Moreover, an extensive nevus flammeus involved his face, neck, upper part of the chest, and the left arm [Figure 1a]. Histopathological examination of biopsies obtained from the two skin lesions showed findings compatible with segmental dermal melanocytosis and nevus flammeus. On the left side, an accessory preauricular tragus was noted [Figure 1b]. In the presternal and epigastric area, there was a thick, cord-like varicosity from which multiple thinner varicosities were radiating like roots of a tree. The legs showed marmorations as seen in cutis marmorata telangiectatica congenita [Figure 1c].

Fundus examination revealed absent macular foveal reflex, and the periphery of retina was tessellated. Hemoglobin was 6.4 g, total leukocyte count was 15,400/mm³, and platelet count was 161,000. His liver profile was abnormal with bilirubin 16.6 mg/dl, serum glutamate oxaloacetate transaminase 1072, serum glutamic pyruvic transaminase 234, alkaline phosphatase 481, and gamma-glutamyl transferase 102. Proteins were normal. His 25-hydroxy Vitamin D level was 3 ng/ml. Venereal disease research laboratory, rapid plasma reagin, TORCH tests were negative. The urine showed precipitation. Ultrasonography of the brain did not show any calcification or hydrocephalus. No intra-abdominal abnormality was seen apart from an undescended testis in the right iliac fossa. Echocardiography showed four tiny muscular ventricular septal defects with a left-to-right shunt. X-rays of limbs and thorax showed normal mineralization of bones with normal joint spaces and alignment. Bone length was normal, and no lytic or sclerotic lesion was present. Heart and aorta appeared normal on X-rays. The left brachiocephalic vein, and the major deep veins of the left arm were obliterated [Figure 2a-c]. The venous flow from the left internal jugular vein and arm was diverted into the right brachiocephalic vein through internal mammary collateralization. Contrast-enhanced computed tomography scan showed multiple anomalies involving the left subclavian, left brachiocephalic, and right inferior jugular veins [Figure 2d].

A diagnosis of unclassifiable type of PPV (phacomatosis cesioflamma overlapping with phacomatosis cesiomarmorata) was made. The parents of the child refused permission to obtain any more tissue samples for molecular analysis.

**Discussion**

The rather uncommon clinical presentation of this boy fulfills the criteria of PPV, but because of overlapping features, it is difficult to categorize this multisystem disorder within the present classification of PPV. Currently, this list includes four distinct types as summarized in Table 1. We prefer this new categorization.
to the time-honored classification of Hasegawa and Yasuhara because today, their Type I can no longer be accepted as a particular form of PPV, whereas some new types have meanwhile been described [Table 1].

For heuristic purposes, our patient’s disorder should be listed, for the time being, within the group of unclassifiable PPV, together with some previous reports on phacomatosis cesioflammea overlapping with CMTC-like lesions and on other unusual phenotypes. From a dermatological point of view, the present phenotype may represent a mixture of phacomatosis cesioflammea and phacomatosis cesiomarmorata. So far, however, it would be premature to describe such cases as a distinct entity with a specific name such as “phacomatosis cesio-flammeo-marmorata.” Future molecular research may throw more light on this issue. A limitation in the workup of the present case was the refusal of the parents to give permission to obtain additional tissue samples for molecular testing. Hence, the categorization of such unusual examples of PPV remains unsettled, so far.

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**Conflicts of interest**
There are no conflicts of interest.

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**What is new?**
- Herein we describe a further example of unclassifiable phacomatosis pigmentovascularis showing features of both phacomatosis cesioflammea and phacomatosis cesiomarmorata.
- This seems remarkable because similar phenotypes have previously been reported. Further molecular research may show whether these peculiar examples of phacomatosis pigmentovascularis deserve to be categorized as an arbitrary coincidence, or whether they represent a distinct entity that we propose be called “phacomatosis cesio-flammeo-marmorata.”

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