Phacomatosis Cesioflammea: A Case Report of a Newborn with an Unusual Mongolian Spot and Port Wine Stain

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Abstract
Phacomatosis cesioflammea is a rare congenital cutaneous disorder that presents with aberrant Mongolian spot and port-wine stain in a newborn. About half of reported cases develop extracutaneous symptoms, especially involving the central nervous system, so early diagnosis is key in managing these patients so that appropriate referral to a specialist is promptly initiated. This case report documents the process of evaluating a newborn with an unusual Mongolian spot and port-wine stain. A thorough list of differential diagnoses, including nevus simplex, arteriovenous malformations, infantile hemangiomia, Klippel-Trenaunay syndrome and Sturge-Weber Syndrome, was ruled out before ultimately diagnosing the patient with phacomatosis cesioflammea. After a year of close neurodevelopmental monitoring, the patient has not manifested any systemic complications, and his prognosis remains good.

Introduction
Phacomatosis cesioflammea is the most common subtype of a group of rare congenital cutaneous abnormalities known as phacomatosis pigmentovascularis (PPV). The Latin translation of phacomatosis cesioflammea, meaning “bluish gray” and “flame,” appropriately describes the classic appearance of congenital dermal melanocytosis (Mongolian spots) and nevus flammeus (port-wine stain). Cutaneous lesions alone are largely asymptomatic, but approximately 50% of cases have systemic involvement, which usually presents within the first months of life. For this reason, a complete physical, including a dilated ocular exam by an ophthalmologist, and close neurodevelopmental monitoring are imperative parts of management. Furthermore, keeping in mind a broad differential is prudent when diagnosing any rare disorder so as not to overlook a more common condition with similar presentation. This case report documents the process of diagnosing a newborn with phacomatosis cesioflammea and subsequent management considerations.

Case Report
A healthy term African-American male, born vaginally after an uncomplicated pregnancy to a 23-year-old G1P1, presented with unusual skin findings on initial newborn exam (Figure 1). An extensive Mongolian spot covered his right flank, buttock, and thigh (Figure 2), and a large port-wine stain extended from his chest to the fingertips of the right extremity (Figure 3). A 6 mm x 20 mm café-au-lait spot was also noted on the right lower back. Limbs were symmetric, without leg-length or limb-girth discrepancies. History and clinical exam were otherwise unremarkable. Family history was significant only for eczema in his mother.

The first task at hand was to formulate a list of differential diagnoses. Vascular birthmarks such as port-wine stains are common findings in a newborn, either in the absence of or in association with congenital cutaneous syndromes. Port-wine stains are low-flow capillary malformations that present as blanchable, red or pink patches in 0.1% to 2% of newborns. Nevus simplex, also known as “salmon patch” or “stork bite,” is evident in 80% of newborns and may be similar in appearance to a port-wine stain. Unlike this patient’s vascular markings, nevus-simplex patches have indistinct borders, favor the midline such as the nape of the neck or eyelids, and resolve spontaneously. Arteriovenous malformation, another vascular cutaneous finding, may present as macular-vascular patches that generally possess a thrill and grow over time. Infantile hemangiomas, the most frequently encountered type of vascular tumor, often appear at birth as telangiectasia with surrounding pallor due to vasoconstriction. These lesions may resemble port-wine stains in early stages and then enlarge in the first few years of life before spontaneously resolving.

The prominence and unilaterality of the patient’s port-wine stain, preferentially distributed to the right upper extremity, raised concern for presence of an associated syndrome such as Klippel-Trenaunay syndrome (KTS) or Sturge-Weber syndrome (SWS). KTS is a congenital malformation of the capillary, venous, and lymphatic systems in the extremities. Cutaneous findings classically present with unilateral extremity enlargement from underlying musculoskeletal hypertrophy, visceral hemangiomas, and venous varicosities. SWS presents with facial port-wine stain, leptomeningeal capillary malformations, and central nervous system (CNS) abnormalities including seizures, mental retardation, glaucoma or neurologic deficits. Cutaneous manifestations are often progressive and
bilateral. After further evaluation, KTS and SWS were placed low on the list of differential diagnoses given that the patient had no note of leg- or arm-size abnormalities and no facial rashes, and these diagnoses would not adequately explain the patient's extensive Mongolian spot.

Mongolian spots are the most common type of hyperpigmented lesions in a newborn, especially in Asian, African American, and Hispanic populations. These lesions are benign and present as blue-to-gray macules due to delayed disappearance of dermal melanocytes deep in the dermis. Pigment is usually located near the sacral and buttock area and fades within the first two years of life. Lesions located in extrascral areas are known as "aberrant" and may raise concern for underlying disorders. For example, perioral Mongolian spots have been reported in 20% to 50% of patients with cleft lip. There have also been cases of persistent ventrally and dorsally distributed Mongolian spots associated with certain lysosomal-storage disorders.

The patient was eventually given a working diagnosis of phacomatosis cesioflamaemea, which was later confirmed by dermatology consultation. This cutaneous disorder adequately explained the patient's unusual presentation of Mongolian spot and port-wine stain. The overall anticipated prognosis for this particular patient is good. The absence of systemic involvement is especially encouraging. Close contact has been maintained with the patient's mother and pediatrician, who report he is happy and developing appropriately. He had a dilated ocular exam per ophthalmology, which was normal, and is to follow up annually with dermatology to monitor cutaneous lesions.

**Discussion**

Phacomatosis pigmentovascularis, or PPV, is a group of rare congenital cutaneous abnormalities diagnosed clinically by the coexistence of pigmented nevi and vascular malformations. The first case of PPV was described in 1947 by Ota et al., who categorized the disorder into types I through V, with subtype "a" for cutaneous involvement only and "b" for presence of extracutaneous findings. In 2005, a simpler classification system was established by Happle involving four main groups: phacomatosis cesioflamaemea, phacomatosis spilorosea, phacomatosis cesiomarmorata, and unclassifiable PPV. Phacomatosis cesioflamaemea, or PPV type II, is diagnosed by the presence of aberrant Mongolian spots and port-wine stain. Additional cutaneous findings may include nevus anemicus (hypopigmentation due to permanent vasoconstriction), nevus of Ota (pigmentation along the first or second branches of the trigeminal nerve), cafe-au-lait macules, CNS involvement or ocular symptoms. Prognosis of the disorder largely depends on the presence of systemic disease.

Roughly 250 total cases of PPV have been reported worldwide, with phacomatosis cesioflamaemea accounting for 77% of these cases. Studies reveal a slight female predominance as well as an increased incidence in Argentinian, Hispanic, and Japanese populations. Limited literature of twin studies in PPV strongly suggest twin discordance, in which monozygotic twins of PPV patients are unaffected.

The pathogenesis of PPV is largely unknown. The most promising hypothesis involves "twin spotting" or didymosis, a phenomenon well-studied in plants and animals. Didymosis represents a specific form of somatic recombination whereby two neighboring but genetically different mutant clonal cells sporadically cross over to form distinctive homozygous cell lines. In the case of PPV, this process likely occurs in genes coding for vessel and melanocyte development, thus resulting in the mosaic appearance of both vascular and pigmented nevi.

Skin lesions alone are largely asymptomatic and may lighten over time. However, approximately 50% of PPV cases have systemic involvement, usually appearing within the first months of life. Research suggests a correlation between the amount of cutaneous involvement and an increased risk for multi-systemic complications. The central nervous system is most commonly affected, presenting with seizures, cerebral atrophy, neurodevelopmental delay, psychomotor retardation, external hydrocephalus, stroke, and intracerebral hemorrhage. Common ocular findings include glaucoma, episcopal vascular malformations, conjunctival melanocytosis, primary acquired melanosis, epiretinal membrane, vitreous hemorrhage, pigmented cataracts, amyloid, and related choroidal melanoma. Other complications include atrial septal defect, renal agenesis, umbilical hernia, idiopathic facial paralysis, diabetes insipidus, vitiligo, hyper IgE, IgA deficiency, pyogenic granuloma, cavernous hemangioma, scoliosis, premature tooth eruption, macrocephaly, Arnold-Chiari type I, sydactyly, bilateral deafness, and eczema. Some reports note an association with KTS and SWS.

Initial workup should include a complete physical exam, close neurodevelopmental monitoring, and a thorough dilated ocular exam by an ophthalmologist. No treatment may be warranted in patients with cutaneous findings only, but for cosmetic purposes a pulsed dye laser can be used for nevus flammeus and a Q-switched laser for pigmented nevi. These procedures should be performed in childhood before school age for the best results. Evidence of extracutaneous involvement may require further evaluation with early referral and prompt treatment to optimize patient outcome.

**Conclusion**

Mongolian spots and port-wine stains can be common findings on initial newborn exams. Special attention should be paid when dealing with atypical presentations of these otherwise-benign pigmented and vascular birthmarks, or if the two present simultaneously such as in phacomatosis cesioflamaemea. Upon diagnosis, a thorough physical exam should be performed, including a dilated eye exam by an ophthalmologist and close monitoring for signs of neurodevelopmental delay, to assess for extracutaneous manifestations. In patients with cutaneous findings alone, prognosis is good, and treatments such as pulsed dye laser or Q-switched laser are optional for cosmetic purposes. Patients with extracutaneous findings, which mainly involve the central nervous system, may require referral to a specialist for further management as indicated. While phacomatosis cesioflamaemea is a rarely reported disorder, physicians should keep it in mind when evaluating any newborn with prominent and unusual birthmarks.

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