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CASE REPORT – OPEN ACCESS

Fatal Blue Rubber Bleb Nevus Syndrome in a Newborn

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ABSTRACT

Background: Blue rubber bleb nevus syndrome (BRBNS) is a rare, multifocal venous malformation. It most commonly affects the skin and the subcutaneous tissues or the viscera, especially the gastrointestinal tract, and less often the central nervous system. Diagnosis is based on clinical, radiological, and histopathological features. There is currently no medically curative treatment; however, sirolimus, an oral immunosuppressant drug, has recently been used effectively in patients with BRBNS.

Case Report: Presently described is a case of neonatal BRBNS. The infant was born with diffuse skin and visceral organ involvement. In addition to supportive therapy, such as blood product transfusions, and excisions of the lesions, propranolol, corticosteroid and sirolimus treatment was administered, but without response.

Conclusion: The patient died as a result of massive bleeding in the endotracheal tube, possibly due to lesions located in the lungs. To the best of our knowledge, this has not previously been reported in the literature.

Keywords: Hemangiomas, neonatal, vascular malformation, vascular tumors

INTRODUCTION

Blue rubber bleb nevus syndrome (BRBNS) is a rare, multifocal venous malformation that may appear at birth (30%), in infancy (9%), or early childhood (48%). It most commonly affects the skin and the subcutaneous tissues (93%), or the viscera, particularly the gastrointestinal (GI) tract (76%), and less often, the central nervous system (13%). Approximately 15% of cases have a family history of BRBNS, and it has been associated with an autosomal dominant pattern of inheritance. The most common symptoms are GI bleeding and secondary iron deficiency anemia. Diagnosis of BRBNS is based on clinical, radiological, and histopathological features. There is currently no medically curative treatment. In addition to surgical removal of the lesions, several traditional treatment modalities with anti-angiogenic drugs, such as corticosteroids, propranolol, interferon-alpha, and octreotide, have been used, but the results have been poor. Recently, sirolimus, an oral immunosuppressant drug used in kidney transplant to prevent rejection, has been used effectively. This novel therapeutic agent seems to offer the advantage of being well-tolerated and has controlled the major morbidities of the syndrome (1–4).

This report describes a case of neonatal BRBNS. The infant was born with diffuse skin and visceral organ involvement, and despite various therapeutic interventions, she died due to massive bleeding in the endotracheal tube.

CASE REPORT

A full-term, female newborn delivered by elective cesarean section in a secondary hospital was admitted to the neonatal intensive care unit on the second day of life due to disseminated dermatosis. The family history revealed no consanguinity or significant history of vascular disorders, other than thalassemia carriage in the mother.

The results of a physical examination were a weight of 4210 g, a body temperature of 37°C, a respiratory rate of 56/minute, a capillary refilling time of <3 seconds, and a blood pressure of 60/34 (42) mmHg with a systolic murmur (grade ≤3/6, localized on the left side of the sternum). There was also edema on the right side of the labia major and the lower limbs. Furthermore, there were multiple bluish, rubbery skin lesions on the face, trunk, upper and lower limbs, palms, soles, buttocks, and vulva, some of which were pedunculated and hemorrhagic (Fig. 1).

Laboratory tests revealed a hemoglobin level of 10.2 g/dL and a platelet level of 19.000 µ/L. The other parameters of a complete blood count, coagulation profiles, and biochemical results were within the normal range. Imaging studies (abdominal ultrasound, thoracic/abdominal computed tomography, abdominal/pelvic and brain magnetic resonance imaging) showed diffuse visceral solid organ involvement (brain, lungs, liver, spleen, and kidneys) with multiple vascular malformations and rounded lesions (Fig. 2).

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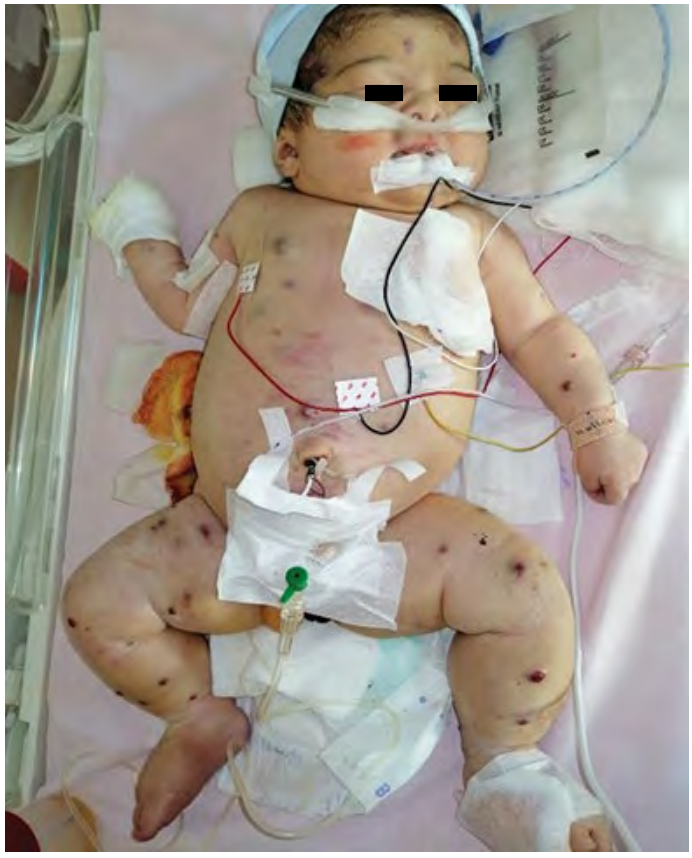

Figure 1. Multiple bluish, rubbery skin lesions on the face, trunk, upper and lower limbs, palms, soles, buttocks, and vulva, some of which were pedunculated and hemorrhagic

Once pathological evaluation confirmed lesions consistent with hemangioma, the patient was diagnosed with BRBNS.

Due to bleeding from the skin lesions, GI tract, and into the endotracheal tube, blood product (erythrocyte, platelet, and fresh frozen plasma) transfusions were required as often as every 2–3 days. In addition to the transfusions and excision of the pedunculated lesions, topical surgical blood stopper agents were also used. Despite these interventions, she remained severely anemic.

Daily propranolol therapy was initiated at a dose of 1 mg/kg/day on the 3rd day of life and the dose was increased to 2 mg/kg/day on the 6th and 3 mg/kg/d on the 24th day of life. After the first week of propranolol therapy, a steroid was added at a dose of 2 mg/kg/day due to an increase in size and number of lesions. At the third week, a trial of daily sirolimus therapy was initiated at a dose of 0.2 mg/ml/day (equal to a dose of 0.05 mg/kg/day) and gradual reduction of the steroid was planned. Within 3 days of sirolimus therapy, the dosage was increased to 0.4 mg/ml/day. The infant died on the fourth day of sirolimus therapy (postnatal 38th day of life), due to massive bleeding into the endotracheal tube.

DISCUSSION

Vascular malformations are often congenital lesions derived from an interrupted or uncommon development of vascular structures. The International Society for the Study of Vascular

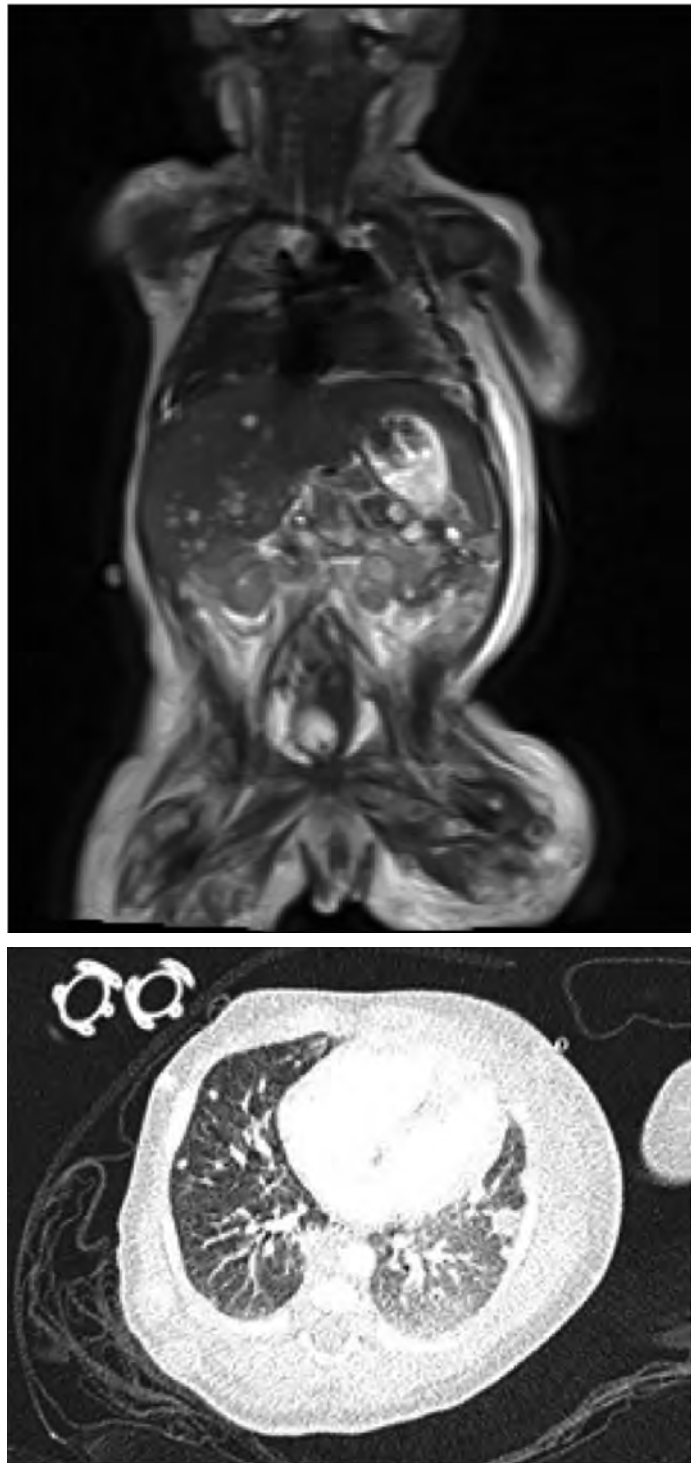

Figure 2. Magnetic resonance and computerized tomographic images revealing diffuse subcutaneous and visceral solid organ involvement with multiple rounded vascular lesions consistent with hemangioma

Anomalies (ISSVA) classification system divides vascular anomalies into 2 main categories: vascular malformations and vascular neoplasms. Vascular malformations are further subdivided into 2 groups: slow-flow malformations (with venous, capillary and/or lymphatic components) and fast-flow malformations (with arterial components) (3, 4).

BRBNS is classified in the slow-flow venous malformation subgroup. In addition to the typical cutaneous lesions of the syndrome usually present at birth or developing in early childhood, visceral involvement may present later in life. Most of the literature describes cases in the childhood or adult age groups. To our knowledge, our case is the most severe form of BRBNS ever reported, with the involvement of skin and almost all of the visceral organs at birth (3, 5–9).

In general, BRBNS is known as a sporadic disorder, sometimes associated with an autosomal dominant inheritance pattern with a locus on chromosome 9p. Regrettably, we were unable to conduct a genetic study in this case to investigate the potential presence of any known or new somatic mutation for the disease (7).

Aside from conservative approaches, including excision of the lesions, blood product transfusions, and iron supplementation, there is currently no known curative treatment for BRBNS. Studies have revealed that no therapeutic agents, such as propranolol, octreotide, corticosteroids, interferon alpha, vincristine, thalidomide, and antifibrinolytics, have demonstrated sustained or superior efficacy in reducing vascular malformations (1, 2).

In this case, excisions and multiple blood and fresh frozen plasma transfusions were performed in an effort to control the bleeding from the lesions of both the skin and visceral organs, but it was not sufficient. As the number and size of the lesions continued to increase despite the medical therapies of propranolol and then a corticosteroid, we administered sirolimus based on the few case reports describing it as a successful agent to treat BRBNS (2–4). It is not possible to make a comment on the efficacy of this agent in our case due to the loss of the patient on the fourth day of sirolimus therapy. In our opinion, better results may have been possible if sirolimus therapy had been initiated as early as the first few days of postnatal life.

GI bleeding, thrombotic complications, and coagulopathies have been reported to be the major causes of death or morbidity in BRBNS patients. Our patient died as a result of massive bleeding in the endotracheal tube, possibly due to bleeding of pulmonary lesions. To the best of our knowledge this location has not previously been reported in the literature (9, 10).

In conclusion, additional studies related to the treatment of BRBNS are necessary to improve survival.

Informed Consent: Written, informed consent was obtained from the patient's family for the publication of this case report and the accompanying images.

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