Blue Rubber Bleb Nevus Syndrome Causing Refractory Anaemia

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Abstract

Blue Rubber Bleb Nevus Syndrome (BRBNS) is a rare angiomatosis characterized by distinctive cutaneous and gastrointestinal venous malformations that result in gastrointestinal haemorrhage and iron-deficiency anaemia secondary to the bleeding episodes. We hope to emphasize the possibility of recurrent melaena in BRBNS and heighten physicians' awareness about the disease to contribute to its early detection.

Introduction

Blue rubber bleb nevus syndrome (BRBNS) is an uncommon condition manifested by cutaneous and gastrointestinal venous malformations that usually lead to occult or massive gastrointestinal bleeding and anaemia. We present here a rare case of BRBNS who presented with severe iron-deficiency anaemia, and was diagnosed and managed accordingly.

Case Report

A 17-year-old Muslim boy presented to the Medicine outpatient of RG Kar Medical College, Kolkata on 20th January 2009 with generalised weakness and easy fatigability since last 1 year. He was symptom-free till about a year back when he developed similar complaints, for which he had received 3 units of blood transfusion and had felt better. He gave a history of passing black tarry stool off and on since the last 18 months without any abdominal pain. There was no history of any substance abuse or analgesic intake. Similar complaints were not present in other members of his family and he was not born of a consanguineous marriage. The patient was found to be severely anaemic and was admitted for evaluation of his anaemia, melaena, and for blood transfusion.

On examination, he was found to be severely anaemic and had a pulse rate of 100/minute, regular, and BP of 120/72 mmHg. There were multiple bluish, bluish-black rubbery blebs (nevi), measuring 5 mm to 1 cm on the soles of both feet (Fig. 1), a similar lesion on the palm of the left hand between the thumb and index finger (Fig. 2), and two larger (around 1.5 cm) maculopapular bluish nevi on the glans penis in the 9 o’clock and 3 o’clock positions were noticed (Fig. 3). The lesions were non-tender, compressible with wrinkled surface and had never bled. He had first noticed them around 4 years back when he...
A diagnosis of ‘Blue Rubber Bleb Nevus Syndrome’ was made on the basis of the typical skin lesions which were rubbery discrete compressible blebs increasing in number over the years, features of iron-deficiency anaemia, positive occult blood in stool, multiple bluish nevi in the stomach, oesophagus, duodenum and colon on GI endoscopy, and histological picture of ectatic venous channels (venous malformation) on skin biopsy.

The patient was counselled about the natural history of the disease and the chronicity of the condition which is disabling but not fatal in majority. He was explained about the benign nature of the disease, and the need for iron supplements and blood transfusion. He was given blood transfusion and discharged with iron supplements, along with an advice for regular follow-up.

**Discussion**

‘Blue Rubber Bleb Nevus Syndrome’ or ‘Bean Syndrome’ is a congenital anomaly characterised the presence of multiple venous malformations, mainly in the skin and GI tract, but can be present in any other tissues and organs. It is a very rare condition with less than 200 cases reported world-wide.1 The condition was first identified in 1860 by Gascoyen, but it was described in detail by William Bean in 1958 who distinguished these ‘blue rubber bleb’ lesions from other vascular lesions of the skin and hence the condition is also known as ‘Bean Syndrome’. The actual cause of the condition is still unknown. There has been suggestion of an autosomal dominant mode of inheritance, though most cases seem to be sporadic.

The skin lesions are characterised by the presence of blue, blackish-blue compressible blebs of varying size (5 mm to few centimetres) and in varied hue. Most lesions are non-tender, though some may be occasionally painful. There are three types of skin lesions:2 (a) blue, rubbery, blood-filled blebs with wrinkled surface that are easily compressible, leaving an empty sac that refills on application of pressure, (b) large, cavernous lesions which can compress adjacent structures, (c) blue, irregular macules. They are usually discrete and multifocal, mainly present over the trunk, soles and palms but may be seen anywhere in the skin. The skin lesions rarely bleed. The lesions, being venous malformations and hence of embryonic origin, are present at birth but may be first noticed in childhood or may become apparent later in adolescence. They have a tendency to increase in number as the person grows older and in some patients there may be hundreds to thousands of such lesions.
Lesions in the GI tract always develop in BRBNS, and can be numerous and diffuse, extending from the oral to anal mucosa. In contrast to the skin lesions which rarely bleed, the GI lesions frequently bleed. Most patients bleed mildly but chronically from the GI tract resulting in iron-deficiency anaemia. In some instances, patients may present with acute and massive GI haemorrhage. Sometimes intussusception and volvulus may occur as a result of the GI lesions. The lesions may also be present in nasal cavity, nasopharynx, eyes, thyroid, parotids, central nervous system, skeletal muscles, pleura, peritoneum, pericardium, mesentery, synovium, lungs, kidneys, liver, spleen, penis, vulva and bladder. There may be associated bony deformity due to the mass effect of the adjacent venous malformations. Haematological complications like chronic disseminated intravascular coagulation and consumptive coagulopathy can occur.

The condition is suspected by the presence of typical skin lesions, history of bleeding from the GI tract and features of iron-deficiency anaemia. Patients are positive for occult blood in stool. GI tract lesions can be evaluated by endoscopy, barium studies and nuclear imaging. Endoscopy is preferred to barium studies, as barium studies show polypoid filling defects and cannot identify the vascular nature of the lesion. Upper and lower GI endoscopy show the presence of multiple nodular bluish venous malformations. Lesions in the small intestine can be detected by video capsule endoscopy or push enteroscopy.

Histological examination of the skin and GI lesions show dysplastic venous channels in lower dermis and subcutaneous tissue with large, irregular spaces containing RBCs and fibrinous material. Spaces are lined by a single layer of thin tissue with large, irregular spaces containing RBCs and fibrinous material. There may be associated bony deformity due to the mass effect of the adjacent venous malformations. Haematological complications like chronic disseminated intravascular coagulation and consumptive coagulopathy can occur.

Differential diagnoses include hemorrhagic hereditary telangiectasia (Rendu-Weber-Osler disease), Maffucci syndrome, Klippel-Trenaunay/Parkes-Weber syndrome, and polyposis syndrome like Peutz-Jeghers syndrome. Rendu-Weber-Osler disease is an autosomal dominant condition characterised the presence of telangiectasias on the skin and mucous membranes. Telangiectasias are usually present on the lips, oral and nasopharyngeal membranes, tongue, and periungual areas, and lack of involvement of these sites suggest an alternative diagnosis. The lesions are cherry red in colour and are of the size of millet seeds. Histologically, the capillaries and venules are involved. The condition can be differentiated from BRBNS by the typical appearance, distribution and histological picture. Maffucci syndrome is characterized by benign enlargement of cartilage (enchondromas), bony deformities, and dark, irregularly shaped haemangioma. Klippel-Trenaunay/Parkes-Weber syndrome consists of i) a vascular nevus involving the lower limb, ii) varicose veins limited to the affected side and appearing at birth or in childhood, iii) hypertrophy of all tissues of the involved limb, especially the bones. Symptomatic GI tract involvement is rare and the most common GI symptom is hematochezia. The typical features with bony deformity and lack of significant GI symptoms differentiate it from BRBNS. The vascular nature of the lesion in BRBNS can be easily differentiated from polyposis syndrome like Peutz-Jeghers syndrome.

The treatment of the GI lesions and bleeding is usually supportive and symptomatic in the form of blood transfusion and iron-supplements. Pharmacological agents like interferon, corticosteroids and octreotide have all been tried, and the results have been largely disappointing with either no response or recurrence of GI bleeding after cessation of treatment. Endoscopic sclerotherapy, band ligation and photocoagulation have provided mixed results. Surgical resection of the lesions is rarely successful due to the extensive and diffuse nature of lesions in the GI tract. The skin lesions rarely bleed and require no treatment except for cosmetic reasons. They may be treated with neodymium-yttrium-aluminium-garnet laser. Larger lesions can be treated with cutaneous sclerotherapy with ethanol or sodium tetradecl.

**Conclusion**

BRBNS is a rare condition characterized by venous malformations in the skin and the GI tract. The presence of this condition obviously highlights the importance of endoscopy in young patients presenting with persistent anemia and a positive occult blood test in stool, moreover it also emphasizes the importance of endoscopy in young patients presenting only with iron-deficiency anemia, or anemia with typical skin lesions with or without a positive occult blood test in stool. The presence of cutaneous lesions typical of BRBNS should also alert the physician about the potential for intracranial vascular malformations. The patient should be counselled about the chronicity of this condition and the need for regular follow-up.

**References**