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A CASE OF BLUE RUBBER BLEB NEVUS SYNDROME

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ABSTRACT

We report a 16-year-old Indian boy diagnosed with Blue Rubber Bleb Nevus syndrome, which is a rare venous malformation that goes overlooked in most case scenarios. He had presented with long standing history of fatigue, melena with a past history of surgery for a vascular malformation and also had multiple bluish skin plaques. He was evaluated and was found to have iron deficiency anemia. Considering the history of melena, upper GI endoscopy was done, which revealed multiple vascular malformations, and so did colonoscopy. Patient was offered multidisciplinary team (MDT) approach involving Internal Medicine, Gastroenterology, Dermatology and Plastic surgery

INTRODUCTION

Blue Rubber Bleb Nevus syndrome (BRBNS or Bean's syndrome) is a rare disorder characterized by multifocal venous malformations in the skin and internal organs usually the gastrointestinal tract associated with iron deficiency anemia and intestinal hemorrhage.[1] It was first recognized by Gascoyen 2 in 1860, and 100 years later William Bennett Bean [3] described BRBNS in detail and coined the term Blue rubber bleb nevus syndrome. It is so rare that only 200 cases have so far been reported in the literature. 4 The incidence of reported BRBNS is very low [5]

CASE PRESENTATION

A 16-year-old Indian boy presented with history of fatigue and melena for the past 4 years. At the time of birth, he had a small bluish swelling over the occipital region which had gradually increased in size and at 4 years of age MRI Brain was done which showed it to be a 7.5x5x3cm vascular lesion and it was excised at 4 years of age. On examination he had pallor and had multiple cutaneous bluish raised lesions of rubbery consistency of various sizes over his entire body. The lesions were, bluish, bleb- like, nodular, soft, 0.5-5.0 cms in size, spherical with smooth/verrucous surface. Nodules were partially compressible with feeling of dermal herniation and refilled slowly on releasing the pressure. The lesions were present over his upper and lower limbs, abdomen and face.

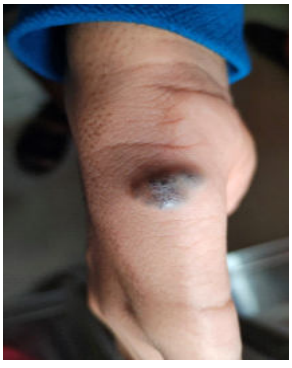

Figure 1: Bluish rubbery lesion over left hand

In view of fatigue and melena, blood tests were done to detect anemia and it showed a picture of iron deficiency anemia (Hemoglobin- 4.5 g/dL, MCV- 56.1 fL, Serum Ferritin- 15.98 µg/L, Serum Iron- 20 µg/dL, peripheral smear showing microcytic hypochromic anemia). As the boy presented with melena, gastrointestinal loss as cause of iron deficiency anemia was considered and evaluated. His stool occult blood was positive. An upper gastrointestinal endoscopy was done, which showed multiple bluish purple vascular lesions in duodenum. Similar lesions were seen in colon and jejunum on colonoscopy and small bowel push enteroscopy. As the boy had bluish rubbery cutaneous lesions, USG of the cutaneous lesions were done, which revealed it to be vascular malformation. X-ray of hands and feet showed no bony abnormalities. In view of vascular malformations of skin and gastrointestinal tract associated with iron deficiency anemia and melena, the possibility of Blue Rubber Bleb Nevus syndrome was considered.

The anemia was corrected, by giving iron supplements and blood transfusions. Biopsy of the cutaneous lesion is planned. Capsule endoscopy/Balloon Enteroscopy is planned for the management of the intestinal vascular lesions.

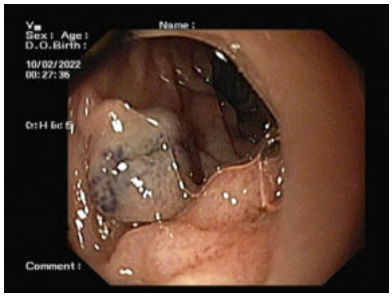

Figure 2: Multiple blueish-purple polypoidal lesions seen, one lesion 0.5x0.5cm in D2, two lesions-1x1cm and 1x0.5cm in proximal and distal D3 respectively

DISCUSSION

Blue Rubber Bleb Nevus syndrome is a rare syndrome of venous malformations that arise in the skin, soft tissues and

gastrointestinal tract. It may involve other organ systems including the liver, spleen, heart, eye, and central nervous system. Due to its low incidence and the haemangioma-like appearance, clinicians often make an incorrect diagnosis. It is usually a sporadic disorder, though autosomal dominant mode of inheritance involving locus on chromosome 9p and somatic mutations (double cis mutations) in TIE2 are also possible. THE TIE 2 gene (also known as TEK) encodes a protein called TEK receptor tyrosine kinase which is a transmembrane receptor involved in multiple steps of angiogenesis. The TEK receptor is constitutively active in the blue rubber bleb nevus syndrome due to somatic activating mutations. This leads to unregulated angiogenesis.6 According to the ISSVA classification of vascular anomalies, this syndrome belongs to the simple venous malformation(non-neoplastic) category.[7]

Patients present at birth or in early childhood with multiple blue to violaceous soft compressible nodules on the skin or mucous membranes. They are often born with a "dominant" lesion and develop numerous venous malformations over their lifetime. The typical skin lesions are described as rubbery in consistency and may be painful or tender when compressed. The size of the lesions ranges from only a few millimetres in diameter to up to 4 to 5 cm in diameter. They can increase in size with time, and more lesions may develop in the skin or gastrointestinal tract. The small bowel is the most common site of gastrointestinal tract involvement. As a result, patients may present with severe iron deficiency anaemia from recurrent gastrointestinal haemorrhage. Venous malformations are slow-flow lesions, making them prone to thrombosis. Thrombosis presents as an erythematous, warm swelling that may be tender to palpation.[8]

Ultrasound is the initial diagnostic study of choice as it is the least invasive. Ultrasound may be performed endoscopically if gastrointestinal venous malformations are suspected. Other important investigations include computed tomography (CT), barium studies, dermoscopy, skin biopsy, fecal occult blood tests, complete blood counts, iron panels.[9]

Differential diagnosis includes other congenital vascular malformation syndromes such as diffuse neonatal hemangiomatosis, familial glomangiomatosis, Klippel-Trenaunay-Weber syndrome, Maffucci syndrome, and mucosal venous malformation syndrome.10 11 Complications include severe gastrointestinal hemorrhage and intestinal intussusception. As a result, patients often require multiple blood transfusions throughout their lifetime.[12]

Treatment is largely symptomatic. Patients may benefit from iron replacement or transfusions if iron deficiency anaemia occurs from gastrointestinal bleeding. Other treatment options for vascular malformations include endoscopic sclerotherapy, band ligation, or laser photocoagulation. Resection of portions of the gastrointestinal tract may become necessary if there is significant intestinal involvement in order to prevent life-threatening gastrointestinal hemorrhage.[13]

Pharmacologic agents include octreotide, corticosteroids, interferon-alpha, IVIG, vincristine and Sirolimus. Somatostatin analogues like subcutaneous octreotide can be used to decrease splanchnic blood flow in patients with gastrointestinal haemorrhage. This may help decrease the need for blood transfusions in these patients. Sirolimus is an angiogenesis inhibitor that has been used to avoid blood transfusions in these patients, who often require multiple in their lifetime.[14]

CONCLUSION

Our case highlighted the importance of clinical correlation of symptoms. The symptoms of anemia, iron deficiency laboratory findings, cutaneous and intestinal vascular lesions were correlated leading to a faster diagnosis and early initiation of treatment. We wish to raise awareness of this rare disease which often goes misdiagnosed or undertreated, so that prompt treatment would be available for the patients in the future.

REFERENCES

1. Dobru D, Seuchea N, Dorin M, et al. Blue rubber bleb nevus syndrome: case report and literature review. https://pubmed.ncbi.nlm.nih.gov/15470538/ (2004, accessed 14/08/2022)
2. Gascoyen GG. Case of nevus involving the parotid gland and causing death from suffocation: nevi of the viscera. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8474085/ (2021, accessed 14/08/2022)
3. Bean WB. "Blue rubber bleb nevi of the skin and gastrointestinal tract" In: Bean WB, editor. Springfield, IL, United States: Charles C Thomas, Vascular Spiders and Related Lesions of the Skin; 1958. pp. 178–185. https://link.springer.com/chapter/10.1007/978-3-211-69500-5_13 (2008, accessed 14/08/2022)
4. Agnese M, Cipolletta L, Bianco MA, Quitadamo P, et al. Blue rubber bleb nevus syndrome, Acta Paediatr. https://pubmed.ncbi.nlm.nih.gov/19958301/ (2009, accessed 14/08/2022)
5. Terata M, Kikuchi A, Kanasugi T, et al. Association of blue rubber bleb nevus syndrome and placenta previa: report of a case. https://pubmed.ncbi.nlm.nih.gov/23055293/ (2013, accessed 14/08/2022)
6. Baigrie D, Rice AS, An IC. Blue Rubber Bleb Nevus Syndrome. https://www.ncbi.nlm.nih.gov/books/NBK541085//(2022, accessed 14/08/2022)
7. Gaillard, F., Weerakkody, Y. ISSVA classification of vascular anomalies. (2022, accessed 14/08/2022)
8. Jin XL, Wang ZH, Xiao XB, et al. Blue rubber bleb nevus syndrome: a case report and literature review. https://pubmed.ncbi.nlm.nih.gov/25493043/ (2014, accessed 14/08/2022)
9. Kassarjian A, Fishman SJ, Fox VL, et al. Imaging characteristics of blue rubber bleb nevus syndrome. https://europepmc.org/article/MED/14500226 (2003, accessed 14/08/2022)
10. Kaur T, Singh S. Blue rubber bleb nevus syndrome: a case report. https://pubmed.ncbi.nlm.nih.gov/24470675/ (2014, accessed 14/08/2022)
11. Rodrigues D, Bourroul ML, Ferrer AP, et al. Blue rubber bleb nevus syndrome. https://europepmc.org/article/MED/10881076 (2000, accessed 14/08/2022)
12. Ertem D, Acar Y, Kotiloglu E,et al. Blue rubber bleb nevus syndrome. https://europepmc.org/article/MED/315078 (2001, accessed 14/08/2022)
13. Arena M, Virdis M, Morandi E, et al. Blue rubber bleb nevus syndrome: combined surgical and endoscopic treatment. https://pubmed.ncbi.nlm.nih.gov/26273767/ (2015, accessed 14/08/2022)
14. Wang KL, Ma SF, Pang LY, et al. Sirolimus alternative to blood transfusion as a life saver in blue rubber bleb nevus syndrome: A case report. https://www.ncbi.nlm.nih.gov/books/NBK541085/ (2018, accessed 14/08/2022)