Available online at www.elixirpublishers.com (Elixir International Journal)

Physiology and Anatomy

Elixir Physiology and Anatomy 177A (2023) 56815 - 56817

ISSN: 2229-712X

Blue Rubber Bleb Nevus Syndrome: A Case Report and Literature Review

F.Nejjari, M.Moussa, S.Berrag, T.Adioui and M.Tamzaourte

Department of gastroenterology, Military Hospital Mohammed V of Rabat, Morocco

ARTICLE INFO

Article history:

Received: 10 March 2023;

Received in revised form:

10 April 2023;

Accepted: 20 April 2023;

Keywords

Blue Rubber Bleb Nevus,

Anemia,

Venous Malformations,

Gastrointestinal Tract.

ABSTRACT

Blue rubber nevus syndrome also known as Bean syndrome, is a rare vascular congenital condition responsible for multiple venous malformations that usually concern the skin and the gastrointestinal tract, rarely reported affecting the central nervous system, lung or the thyroid gland. We herein present a case of an 80-year-old male, diagnosed with Biermer's disease since 2006, he latter on was subject to an aggravation of his anemia leading the investigations to discover multiple gastrointestinal (GI) 'blebs' causing recurrent haemorrhages.

Introduction

Blue Rubber Bleb Nevus Syndrome (BRBNS) is a rare congenital medical condition. It consists of multiple venous malformations in the skin, gastrointestinal (GI) tract and/or other visceral organs. The first person to report it was George Gaskoin in 1860, an English dermatologist. In 1958, William Bennett Bean reported eight cases with hemangiomas on the skin and GI, because of their blue to bluish purple color and rubbery consistency, he called these lesions "Blue Rubber Bleb Nevi" [1]. But the term Blue Rubber Bleb Nevi Syndrome or latter on referred to as Bean's syndrome, was first used by Rice et al., in order to describe the presentation of bluish macules and hemangiomas in the GI tract, giving as a result chronic iron deficiency anemia (IDA) [2]. Which are the main symptoms that lead to the discovery of BRBNS in our patient. Unfortunately, since the disease's pathogenesis is still unclear, there is no treatment for this rare syndrome outside the symptomatic management of the itsconsequences.[3]

Case Report

An 80-year-old male patient diagnosed with Biermer's disease in 2006 based on three arguments: clinical (anemic syndrome), biological (macrocytic anemia) and an immunological confirmation. His treatment was based on Vitamin B12 and folic acid. The patient was noncompliant and stopped taking his medication since 2020.He was admitted to our Military hospital of rabat for an assessment of a recurrent chronic fatigue that has been endured for 3months prior to this consult. His symptoms raged from: asthenia, skin pallor, palpitations to feet's tingling all cardinal signs of anemia. The physical examination reveals anterior cervical swollen lymphnoeads on the right upper side of the neck, atrial fibrillation on the patient's electrocardiogram (EKG) as well as benign thyroid nodules on the cervical ultrasound, none is responsible of his current condition. The patient underwent esophago-gastro-duodenoscopy and colonoscopy which showed(Figure 1 to 4): multipleblebswithout bleeding that seemed who can be the root of his symptoms, the biopsies revealed an autoimmune gastritis related to Biermer's disease.

Results of the patient's lab analysis

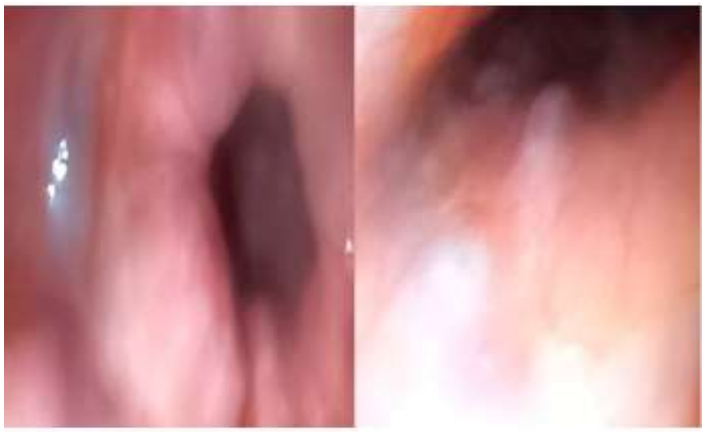

Figure 1& 2. . Esogastroduodenoscopy identified venous malformations (Ectasia) in the Esophagus and Stomach.

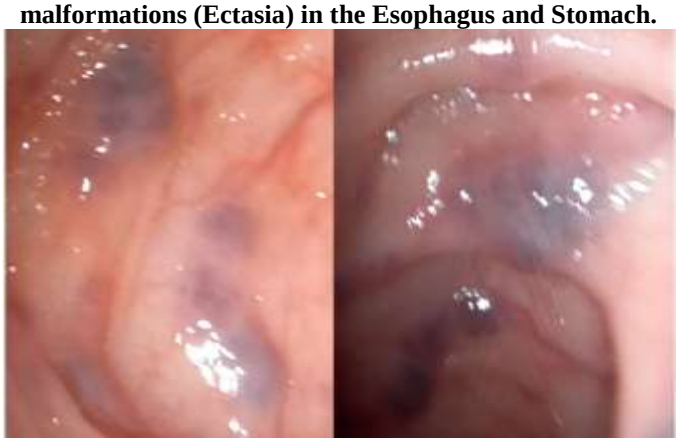

Figure 3 & 4. Multiple Purplish Lesions in The Left Colon on Colonoscopy Without Bleeding

Tele:

E-mail address:mandaikmoussaa@gmail.com

Discussion

Blue rubber bleb nevus syndrome (BRBNS) is a congenital condition characterized by multiple blue to bluish purple soft compressible nodules on the skin or mucous membranes. The nodules grow in number and size with increasing age. Most cases occur sporadically; however, TEK gene mutations may also cause BRBNS with autosomal dominant inheritance. [4]

The most recent literature review in 2021 found around 350 cases of BRBNS with diverse clinical presentations. 21% of the patients were from US, 11,7% from China, 8,9% from Japan, 7,6% from Spain, 7% from India, 5,2% from Turkey, 4.3% from France, there were also reports from other countries, such as Germany, Portugal, Italy, Canada, etc. It has been identified in all races, with Caucasians most frequently affected. It's a very rare systemic vascular malformation, with a low estimated incidence, only 1/14000 births [5]. This syndrome has no sex predilection, and it can occur at any age, the maximum age of diagnosis was 89 years old, reported in 2018 [6]

After the skin, the gastrointestinal tract (GIT) is the second most frequently involved organ, with most lesions found in the small intestine followed by the colon. GIT nevi may cause overt or occult gastrointestinal bleeding, iron deficiency anemia (IDA), or rarely intussusception and ischemic gut. Cutaneous nevi vary in size and number and are usually asymptomatic but can cause pain or hyperhidrosis. Nevi may also involve other organs, including the central nervous system, eyes, thyroid, kidney, spleen, and musculoskeletal system. [7]

GI involvement occurs in 76% of cases, it can affect any portion of the GI tract from the mouth to the anus, the lesions cause diverse clinical manifestations like: melena or rectal bleeding, in some cases the only manifestation is hidden bleeding that engender IDA [6]. The bleeding and severe IDA could be fatal without effective treatment [8]. It rarely leads to CI complications such as intussusception, perforation, volvulus with occasional associated mortality [9]

In the case we're reporting, the only manifestation was esophageal varices and gastro intestinal vascular ectasia. The anemia may be caused by the simultaneous incurrence of Biermer's disease and BRBNS. [10]

The syndrome is easy to misdiagnose because of its low incidence and diverse clinical presentations. So, for our patient here, either it was misdiagnosed; which is highly suspected especially with the absence of cutaneous lesions and the presence of macrocytic anemia, or the syndrome occurred at a very late age which only has been a hand full of cases reporting a late discovery of the syndrome. [11-12]

Histologically, these lesions appear as dilated vascular spaces lined with cuboidal epithelium with an increased number of sweat glands and presence of smooth muscle fibers. It is also composed of thin walled ectatic veins. [13] Thrombosis can be observed. There is no specific immunohistochemical marker to diagnose BRBN histologically. [15]

The disease's pathogenesis is still unclear and up to now there is no standard treatment. Management of GIT nevi is often supportive with iron supplementation and blood transfusions, however endoscopic therapy for bleeding lesions may be required, including bipolar or argon plasma coagulation, banding, cyanoacrylate glue, sclerotherapy, or snare polypectomy. [14] Forinstance, symptomatic gastrointestinal lesions should be first treated conservatively with oral iron supplementation and blood transfusions, especially when there is occult blood loss. Management of serious chronic bleeding should be treated by endoscopic approaches with sclerotherapies and/or resection of the venous malformations. [17] Systemic steroids, octreotide and interferon a-2a are currently not used as it has shown only limited success in managing the growth of the intestinal lesions. Surgical resection of the GI lesions is recommended when conservative management fails, regardless of the number and location of lesions. Complete eradication may avoid the need for repeated operations, but it is not always possible due to the extension of the lesion. [16]

Cutaneous nevi are often managed conservatively; however, surgery, sclerotherapy, or laser therapy may be used for cosmetic purposes. There are no widely available systemic therapies, although case reports of successful treatment with interferon-beta, octreotide, and sirolimus exist. [19-20] Sirolimus can be considered as a promising drug therapy for this syndrome. In Peking University Third Hospital in China, after a 3-month sirolimus treatment, a patient's haemoglobin increased and the fecal occult blood test was rechecked three times after the sirolimus treatment and the results were all negative [18].

Most patients with BRBNS have a normal life expectancy; however, quality of life may be impaired by symptomatic nevi. In our case the patient is still alive as of the writing of this article.

Conclusion

Bean's syndrome is a systemic vascular malformation, easily misdiagnosed because of its unspecific clinical manifestations and very low incidence. Early diagnosis is important because the GI lesions' complications can be fatal. Diagnosis is based on clinical examination with characteristic blue, rubbery lesions on the skin associated with neurologic features and pathologic neurologic imaging. The involvement of multiple organ systems, such as the neurologic system, in BRBN underscores the need for careful examination for the various signs and symptoms, so that proper follow-up and timely management can be organized.

References

1. Bean WD: Blue rubber bleb nevi of the skin and gastrointestinal tract, in "Vascular Spider and Related Lesion of the Skin" by Charles C Thomas Publisher, Springfield, Ill, 1958, p 175
2. RiceJS, et al: blue rubber-bleb nevus syndrome. Arch Derm 86: 503, 1962
3. Xia H, Wu J, Huang Y. Blue rubber bleb nevus syndrome: a single-center case series in 12 years. Transl Pediatr 2021;10(11):2960-2971. Doi: 10.21037/tp-21-23
4. Martinez CA, Rodrigues MR, Sato DT, et al. blue rubber bleb nevus syndrome as a cause of lower digestive bleeding. Case Rep Surg 2014; 2014:683684
5. Aron J, Couturier A, Sinayoko L, et al. An unusual cause of gastrointestinal bleeding in a hemodialysis patient. Hemodial Int 2018;22: E60-2
6. 5]Gilbey LK, Girod CE. Blue rubber bleb nevus syndrome: endobronchial involvement presenting as chronic cough. Chest2003;124(2):760–3. doi:10.1378/chest.124.2.760.
7. Amyere M, Aerts V, Brouillard P et al. (2013). Somatic uniparental isodisomy explains multifocality of glomuvenous malformations. Am J Hum Genet 92: 188–196.
8. Apak H, Celkan T, Ozkan A et al. (2004). Blue rubber bleb nevus syndrome associated with consumption coagulopathy: treatment with interferon. Dermatology (Basel, Switzerland) 208: 345–348.

9. Bean WB (1958). Blue bleb rubber nevi of the skin and gastrointestinal tract. In: CC Thomas (Ed.), Vascular Spiders and Related Lesions of the Skin. Oxford, Springfield, IL, pp. 17–185.
10. Boente MD, Cordisco MR, Frontini MD et al. (1999). Blue rubber bleb nevus (Bean syndrome): evolution of four cases and clinical response to pharmacologic agents. Pediatr Dermatol 16: 222–227.
11. Boon LM, Mulliken JB, Vikkula M et al. (1994). Assignment of a locus for dominantly inherited venous malformations to chromosome 9p. Hum Mol Genet 3: 1583–1587.
12. Boscolo E, Limaye N, Huang L et al. (2015). Rapamycin improves TIE2-mutated venous malformation in murine model and human subjects. J Clin Invest 125 (9): 3491–3504.
13. Brouillard P, Boon LM, Mulliken JB et al. (2002). Mutations in a novel factor, glomulin, are responsible for glomuvenous malformations (“glomangiomas”). Am J Hum Genet 70: 866–874.
14. Bean W (ed). Blue rubber-bleb nevi of the skin and gastrointestinal tract. In: Vascular Spiders and Related Lesions of the Skin. Springfield Ill Charles C Thomas; 1958: 17-185.
15. Fishman SJ, Smithers CJ, Folkman J, et al. Blue rubber bleb nevus syndrome: surgical eradication of gastrointestinal bleeding. Ann Surg. 2005;241(3):523-528
16. Starr BM, Katzenmeyer WK, Guinto F, Pou AM. The blue rubber bleb nevus syndrome: a case with prominent head and neck findings. Am J Otolaryngol. 2005;26(4):282-284.
17. Gallione CJ, Pasyk KA, Boon LM, et al. A gene for familial venous malformations maps to chromosome 9p in a second large kindred. J Med Genet. 1995;32(3):197-199.
18. Fretzin DF, Potter B. Blue rubber bleb nevus. Arch Intern Med. 1965;116(6):924-929
19. Crepeau J, Poliquin J. The blue rubber bleb nevus syndrome. J Otolaryngol. 1981;10(5):387-390.
20. Sullivan CA. Blue rubber bleb nevus syndrome. Anesthesiology. 2018;129(6):1169.

APPENDIX

Biological assessment		Results	Normal Values
Hemogramm	White blood cells	6,1 *10^3	4-10 / uL
	Hemoglobine	11,5	12-16 g/dl
	Hematocrite	38	36-47%
	MCV	109	82-98 fl
	MCHC	35	32-36 g/dl
	Platelet Count	243	140-450 / uL
Hemostasis	TP	85	70-100 %
	Activated cephalin time ratio	1,1	〈 1,2
Biochemistry	Blood urea	0,39	0,15 - 0,38 g/l
	serum creatinine	9	6 - 13 mg/l
	creatinine clearance	80,38	80 - 120 ml/min
	Uric acide	71	39 - 78 mg/l
	Alkaline Reserve	25	21 - 28 mmol/l
	Blood sodium	141	135 - 145 mmol/l
	Blood potassium	4,4	3,7 - 5,3 mmol/l
	Chloride	101	95 - 110 mmol/l
	Total calcium	88	80 - 105 mg/l
	Albumin	45	35 - 50 g/l
	Protidemia	68	64 - 83 g/l
	Lipasemia	31	〈 78 UI/l
	Blood sugar	0,92	0,7 - 1,05 g/l
Inflammatory assessment	CRP	3	〈 5 mg/l
	Ferritin	10	11-336 ng/ml
Lipid profile	NORMAL		
hepatic check	ALT or TGP	20	〈 40 UI/L
	AST or TGO	20	〈 35 UI/L
	GGT	30	〈 32 U/L
	PAL	98	40 - 150 U/L
	Total Bilirubin	7	3 - 10 mg/L
	Conjugated Bilirubin	4	1 - 5 mg/L
	LDH	231	190 - 400 UI/L

Hormonal Balance	**Ultrasensitive TSH**	**0,99**	**0,4 - 4 uU/ml**
	FT4	**0,72**	**0,70 - 1,48 ng/dl**
	FT3	**3,2**	**2 - 6 ng/l**
	Thyroglobulin	**1,4**	**1 - 2 ng/ml**
	Cortisol (8h)	**12**	**5 - 23 ug/dl**
	Parathyroid hormone	**36**	**6 - 50 pg/ml**
Hepatitis A serology	**Anti-HVA antibodies**	**Negative**	
Hepatitis B serology	**HBS Antigen**	**Negative**	
	Anti-HBC antibodies	**Negative**	
	Anti-HBS antibodies	**Negative**	
Hepatitis C serology	**Anti-HVC antibodies**	**Negative**	
EBV	**IGM AND IGG type antibodies**	**Negative**	
CMV	**IGM AND IGG type antibodies**	**Negative**	
HSV1	**IGM AND IGG type antibodies**	**Negative**	
HSV2	**IGM AND IGG type antibodies**	**Negative**	
Immunological assessment	**Anti-smooth muscle antibodies**	**Negative**	
	FAN or ANA	**Negative**	
	Anti-ACTIN	**Negative**	
	P-ANCA	**Negative**	
	Anti-LKM-I	**Negative**	
	Anti-LC-I	**Negative**	
	Anti-mitochondria antibodies	**Negative**	
	Anti-SCL-70 antibodies	**Negative**	
	Anti-SLA/ LP	**Negative**	