



CASE STUDY

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A case report of a patient with blue rubber bleb nevus syndrome presenting with severe gastrointestinal bleeding

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ABSTRACT

Blue rubber bleb nevus syndrome (BRBNS) is an uncommon condition presenting with multiple cutaneous and visceral vascular malformations, predominantly in the gastrointestinal (GI) tract. Typical skin lesion consists of a blue, soft tumor of a rubber like cohesiveness, that is easily compressible and refills slowly on release of pressure. The GI lesions are more clinically relevant, as they may induce chronic bleeding or even life threatening massive hemorrhages. This report presents a case of BRBNS diagnosed in a 52-year-old male with signs of lower gastrointestinal bleeding. The patient presented with melena, fatigue and severe anemia, which were treated by numerous blood transfusions and iron supplementation. Multiple vascular changes were visualized in the small intestine. A typical skin lesion was also present in the skin. Additionally, this report describes the clinical aspects of the syndrome, diagnostic preferences, as well as possible critical complications.

Keywords: blue rubber bleb nevus syndrome, gastrointestinal bleeding, anemia.

Introduction

Blue rubber bleb nevus syndrome (BRBNS) is a rare vascular disorder characterized by multifocal venous malformations. Numerous changes of variable size and structure are most prominent in the skin and gastrointestinal (GI) tract, but can frequently be observed in other locations such as central nervous system (CNS) [1].

The entity was originally described by Gascoyen in 1860, who first noted the association of cutaneous and GI lesions with bleeding [2]. Almost a century later, in 1958, William Bean further investigated and characterized these vascular anomalies, thereby giving rise to the eponym Bean's syndrome [3].

Here we report a patient with multiple intestinal lesions presenting with episodes of severe GI bleeding and iron deficiency anemia.

Case Report

A 52-year-old male patient was admitted to the Department of Gastroenterology, Medical University of Lodz, in April 2014. Patient's main complaint was disturbing melena observed for five days preceding the admission accompanied by dizziness, excessive fatigue and stenocardial pain on exertion. Hematemesis or recurrent epistaxis were denied. The patient had a medical history of non-steroid anti-inflammatory drugs (NSAIDs) intake, administered for upper respiratory tract infection a month prior to hospitalization. Additionally, the use of other NSAIDs due to persistent back pain was ascertained.

Existing concomitant disorders, being hypertension and benign prostate hypergrowth were determined. For each, relevant treatment had been introduced, including antiplatelet aminosalicylic acid therapy.

Past medical history was otherwise unremarkable. Family history was negative for similar GI disorders episodes. However, the existence of a skin hemangioma in patient's daughter was confirmed.

At the physical examination patient appeared pale with anemic mucosa, tachycardia and presented a bluish, soft, single nodule in the area of left scapula (**Figure 1**). The abdomen examined palpably emerged as soft and non-tender, without liver or spleen enlargement. Performed per rectum examination confirmed melena. Rest of the physical examination did not reveal any abnormalities.

According to laboratory data, performed routine blood analysis showed a significant decrease in hemoglobin (Hgb) concentration, lowered hematocrit (Hct), mean cell volume (MCV) and serum iron level. Moreover, blood cell counts revealed decreased level of red (RBC) and white (WBC) cells. In response to those values indicating severe anemia, blood transfusion of packed red blood cells and iron replacement therapy were administered. Applied medication resulted in significant improvement in blood parameters controlled at hospital discharge. During hospitalization patient underwent both upper and lower GI endoscopy. None of those imaging studies however, revealed abnormalities. Clinical evidence of GI bleeding required locating the exact source of bleeding. Therefore, the patient was scheduled for capsule endoscopy. The study showed multiple nodules with intensified vascular pattern in the wall of small intestine, which were referred to as varices of jejunum (**Figure 2**).

Complex diagnosis required additional examination of other potential locations affected with venous malformations. For this reason, successive actions



Figure 1. Skin hemangioma in the area of left scapula



Figure 2. Capsule endoscopy image- intestinal nodules with intensified vascular pattern

involved extending diagnostics with further imaging studies including spine nuclear magnetic resonance (NMR) of the abdomen and head computed tomography with angiography (CTA)

Performed in the first instance spine NMR revealed a hemangioma in the body of L1 vertebra, partially explaining the origin of the persistent lower back pain reported by the patient.

The head CTA with a normal image did not confirm the suspicions of probable malformations presence. Oppositely, the abdomen scan revealed multiple, varying in size nodules, not associated with vessels in the mesentery (**Figure 3**). The unclear image of internal structures, orientated diagnosis towards lymphoma which consequently ended with laparoscopic mesenteric lymph node harvesting. In the laparoscopic surgery access enlarged mesenteric lymph nodes, grouped and surrounded by thick crown of vascular plexuses of cyanotic color were observed. The harvested tissue was microscopically analyzed. Regardless of the fragmentary material, elements of adipose tissue with venous malformation were identified. Continuing with the broadened diagnosis, the patient underwent another lymph node biopsy procedure. The investi-

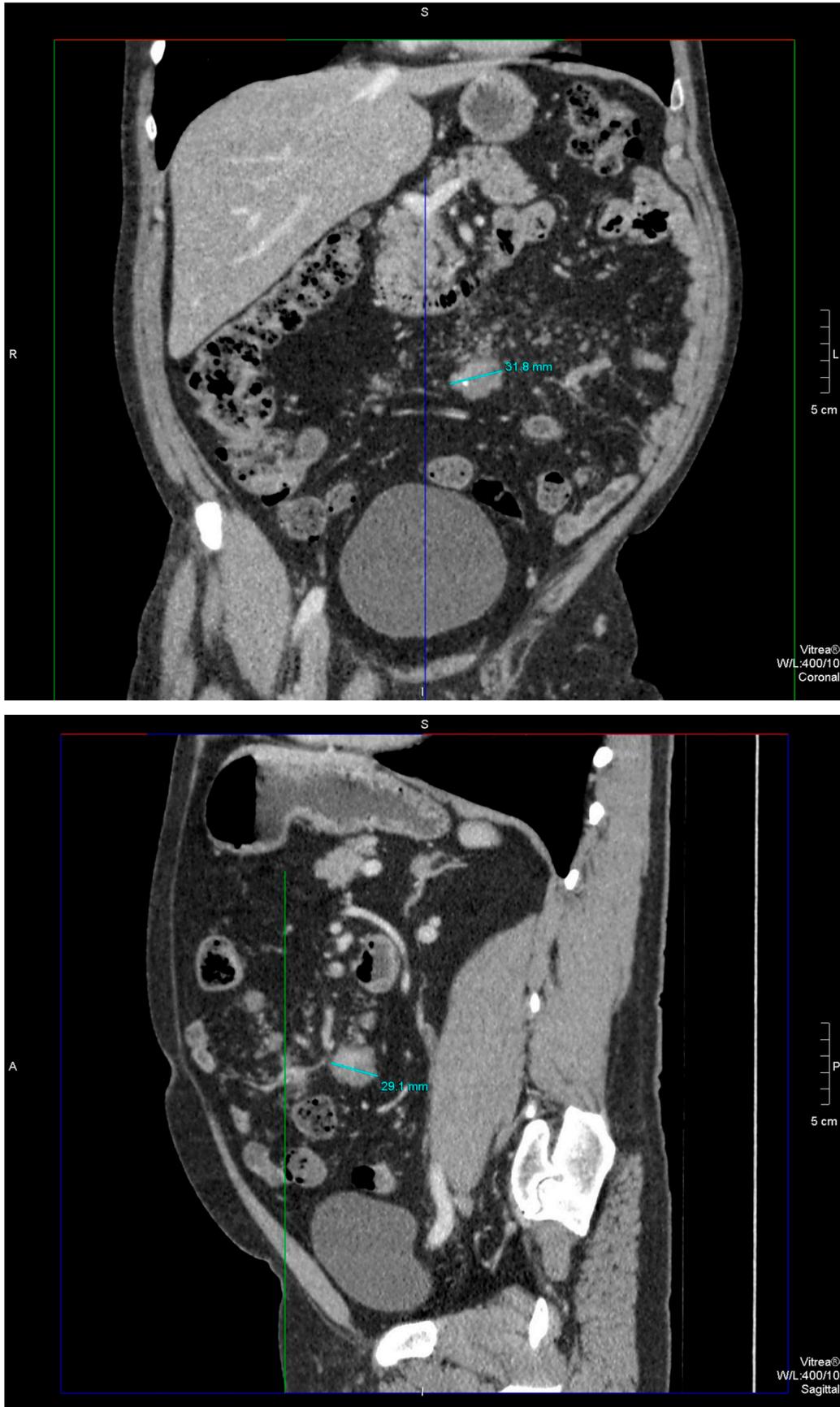


Figure 3. Abdominal angiotomography image – nodules not associated with vessels in the mesentery

gated right groin lymph node image was described as consistent with a reactive state structure.

All of the performed actions proved BRBNS to be the origin of the multifocal malformations. Having received essential treatment, the patient was discharged and educated for observation of early signs of GI bleeding and asked to attend outpatient follow up regularly.

Discussion

The initial report of the disease dates back to 1860, when Gascoyen reported the correlation of skin lesions and GI bleeding [4]. The description did not receive much clinical attention until 1958, when William Bean in detail described a condition with similar presentation and coined the term BRBNS, giving an adequate image of the typical blue, rubbery, bleb like vascular lesions [5].

Bean's description of the findings present in the disease might be in fact considered as inaccurate regarding their true nature. Although, both the original author and multiple contemporary scientists continue to inappropriately classify those as hemangiomas [6], in fact histologically they are considered venous malformations. According to a proposed biologic classification system, vascular anomalies are divided into hemangiomas representing neoplastic lesions with endothelial hyperplasia and vascular malformations, which are congenital lesions with normal epithelial turnover [7].

Cumulating evidence suggest that the lesions found in BRBNS then, should not be referred to as typical hemangiomas, but rather venous malformations [3]. Such changes can be found on any cutaneous surface but are most predominant in the trunk and upper extremities [8]. Altogether, 3 types of such malformations have been described [9]. Type I is a large disfiguring venous malformation that may increase in size and obstruct vital tissues. Type II, the most common finding, is a nontender soft nodule of bluish color which when compressed refills with blood rapidly (blue rubber nipple). Type III is an irregular blue-black macule or papule [10]. These lesions may be punctate, merge with adjacent pigmented nevi and rarely blanch on pressure [11].

Cutaneous malformations do not have a tendency to bleed spontaneously [6]. With the diameters ranging between few millimeters and several centimeters, they can number from several to more than a hundred with a tendency to escalate in size and quantity with age.

In general, venous malformations in the skin are usually first noticed at neonatal period or infancy, but

can sometimes be latent until adulthood [12]. The latter mechanism corresponded with the described patient, who observed the presence of a skin hemangioma since early childhood. The presence of cutaneous lesions typical of BRBNS should alert the clinician for potential internal vascular malformations [13]. Analogous venous anomalies, to those in the skin, may be located throughout the GI tract. Although, possible to observe in any position from oral cavity to anus they are most prevalent in small intestine and distal colon [14]. In contrast to skin lesions, intestinal malformations are more susceptible to bleeding often resulting in iron deficiency anemia, which may require supplementation and blood transfusions [15]. Occasionally patients develop severe complications such as rupture, intestinal torsion, and intussusceptions [16]. GI tract appears as the second most involved organ in the disorder following the skin. However, case reports have demonstrated other tissues and organs involved in the pathology including the central nervous system, thyroid, parotid, eyes, oral cavity, musculoskeletal system, lungs, kidney, liver spleen and bladder, all of which being a potential cause of severe complications [17]. The presented patient showed no involvement of other internal organs except small intestine. There was also a spinal involvement and later on a vascular malformation in head magnetic resonance imaging (MRI) was found. Although most cases of BRBNS develop sporadically, a genetic model of inheritance has been proposed. Evidence suggest the disorder to have autosomal dominant transmission associated with gene located on chromosome 9 [18]. Furthermore, within the structure of the same gene, a locus associated with familiar venous malformations was identified, thus suggesting categorizing BRBNS in the category of familiar venous malformations [19]. In relationship to a typical BRBNS skin lesion present in patient's daughter, this model seems worth considering. Diagnosis of BRBNS can be often made by visual inspection of the skin lesions, and therefore biopsy is not routinely necessary [20]. Nevertheless, basic evaluation includes a complete history and physical exam, blood count and fecal occult blood (FOB) test to detect blood loss from GI lesions. Positive test result combined with anemia obligate to a full investigation of the GI tract to locate bleeding sites. This evaluation can be accomplished through various methods. Barium contrast studies are considered useful diagnostic tool, showing filling defects if a GI lesion is present. Also computed tomography (CT) and MRI are described to be highly specific diagnostic tools. The latter has proven to be a useful method for screening asymptomatic family members [6].

Compared with these techniques, GI endoscopy emerges as a superior modality as it provides the possibility of curing the lesions. At the other side of the spectrum, it is considered to be an invasive technique and its use within small intestine is limited [21]. To overcome these negative aspects, while keeping the high of the study a new, noninvasive tool - capsule endoscopy, is highly recommended [22]. In fact, capsule endoscopy was the technique to fully confirm BRNNS in our patient, with both upper and lower GI endoscopy showing no abnormalities. BRBNS should be differentiated from other clinical entities including hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome), Klippel-Trenaunay syndrome, and Maffucci syndrome all characterized by different vascular malformations [23]. Osler-Weber-Rendu syndrome is described as episodes of recurrent epistaxis and gastrointestinal, punctiform lesions, morphologically and histologically different from those observed in BRBNS. Additionally, it is known to have positive family history [24]. Klippel-Trenaunay syndrome presents a characteristic triad of varicosities, port-wine stains and soft tissue and bone deformities generally located in just one of the extremities [25]. Lastly, Maffucci syndrome manifested by diffuse lesions in the skin and soft tissues accompanied by bone malformations and chondrodysplasias [26].

The management of cutaneous lesions includes laser ablation or cryotherapy. Surgical removal is usually not necessary and often limited to cosmetic indications [27]. Treatment for patients with visceral involvement largely comprises symptomatic treatment of iron deficiency anemia [15].

Although with results based only on case reports, the use of several medical agents for treating BRBNS have been documented. Such therapies were performed with the use of octreotide, interferon- α 2a or sirolimus [29, 30].

Specialist suggest endoscopic sclerosis and laser photocoagulation of symptomatic lesions or segmental resection of the involved area as a prophylactic action against bleeding [31, 32]. Operative management however, should not underestimate the risk of significant hemorrhage and possible life-threatening complications. Still, in the event of massive hemorrhage radical steps involving partial resection should be taken [33].

Our patient showed significant involvement of small ileum and jejunum. Preventive surgical resection was not considered as a treatment option due to possible development of short bowel syndrome. The actions were limited to regular outpatient visits, blood and FOB

tests, with mandatory imaging studies in an event of laboratory or clinical symptoms of internal bleeding. Furthermore, to minimize the influence on the hemostasis, instructions for avoiding use of any NSAID were implemented.

Conclusions

The presentation of this case demonstrates the invaluable role of an integrated approach to a patient. Thorough physical examination combined with patients medical history provide an opportunity for early diagnosis, management and complications prevention.

The role of used medication, established to influence the hemostasis, should also not be diminished. The report represents possible correlation between the GI lesions bleeding and using substantial amounts of NSAIDs. Vital in arriving at the diagnosis is the extensive search for the exact origin of the symptoms, which in the presented case required the use of 4 different imaging studies (conventional and capsule endoscopy, abdominal and head CT scans with angiography and MRI).

Several disorders involving vascular anomalies, all varying in medical approach to a patient, should be differentiated with BRBNS. Therefore, early recognition of typical cutaneous vascular lesions may bring rational benefits in patient treatment and preventing possible life threatening complications.

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Conflict of interest statement

The authors declare no conflict of interest.

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