Case Report
Étude de cas

Blue rubber bleb nevus syndrome

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Blue rubber bleb nevus syndrome, an uncommon condition, is manifested by gastrointestinal and skin hemangiomas and gastrointestinal hemorrhage causing anemia. The authors report a unique case of the syndrome in association with a congenital cardiac malformation. A 26-year-old woman presented with iron-deficiency anemia after the birth of her first child. She had a history of skin and gastrointestinal hemangiomas and tetralogy of Fallot. Endoscopy revealed multiple new intestinal hemangiomas, which were removed through enterotomies with resolution of the anemia. Iron therapy was prescribed, and her condition was stable at follow-up 5 years later.

Problème rare, le syndrome de Bean se manifeste par des hémangiomes gastrointestinaux et cutanés et une hémorragie gastrointestinale qui cause de l'anémie. Les auteurs décrivent un cas unique du syndrome lié à une malformation cardiaque congénitale. Une femme de 26 ans s'est présentée en état d'anémie sidéropénique après la naissance de son premier enfant. Elle avait des antécédents d'hémangiomes cutanés et gastrointestinaux et de tétralogie de Fallot. L'endoscopie a révélé de multiples hémangiomes intestinaux frais dont on a effectué l'ablation par entérotomie, ce qui a réglé l'anémie. On a prescrit une sidérothérapie et son état était stable après 5 ans de suivi.

Blue rubber bleb nevus syndrome (BRBNS) is an uncommon disorder, defined by gastrointestinal and skin hemangiomas, gastrointestinal hemorrhage and resulting anemia. The syndrome is named for the characteristic appearance of skin lesions, which are soft, blue, compressible masses that become wrinkled when the blood is expressed with pressure and subsequently refill.[1,2] We present a patient with BRBNS associated with tetralogy of Fallot who had been followed up closely since birth.

Case report

A 26-year-old white woman was referred with chronic iron-deficiency anemia after the birth of her first child, who was delivered by elective cesarean section. She had no history of peptic ulcer disease, hematemesis, hematochezia or melena but had intermittent, mild abdominal pain. Her stool was negative for occult blood when tested on one occasion.

Her medical history was significant. At 6 months of age tetralogy of Fallot was diagnosed; she underwent Blalock anastomosis at the age of 2 years. She was admitted for total correction of the tetralogy at the age of 6 years, but her hemoglobin level was only 77 g/L and there was occult blood in the stool. Results of barium studies were normal. At laparotomy no source of gastrointestinal bleeding could be found. The following year she had total correction of the tetralogy, but her hemoglobin level remained low, so iron, taken orally, was prescribed. She was operated on again at 7 years of age, when multiple hemangiomas, 1 to 5 mm in diameter, were discovered in the intestine; they were removed through enterotomies. An accessory spleen was also removed. At the age of 12 years she again had a low hemoglobin level (80 g/L), but sigmoidoscopy revealed no lesions. However, a hemangioma of the right middle finger, 1 cm in diameter, was noted. One year later she had an episode of rectal bleeding. Angiogra-

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phy showed hemangiomas in the small intestine and around the ileocecal valve. Colonoscopy revealed 10 hemangiomas in the distal 60 cm of the descending colon and sigmoid. These varied in appearance, some being exophytic, others being flat. Levophed, 0.5 mL orally, was prescribed. A short time after this she underwent enterotomies to remove 26 hemangiomas in the small bowel and 7 hemangiomas in the large bowel.

She remained well until she was 18 years old, when she was admitted to hospital with a swollen, painful left knee. A synovial thickening was removed arthroscopically, but the findings were unknown.

After the birth of her child, her anemia again became refractory to oral iron therapy, and she underwent endoscopy. Examination revealed two hemangiomas in the second portion of the duodenum, several in the left colon and a pedunculated hemangioma in the transverse colon. Angiography showed tiny tangles of abnormal small vessels, two in the terminal ileum (superior mesenteric artery angiogram) and one in the rectosigmoid (inferior mesenteric artery angiogram) (Fig. 1). At operation, 17 hemangiomas were excised or suture ligated through four enterotomies. A small amount of dark green ascitic fluid was found. Pathological examination revealed hemangiomas with intravascular thrombi involving the lamina propria and submucosa.

She continued her iron therapy and at follow-up 5 years later her hemoglobin level was stable at 109 g/L. She had undergone two repairs of incisional hernias and each time a small amount of ascitic fluid was noted. New skin lesions continued to arise, and some lesions had regressed but not disappeared. She had lesions on both hands (Fig. 2), inside the lower lip, at the base of the left side of the neck and behind the right ear. None required surgical intervention or were cosmetically compromising.

Discussion

BRBNS was first described by Gascoyen in 1860[3,4] and later by Bean in 1958.[1] The components of Bean's definition included hemangiomas of the skin and gastrointestinal tract, and gastrointestinal bleeding leading to anemia.[1,2,4–6]

Genetically, the syndrome is most likely of a sporadic nature;[5] several authors[4,7,8] have described pedigrees showing autosomal dominance, but none of these index cases had evidence of gastrointestinal involvement. All races are affected, and the sex distribution is equal.[2,3,6,9–11]

In addition to the soft, blue, compressible masses, the skin lesions may also be large cavernous hemangiomas or blue-black macules or papules[1,3,12,13] and may number from one to hundreds.[14] They appear at birth or in childhood[15] and increase in size and number with age.[2,3,9,16–18] Lesions may be found anywhere and can be associated with hyperhidrosis and pain[3,6,19,20] but rarely bleed[9,17] and are not known to undergo malignant change.[3, 17,19]

Gastrointestinal lesions are found from mouth to anus[10,11,18] and are thought to be most common in the

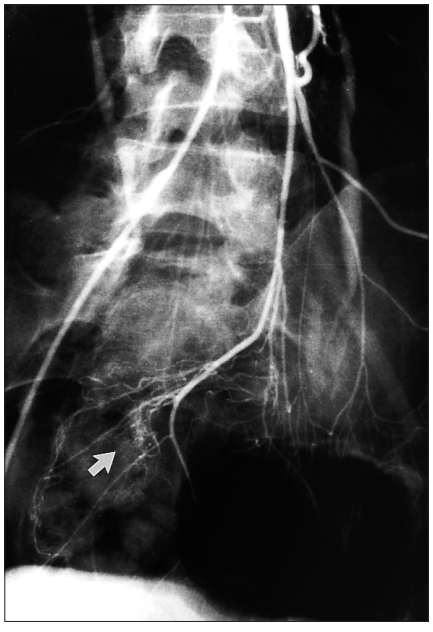

FIG. 1. Inferior mesenteric artery angiogram showing small tangle of abnormal blood vessels (arrow) in rectosigmoid area.

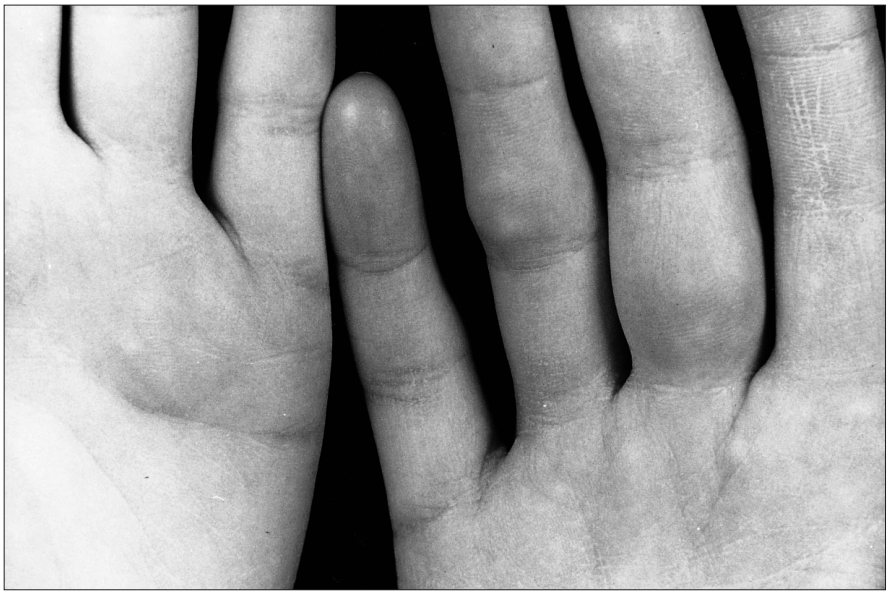

FIG. 2. Volar surface of patient's hands showing swellings, which are soft and bluish, on long and ring fingers and on hypothenar eminence.

small intestine.[6,9] Iron-deficiency anemia secondary to occult gastrointestinal blood loss is the commonest form of presentation.[3,4,6,14,16,19,21,22] Intestinal lesions can cause abdominal pain related to intussusception, volvulus, intramural hemorrhage or infarction.[3,6,13,17,22] Lesions elsewhere can result in hematuria,[10] epistaxis, hemoptysis and menorrhagia.[3,16] Bone deformities caused by pressure effects or hypervascularity result in skeletal bowing, pathologic fractures, bony overgrowth and articular derangement.[5,21] There are reported associations of BRBNS with coagulopathy and deep venous thrombosis,[23] medulloblastoma, pulmonary hypertension, hypernephroma and Maffucci's syndrome.[3,4]

Initially, the diagnosis is made from clinical findings. Abdominal radiographs may show phleboliths in intestinal hemangiomas after thrombosis and organization.[21,22] These are seen in one-third of children with gastrointestinal hemangiomas.[22] Barium studies may show filling defects, most commonly wide-based sessile polyps,[24] but may not show any abnormality.[3,6,14,25] Angiography may reveal hemangiomas missed by barium studies[25] and is most useful in cases of active bleeding.[14] Endoscopy may in turn show those lesions missed by angiography.[3,6,14,26] Endoscopically, the lesions appear as bluish nodules with normal mucosal walls capped by thinned mucosa.[5] Lesions have also been identified by computed tomography and magnetic resonance imaging.[3,10,13]

Pathological findings are typical of cavernous hemangioma.[7,10,14,19,27] There are numerous dilated blood-filled spaces lined with cuboidal epithelium and surrounded by a fibrous stroma with occasional smooth-muscle cells, and there may be a proliferation of sweat glands.[14,19,27]

There are several vascular syndromes similar to BRBNS. In Osler–Weber–Rendu syndrome patients have gastrointestinal and skin lesions, but the latter are telangiectatic and macular and may be subungual.[5,7,9,12,14] Klippel–Trenaunay syndrome includes cutaneous hemangiomas and limb hypertrophy but not gastrointestinal involvement.[12] Maffucci's syndrome associates dyschondroplasia with vascular hamartomas of skin and viscera.[4,9] Glomangiomatosis (multiple glomus tumours) can be identified by pathological examination.[19]

Initial therapy for BRBNS consists of orally administered iron preparations to combat anemia, especially if gastrointestinal blood loss is occult.[3,6,14,18,19,28] Transfusions may occasionally be necessary.[2,19] A full investigation of the entire tract to identify all potential bleeding sites is required before the treatment of symptomatic gastrointestinal lesions. Such lesions can be endoscopically photocoagulated with continuous neodymium: yttrium–aluminum–garnet laser, and mucosa has been shown to heal well without strictures.[2,28] Sclerotherapy is associated with multiple complications, including ulceration and scarring, and is not widely used.[28] Enterotomy and excision of hemangiomas preserve bowel, and large lengths of bowel can be cleared at each enterotomy site.[22] Bowel resection is reserved for serious bleeding, localized lesions and intussusception.[3,6,14,17,19,22] Combining endoscopic photocoagulation with resection and enterotomy may prove valuable.[2] Our case suggests that bowel lesions continue to arise, so patients require follow-up with barium studies and endoscopy when anemia becomes refractory to iron therapy.[17]

Some authors[18,19,29] advocate laser surgery or excision of cosmetically compromising skin lesions, but patients should be warned of the possibility of bleeding or recurrence.[17]

Conclusions

Because BRBNS is rare, most of our knowledge about it is based on anecdotal reports. Our case is unique because it is the first reported association with a congenital cardiac malformation and demonstrates the continuous nature of gastrointestinal hemangioma formation. Patients suffering from BRBNS require conservative treatment with close follow-up to avoid major ablative surgery and its complications.

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