

BLUE RUBBER BLEB NEVUS SYNDROME: A CLINICAL SPECTRUM WITH CORRELATION BETWEEN CUTANEOUS AND GASTROINTESTINAL MANIFESTATIONS

To the Editor,

Blue rubber bleb nevus syndrome (BRBNS) is a rare disorder characterized by distinctive cutaneous and gastrointestinal cavernous hemangiomas. Patients usually present with iron deficiency anemia from occult gastrointestinal bleeding or massive gastrointestinal bleeding in the emergent setting.¹⁻⁹ Optimal management for these patients is unclear as a result of its rarity and anecdotal reporting. The authors recently treated a case of this rare disorder and reviewed the literature on surgically treated cases to define the role for surgical intervention in BRBNS.

The patient is a Chinese boy who first presented at the age of 12 years for long-standing symptomatic anemia. He had a history of multiple hospital admissions for blood transfusions since the age of 5 years. There was no consanguinity and he had no family history of anemia. Clinical examination was unremarkable except for a solitary but prominent cavernous hemangioma over his left heel (Fig. 1). This was tender on compression.

His hemoglobin level on admission was 6.0 g/dL and this was iron deficient in profile. Subsequently, he had multiple readmissions for symptomatic anemia requiring blood transfusions. Extensive investigations that included hemoglobin electrophoresis, Meckel's radio-nuclide scan, gastroscopy, colonoscopy, small bowel enema and a 3-vessel angiogram were normal with no lesion or bleeding noted. The only positive finding was a Technicium (Tc-99) red blood cell tagged scan that showed intermittent bleeding from three foci in the small bowel in 1995. A diagnosis of BRBNS was made and he was followed up closely and given supportive treatment.

He subsequently had five further hospital admissions for occult gastrointestinal bleeding requiring blood transfusions. Repeated upper and lower gastrointestinal endoscopies failed to show any lesions to account for this. Repeat Tc-99m red blood cells tagged scan performed during an admission for symptomatic anemia in 2001 demonstrated mild intermittent bleeding from the small bowel at three similar foci in the small intestines. The decision for operative intervention was made after following him up for 9 years in view of the increasing severity of bleeding episodes and frequent need for blood transfusions.

At laparotomy, two characteristic cavernous hemangiomas were found in the mid-jejunum. An intussusception of one of the hemangioma into the adjacent small bowel was also noted. Detailed examination of the whole gastrointestinal tract with intraoperative endoscopy showed no other hemangiomas and the two affected segments of the small bowel were resected. Pathological examination confirmed dilated cavernous blood-filled spaces in the small intestinal wall. He was well on follow up 20 months after the operation with no further gastrointestinal bleeding. He did not require any further oral iron supplementation and had no limitations of his physical activities.

This is a rare disorder characterized by distinctive vascular malformations of the skin and gastrointestinal



Figure 1 Characteristic cavernous hemangioma over the right ankle. This bluish purple hemangioma is compressible, leaving an empty, wrinkled sac that rapidly refills.

tract. The genetic inheritance follows an autosomal dominant (AD) pattern with high penetrance. However, many cases are sporadic.^{2,3} The primary clinical concern in BRBNS is bleeding from involvement of the gastrointestinal tract, which can be fatal.² Hemangiomas can be found anywhere in the gastrointestinal tract from the oral cavity to the rectum. The most common site involved is the small bowel.¹⁻³ Unlike skin hemangiomas that are usually asymptomatic, gastrointestinal hemangiomas are frequently complicated by bleeding. Affected individuals usually present with massive gastrointestinal hemorrhage or iron deficiency anemia caused by occult gastrointestinal bleeding.^{1,2}

Rarely, BRBNS can present with an acute abdomen as a result of intussusception (noted in our patient at laparotomy), volvulus or bowel infarction.^{1,3}

The role of surgery is dependent on the presentation, location and extent of the hemangiomas. In the emergent setting, the role of surgery is life-saving. Management in the elective setting is much more controversial. It is difficult to predict the extent of bowel involvement and, hence, the extent of surgical resection. Furthermore, the optimal timing for surgery has not been defined. The majority of authors have advised conservative management where possible because of the risk of multiple operations and compli-

Table 1 Correlation between number and distribution of skin lesions and number and distribution of gastrointestinal tract lesions in recently published case reports treated with laparotomy and surgical resection of the involved bowel

Reference	Age (years)/sex	Skin area involved	Digestive organ involved	Treatment and results.
1	22/male	15 cutaneous hemangiomas all over body, including hands, feet, ears and glans penis	Three in the stomach, one in the duodenum, four in the colorectal area and 59 in the small bowel	Excision of gastric, colonic and small bowel hemangiomas. Small bowel segmental resection and right hemicolectomy. Well at follow up
2	19/female	Multiple lesions all over body and mucosal surfaces	Two in the esophagus, four in the stomach, one in the duodenum, multiple in the colon and 82 in small bowel	Endoscopic laser coagulation of gastric and colonic hemangiomas. Small bowel resection. Recurrent gastrointestinal bleeding 4-years later with further bowel resection performed
5	23/male	Multiple skin hemangiomas, including plantar, left inguinal area and oral hemangiomas	Three in the stomach, two in the duodenum, seven in the colon and 35 in the small intestines	Endoscopic polypectomy and laparotomy endoscopic-assisted polypectomy of small bowel hemangiomas
6	21/female	Multiple cutaneous hemangiomas, including right back, right foot, zygomatic arch and right anterior axillary region	Two hemangiomas in the stomach, three in the colon and eight in the small intestines	Multi-endoscope-assisted surgical resection/enucleation of gastrointestinal hemangiomas
7	33/female	Multiple cutaneous hemangiomas mainly found on the limbs	Multiple hemangiomas in the stomach and duodenum and more than 15 in the colon and six in the small intestine	Segmental resection of sigmoid colon and multiple wedge resection of the small intestines. Well at 6-months follow up
8	37/female	Multiple skin lesions. Cosmetic sclerotherapy for a large hemangioma involving her face and neck	Multiple hemangiomas in the stomach, small intestines and colon	Multiple surgical resections for recurrent surgical resections for recurrent gastrointestinal bleeding: partial gastrectomy, right hemicolectomy, small bowel resection and completion colectomy
9	30/female	Right shoulder region hemangioma. No other cutaneous involvement	One hemangioma in the small bowel and one in the stomach. Rest of the gastrointestinal tract was normal	Complete surgical resection. Well at 1-month follow up

cations of extensive bowel resection such as short gut syndrome.⁸

The authors reviewed recently published case reports of BRBNS in which patients were treated with laparotomy and surgical resection of the involved bowel (Table 1). There are three important conclusions that can be drawn. First, there appeared to be a correlation between the number of cutaneous hemangiomas and visceral hemangiomas. All patients with multiple skin hemangiomas were found to have multiple gastrointestinal hemangiomas at laparotomy and vice versa. Nakagawara *et al.*⁴ previously reported a correlation between the number of hemangiomas involving the body surface and the number of cutaneous hemangiomas. Second, the outcome is poorer for those with extensive involvement of the viscera, with more extensive resection needed and a high re-operation rate for recurrent bleeding. Finally, for patients with limited involvement of the gastrointestinal tract, definitive surgery can potentially provide long-term remission of gastrointestinal bleeding.

These data are based on small numbers of anecdotal case reports that lack long-term follow up. However, the natural history of our patient supports the clinical observations made above. He had a solitary left ankle hemangioma with no other cutaneous lesions. We followed him up over a 10-year period with regular gastroscopy and colonoscopy and did not find any new development of hemangiomas. The Tc-99m red blood cells tagged scans in 1995 and 2001 showed corresponding bleeding spots with no interval increase in foci of hemorrhages. Initially, it was decided to treat the patient conservatively. He was relatively stable requiring only occasional blood transfusions from occult gastrointestinal bleeding. However, as severity of bleeding increased, this warranted definitive treatment. Our laparotomy findings concur well with cutaneous manifestation. Only two hemangiomas of the small bowel were discovered and resected. He was well 16-months postoperatively with no further blood loss or progression of disease. The patient probably has a mild form of BRBNS with limited lesions in both the skin and gastrointestinal tract. A similar case was reported by Haiping *et al.*⁹ about a patient with cutaneous hemangioma limited to the shoulder region and found to have only two hemangiomas of the gastrointestinal tract at laparotomy.

The clinical spectrum of BRBNS is heterogenous with variable phenotypic expressivity. Patients with solitary or few cutaneous hemangiomas in a limited area of the skin might represent a milder manifestation of BRBNS with limited gastrointestinal involvement. This subgroup of patients might benefit from early surgical intervention if gastrointestinal hemangiomas are symptomatic as it might be possible to completely excise the involved bowel segments.

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