Blue Rubber-Bleb Nevus Syndrome: A Case Report

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Blue rubber-bleb nevus syndrome (BRBNS) is an uncommon systemic disorder characterized by cutaneous and visceral cavernous hemangiomas. The characteristic rubbery textured and easily compressible lesions usually present in childhood and predominate cutaneously over the trunk and extremities. Gastrointestinal foci appear most commonly in the small bowel, a site that appears to dominate visceral involvement. We review the case of a 23-year-old white woman, whose numerous lesions on her trunk, extremities, and oral mucosa had been present since childhood.

In 1860, Gascoyen[1] first reported the association between cutaneous and visceral hemangiomas and gastrointestinal (GI) bleeding. He described the case of a 44-year-old anemic patient with multiple hemangiomas of the skin, GI tract, and parotid gland. The parotid hemangioma compromised the patient's airway and ultimately led to death, but the relationship of clinical symptoms spurred Gascoyen's interest.

Almost a century later in 1958, Bean[2] presented a case with similar findings and pioneered the descriptive term *blue rubber-bleb nevus syndrome* (BRBNS). Bean described 3 different patterns of cutaneous lesions: (1) multiple protuberant blue bloody sacs that are easily compressible; (2) large hemangiomas that may lead to obstruction of the airway, alimentary canal, or other vital structures; and (3) pleomorphic flat blue lesions, occasionally with black stippling, that merge with adjacent normal skin. Bean's description differentiated BRBNS from a heterogeneous group of vascular lesions.

Since Bean's initial description of BRBNS, fewer than 200 cases have been reported in the literature. This rare systemic disorder affects both men and women of all ages and races. Most cases reported in the literature have sporadic occurrence; however, several families have demonstrated autosomal-dominant inheritance patterns with significant penetrance.[3,4]

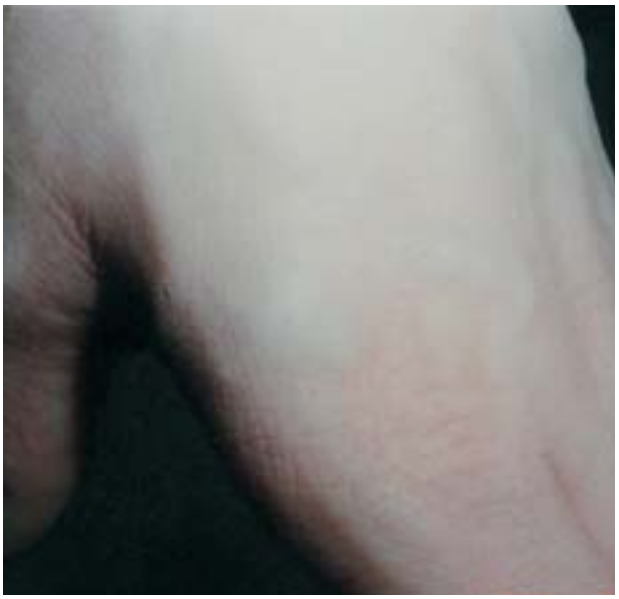

Figure 1. Subcutaneous bluish nodule on the left hand.

Case Report

A 23-year-old white woman was referred to the dermatology department by her family physician for evaluation of numerous nodules on her trunk, extremities, and oral mucosa. These lesions were first noticed during her childhood, at which time 2 of the lesions were excised, 1 of which had since recurred. The pathology results were unknown. The lesions had progressed in number and size over the years. In addition, the patient had a history of rectal bleeding 3 years ago that was attributed to internal hemorrhoids found on colonoscopy. Other past medical history was notable for a uterine cyst and fibroid cysts of the breasts. She denied anemia, melena, or other known GI bleeding episodes. There was no family history of similar lesions.

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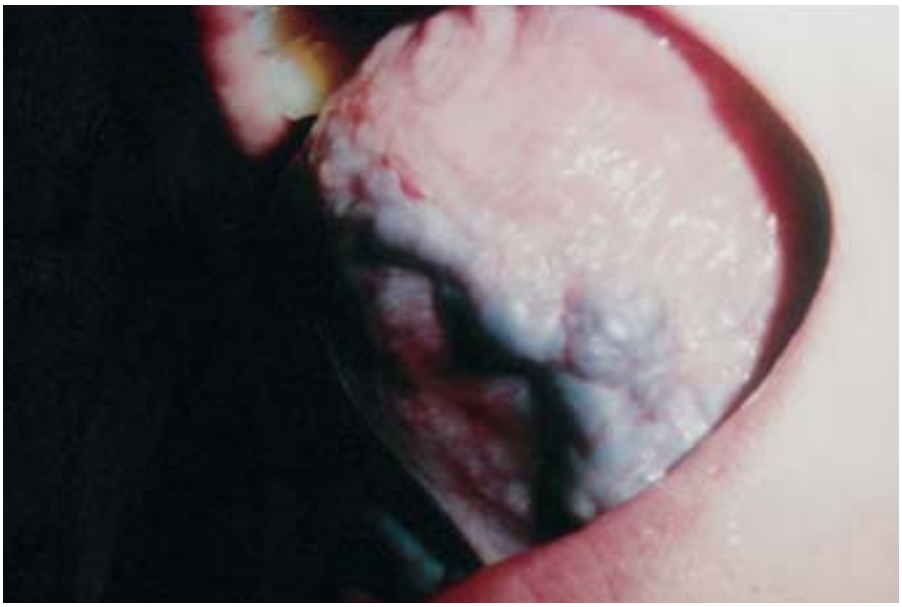

Figure 2. Blue rubbery sublingual nodule.

Findings from the physical examination revealed variably sized, compressible, nonpulsatile, nontender, subcutaneous, bluish nodules located on the patient's right antecubital fossa, right flank, left arm, left hand, and multiple areas of the buccal mucosa and tongue. The variability in size ranged from 1 cm on the hand (Figure 1) to 1.5 cm on the tongue (Figure 2) and antecubital fossa. No skeletal abnormalities were noted.

The patient's most bothersome lesion, located in the right antecubital fossa, was excised and evaluated histologically under light microscopy (Figures 3 and 4). Biopsy results revealed a specimen composed of connective and adipose tissue with a prominent proliferation of ectatic, branching, thin–walled vascular spaces occasionally surrounded by bundles of smooth muscle. No endothelial cell atypia was identified. Although the vascular contour and organization was unusual, size and depth of the vessels were consistent with a cavernous hemangioma. The histopathologic changes observed were compatible with those seen in BRBNS.

Results of a computed tomographic scan of the head were normal. The patient was counseled regarding the related risks of her condition.

Comment

BRBNS is a rare disorder characterized by multiple cutaneous and visceral cavernous hemangiomas. Clinical presentation commonly consists of cutaneous cavernous hemangiomas present at birth or during early childhood that progress in size and number with age. Bean's original work described 3 distinct types of cutaneous and subcutaneous lesions: (1) a blue rubbery blood-filled sac that can be completely or partially emptied of blood by compression; (2) a large cavernous hemangioma that may compress vital structures; and (3) flat blue macules with black stippling. Hyperhidrosis frequently is seen with all 3 types of lesions. Lesions have been documented throughout the entire body surface; however, a literature search reveals a predisposition for the trunk and upper extremities.

In addition to cutaneous involvement, vascular lesions of the GI tract also were present. Cavernous hemangiomas may be present anywhere from the oral mucosa to the anal mucosa, with the highest incidence occurring in the small bowel.[5] Unlike cutaneous lesions, mucosal hemangiomas of the GI tract are friable and highly susceptible to bleeding, resulting in significant occult blood loss and subsequent anemia.[6] The risk for serious bleeding makes BRBNS an important entity to identify.

Although cavernous hemangiomas of the skin and GI tract are the hallmarks of BRBNS, multiple other areas of involvement have been documented in the literature. Hemangiomas have been reported in the brain,[7] conjunctiva, iris, retina,[8,9] oropharynx,[10] nasopharynx,[11] lung,[12] pleura,[13] heart,[14] peritoneal cavity,[12] mesentery, liver,[15] penis,[16,17] uterus, urinary bladder,[18] spleen, joint capsule, and skeletal muscle.[19] Orthopedic involvement with skeletal bowing and pathologic fractures also has been documented.[20]

Histologically, examination of the lesion reveals ectatic vascular channels lined with a single layer of flattened or cuboidal endothelial cells surrounded by a fibromuscular wall. Occasionally, proliferation

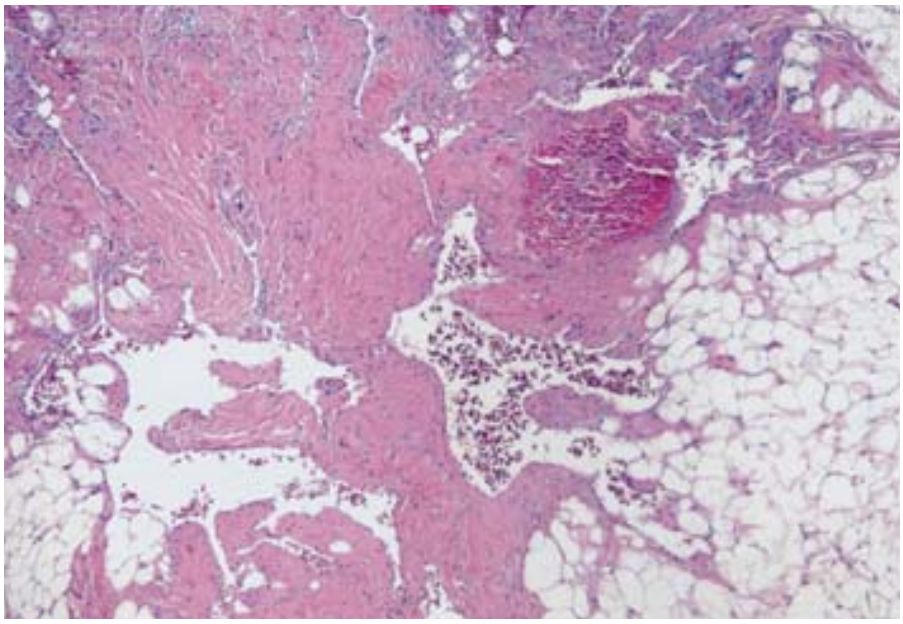

Figure 3. Biopsy of antecubital fossa demonstrates thin-walled vascular spaces surrounded by bundles of smooth muscle (H&E, original magnification ×4).

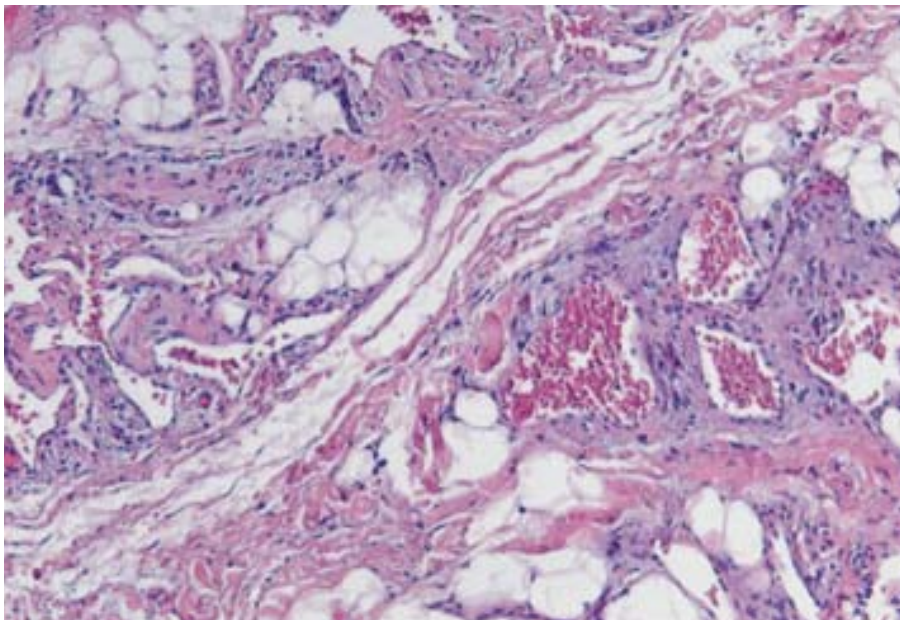

Figure 4. No endothelial cell atypia. Lesion consistent with cavernous hemangioma (H&E, original magnification ×10).

of the eccrine gland has been described,[21] which accounts for the hyperhidrosis observed clinically. Malignant transformation of these hemangiomas has never been described.

BRBNS must be differentiated from hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome), Maffucci syndrome, Klippel-Trenaunay-Weber syndrome, Sturge-Weber syndrome, multiple glomus tumor, and Kaposi sarcoma. The case presented here does not have the clinical or histologic characteristics of these syndromes.

The diagnosis of BRBNS remains a clinical and histologic diagnosis. The discovery of cutaneous hemangiomas indicates further testing for anemia, occult blood loss, and visceral involvement. Magnetic resonance imaging and other imaging techniques have proved pivotal in describing the extent of visceral involvement. Recently, the role of labeling red blood cells with technetium Tc 99m to quantify visceral involvement has been described.[22] The stasis produced by the dilated venous malformation promotes focal accumulation of the labeled red blood cells in the skin and GI tract. Magnetic resonance angiography has recently shown promising results in identifying vascular abnormalities. These imaging techniques may prove to be efficacious in determining visceral involvement in BRBNS.

Cutaneous hemangiomas are treated infrequently unless they are cosmetically disfiguring or functionally disabling. Cosmetically unacceptable lesions may be excised or ablated with laser radiation therapy.[23] Carbon dioxide laser ablation appears to be efficacious, demonstrating decreased scarring and decreased recurrence rate in comparison to excision. GI involvement needs to be evaluated for the extent of the bleeding. If blood loss is significant and focal lesions are identified in an accessible area, laser photocoagulation (Nd:YAG) is indicated and preferred to other techniques because the procedure stops the bleeding immediately and is minimally invasive. Other techniques described in the literature are sclerosing techniques, which have fallen out of favor because of an increased incidence of ulceration and stricture formation in comparison with alternative modalities. When traditional methods fail and vascular lesions are confined to a segment of the alimentary canal, resection of the involved segment may be indicated.[24] Historically however, involvement of the GI tract has been extensive with mild, chronic blood loss requiring conservative treatment with continuous oral iron therapy.[25]

We conclude that in the case of a patient with cutaneous and oral vascular lesions, BRBNS must be considered in the differential diagnosis. Early recognition is critical to provide appropriate medical intervention and possible genetic counseling.

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