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Case Report

Angiomyolipomas As A Cause of Abnormal Uterine Bleeding In A Patient with Tuberous Sclerosis

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Precis: Angiomyolipomas are a rare cause of abnormal uterine bleeding in women with tuberous sclerosis and may be distinguished from uterine fibroids by histologic and immunohistochemical characteristics.

Abstract

Background: Angiomyolipomas have a strong genetic association with tuberous sclerosis and are most frequently found in the kidney. However, these benign tumors can also be found in the uterus, where they can have the sonographic appearance of leiomyomata. Additionally, they are frequently associated with symptoms such as pain and abnormal bleeding, further confounding the diagnosis. Indeed, angiomyolipomas can grow rapidly and larger tumors portend an increased risk of significant hemorrhage.

Case: A 46-year-old woman with tuberous sclerosis presented with several years of dysmenorrhea and irregular, heavy vaginal bleeding. Transvaginal ultrasonography revealed uterine masses consistent with benign leiomyomata. She underwent total laparoscopic hysterectomy after failure of conservative management. An unusual intraoperative appearance of the mass led to careful pathologic examination, which confirmed a diagnosis of uterine angiomyolipoma.

Conclusion: Uterine angiomyolipomas should be considered in the differential diagnosis of symptomatic fibroid-like uterine masses in patients with tuberous sclerosis. As there is a potential for adverse sequelae and conservative therapies for abnormal bleeding may not be effective in this setting, increased suspicion for angiomyolipomas may appropriately led to more aggressive surgical management in this patient population.

Keywords: Angiomyolipoma; Leiomyoma; Tuberous Sclerosis; Abnormal Uterine Bleeding

Abbreviations

TSC: Tuberous Sclerosis Complex;
TSC-1: Tuberous Sclerosis-1 Tumor Suppressor Protein, Hamartin;
TSC-2: Tuberous Sclerosis-2 Tumor Suppressor Protein, Tuberin;
AML: Angioleiomyolipoma;
HMB-45: Antibody to Human Melanin Black-45;
CD10: Antibody to Neprilysin, Cluster of Differentiation-10;

ER: Antibody to Estrogen Receptor;
PR: Antibody to Progesterone Receptor;
E-cadherin: Antibody to Epithelial Cell Adhesion Molecule;
h-caldesmon: Antibody To High Molecular Weight Caldesmon;
S-100: Antibody to Acidic Ammonium Sulfate Soluble Calcium Binding Protein

Introduction

Tuberous Sclerosis Complex (TSC) is an autosomal dominant disorder characterized by benign tumors in multiple organs, most frequently the skin and kidneys. This is associated with functional loss of tumor suppressors TSC1 and TSC2. Angiomyolipomas (AMLs) are usually slow-growing hamartomas rich in muscle, fat, and blood vessels that are present in approximately 80% of patients with TSC [1]. These tumors exhibit high-grade mitotic activity, pleomorphism, and necrosis [3], making them susceptible to rupture and hemorrhage [2]. While distribution of angiomyolipomas has been well described in nervous, renal, hepatic, cardiovascular, and integumentary systems, conspicuously few cases of angiomyolipoma involving the uterus have been reported in this patient population [4]. However, as these tumors may have the sonographic, gross and microscopic appearance of fibroids, the incidence may be markedly under-reported.

Clinical Case

A 46-year-old woman with tuberous sclerosis complex (TSC) presented with several years of dysmenorrhea and irregular, heavy vaginal bleeding. Transvaginal trasonography revealed uterine masses consistent with leiomyomas and she was counseled regarding multiple treatment options. After conservative medical therapy with nonsteroidal anti-inflammatory and hormonal medications failed to control her symptoms, she elected to proceed to surgical management. She underwent an uncomplicated total laparoscopic hysterectomy for definitive management. Intraoperatively, an unusual vascular and polypoid appearance of a presumed subserosal fibroid (Figure 1a) prompted a request for special attention to the pathologic examination of the specimen.

Materials and Methods

The patient described herein provided consent for publication and the case investigation and report received an exemption from our institutional IRB. Gross uterine examination revealed multiple subserous, intramural and submucosal nodules ranging in size from 0.5- 4.5 cm with focal soft and mottled areas on cut surfaces grossly consistent with leiomyomata. Representative samples were processed for routine histological examination with hematoxylin & eosin staining. Further investigation was undertaken using routine immunohistochemical staining techniques with a battery of peroxide-labeled antibodies against HMB-45, smooth muscle actin, CD10, ER, PR, E-cadherin, membranous beta-catenin, h-caldesmon, and S-100. Nuclei were counterstained using hematoxylin. Tissue sections were incubated with specific antibody and unbound antibody rinsed away. Bound antibody was identified through a peroxidase reaction resulting in a brown precipitate in either the nucleus or cytoplasm of the positive-staining cells.

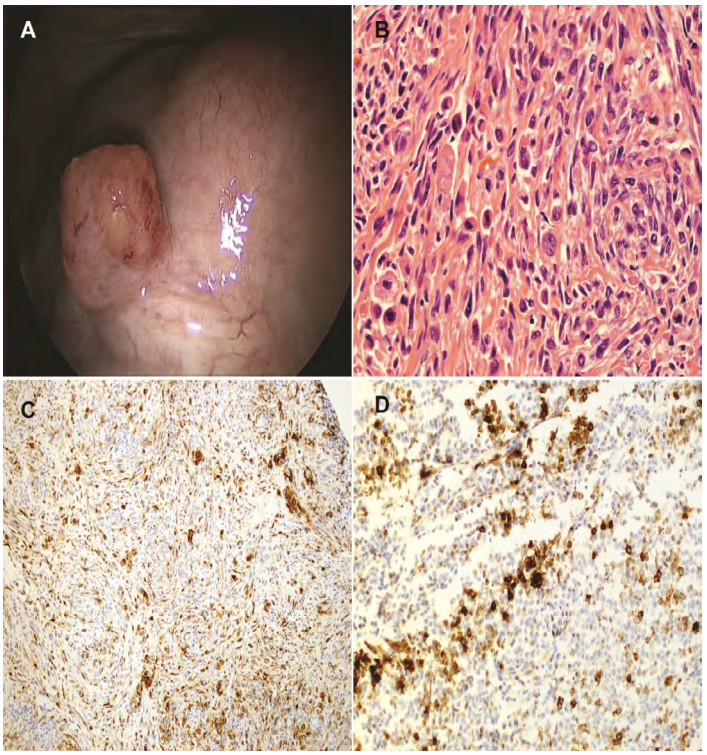

Figure 1.

A. Laparoscopic image of uterine lesion
B. Hematoxylin and eosin stain, mag x200
C. HMB-45 immunohistochemical stain, mag x200
D. H-Caldesmon immunohistochemical stain, mag x200

Lack of antibody binding was identified by the absence of brown precipitate staining with uptake of only the hematoxylin counterstain.

Discussion

Initial microscopic examination supported a diagnosis of benign leiomyomata. However, a more critical evaluation prompted by the unusual intraoperative gross appearance, revealed bundles of smooth muscle in a fascicular pattern with focal thick walled blood vessels and fibrinoid degeneration reminiscent of an endometrial stromal lesion. Pleomorphic epithelioid cells with eosinophilic cytoplasm and prominent bizarre nuclei were identified (Fig 1b) and were strongly positive for immunohistochemical staining using the melanogenic marker HMB-45, which is diagnostically characteristic of angiomyolipoma (Fig 1c). SMA, CD10, ER, PR, E-cadherin, membranous beta catenin, and (focally) h-caldesmon were also more diffusely positive (Fig 1d); S-100 was negative. This

immunohistochemical staining profile distinguished these tumors as angiomyolipomas (AML) rather than leiomyomas with epithelioid features.

Uterine angiomyolipomas may appear sonographically and grossly like fibroids. However, as with this patient, conservative therapies for abnormal bleeding may not be effective. Nor would they necessarily be anticipated to degenerate or become less symptomatic after menopause. Importantly, due to the rare cases of uterine angiomyolipomas reported, the clinical course and implications cannot be fully predicted.

Unlike renal angiomyolipomas, uterine angiomyolipomas in the setting of tuberous sclerosis are thought to be an uncommon tumor. On the other hand, it is possible the incidence is under-reported due to the similarity in anatomic features leading to missed diagnoses. Indeed, it was only after communication between the surgeon and pathologist regarding the unusual intraoperative appearance of these lesions that the immunohistochemical investigation, including HMB-45, was initiated to confirm the diagnosis. Accordingly, angiomyolipomas should always be in the differential diagnosis of uterine masses in this patient population.

Not only is accurate diagnosis important for patients presenting with these features, it should be useful in counseling family members as well. This patient's sister, who also has abnormal uterine bleeding and tuberous sclerosis, is currently undergoing evaluation.

Conclusion

Uterine angiomyolipomas should be considered in the differential diagnosis of symptomatic fibroid-like uterine masses in patients with tuberous sclerosis. Given their cellular composition, conservative therapies for abnormal bleeding are unlikely to be effective in this setting. Considering their potential for adverse sequelae, an increased suspicion for angiomyolipomas may appropriately lead to more aggressive surgical management in this patient populatiion.

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