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Extensive pelvic lymphatic malformations presenting with hematospermia: A case report

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ABSTRACT

Lymphatic malformations are rare vascular abnormalities that usually occur in the head and neck but can occur elsewhere in the body. Here, we present an unusual case of a 14-year-old male who presents with hematospermia, hematochezia, and hematuria. Following work-up which included urinalysis, ultrasound, and magnetic resonance imaging (MRI), the patient was diagnosed with pelvic lymphatic malformations (LMs), including a perirectal lesion and a lesion involving the right spermatic cord. He was started on sirolimus therapy, which resolved the hematospermia and hematuria, and decreased the frequency of the hematochezia. However, the hematochezia did not resolve completely and the patient wished to discontinue sirolimus. The decision was made to pursue doxycycline sclerotherapy for the perirectal lesion. The hematochezia resolved for two weeks following sclerotherapy, but resumed soon thereafter. Options to further manage the patient's symptoms include re-starting sirolimus or repeating doxycycline sclerotherapy. To our knowledge, this is the first report of a lymphatic malformation presenting with hematospermia. Pelvic lymphatic malformations should be considered as a possible etiology for otherwise unexplained bleeding episodes in the adolescent genitourinary system.

Key Words: Pelvic lymphatic malformations, hematospermia, mTOR, sirolimus, sclerotherapy.

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Introduction

Lymphatic malformations (LMs) are rare benign low-flow vascular abnormalities that occur in one out of 2000-4000 live births [1]. These lesions develop as embryologic disturbances during the formation of the lymphatic system. While LMs can occur in any area of the body, these lesions tend to occur in the lymphatic-rich areas of the body such as the head and neck, axilla, groin, mediastinum, and retroperitoneum [2].

The symptoms associated with LMs are generally due to infection or local mass effect on surrounding tissues. Treatment strategies depend on the location, characteristics, and extent of the LM. Treatment options include observation, medical therapy, surgery,

sclerotherapy, and ablation. Medical therapy targets the mammalian target of rapamycin (mTOR) pathway, an important regulator in lymphangiogenesis. Herein, we present a case of extensive pelvic LMs presenting with hematospermia, hematuria, and hematochezia treated with sirolimus and sclerotherapy.

Case report

A 14-year-old male with a past medical history significant for hematochezia since infancy presented with a 2-month history of hematospermia. The patient had a long history of hematochezia of unknown etiology resulting in iron-deficiency anemia. Hematologic work-up was negative, and the patient ultimately had a colonoscopy at age 7 which was unrevealing. Recently, he reported that each morning the front of his underwear were heavily spotted with blood. Additionally, he noticed hematospermia and hematuria.

Upon urologic evaluation, physical examination was remarkable for varicosities on his glans penis with no evidence of blood per urethra. Urine analysis was negative for blood, leukocyte esterase, or nitrites. Sonogram of the bladder and kidneys revealed no pathology. Magnetic resonance imaging (MRI) of the abdomen and pelvis revealed a multispacial LM involving not only the pelvic peritoneum, but also the soft tissues adjacent to the coccyx and medial to the right obturator internus muscle (Fig. 1A). The LM also had a microcystic component involving the right spermatic cord with extent adjacent to the right testicle and penis, including the corpora cavernosa and glans (Fig. 1B).

After multi-disciplinary discussions, the consensus recommendation was to start therapy with a mammalian target of rapamycin (mTOR) inhibitor while continuing to explore

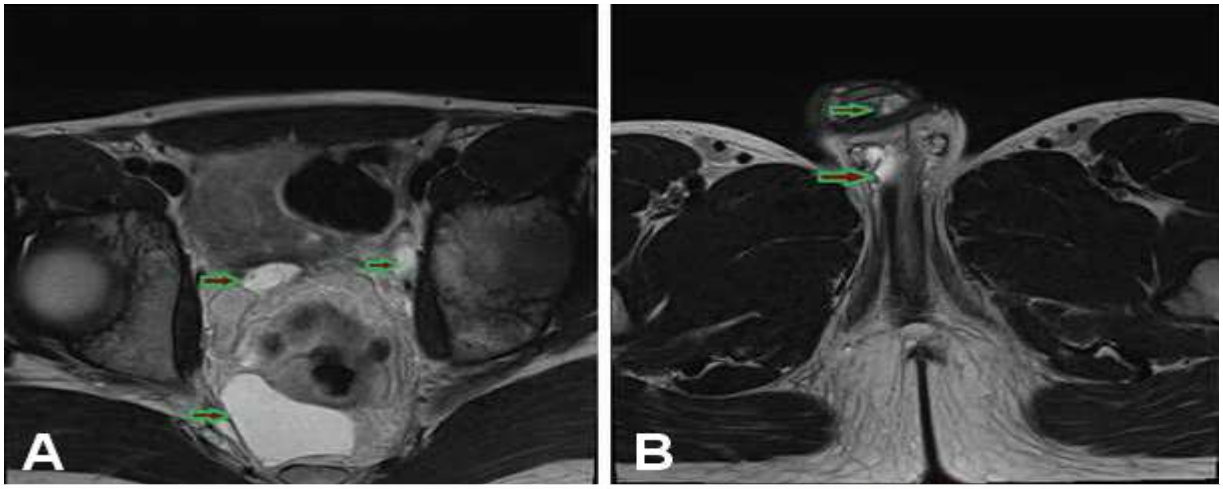

Fig. 1. **A)** Multispacial perirectal LM involving the pelvic peritoneum and soft tissues adjacent to the coccyx, initial MRI. **B)** Microcystic LM with extent in the corpora cavernosa and spermatic cord, initial MRI.

He noted that the hematuria was asymptomatic and exacerbated by strenuous activity such as sports but could also occur at rest. The patient denied other sources of bleeding such as epistaxis, gum bleeding, and hemarthrosis.

options for the large perirectal lesion. The patient was started on sirolimus. After 2 weeks of therapy, he had significantly less volume and frequency of penile bleeding and by 1 month had complete resolution of

hematospermia and hematuria. The patient initially reported decreased rectal bleeding as well, and by 5 months it had slowed to infrequent episodes.

After one year of therapy, the family discontinued the sirolimus and wished to pursue management for the macrocystic lesion. The patient underwent repeat MRI showing a significant decrease in the size of the pericoccyx LM, with no significant changes to the other lesions (Fig. 1-3). The decision was made to pursue doxycycline sclerosis for the perirectal lesion. Following the procedure, the patient had no rectal bleeding for 2 weeks, but the bleeding soon resumed. There continued to be no penile bleeding.

The patient planned to undergo another MRI to assess the response to the sclerosis and have a discussion regarding repeat sclerosis or resuming sirolimus therapy.

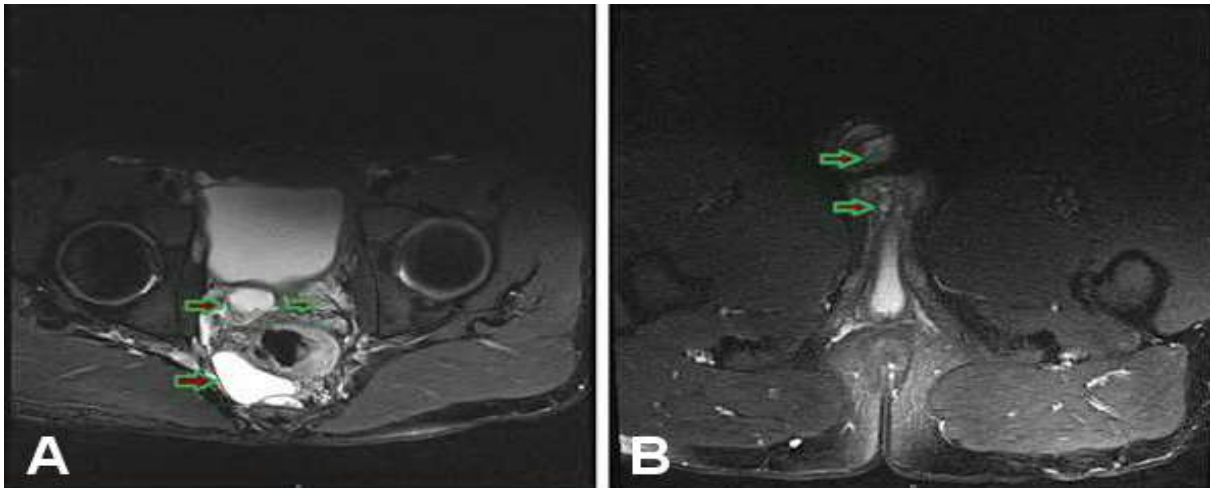

Fig. 2. Repeat MRI after 13 months of Sirolimus therapy. **A)** Unchanged LM near rectum and obturator internus. **B)** Unchanged LM of glans penis and corpora cavernosa.

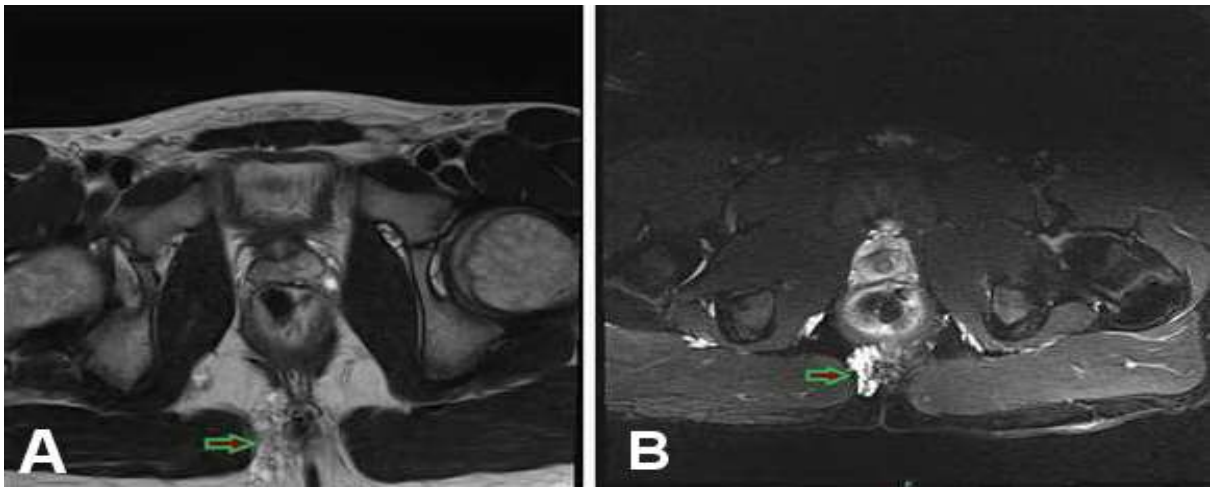

Fig. 3. **A)** Peri-coccyx LM on initial MRI. **B)** Decreasing size of peri-coccyx LM on repeat imaging 13 months later.

Discussion

Lymphatic malformations (LMs) cause significant morbidity depending on their location and involvement of surrounding structures [3]. To our knowledge, this case represents the first report of LMs presenting with hematospermia.

In general, vascular malformations are classified based on the type of blood flow: slow-flow (capillary, venous, and lymphatic lesions), high-flow (arterial) lesions, and combined slow/fast-flow lesions. In this case, the diagnosis of LM via MRI was made on the basis of the numerous microcystic and macrocystic components of the lesions, which are characteristic of LMs and not present in other vascular anomalies. While Doppler ultrasound can be used to confirm the flow of the lesion, these studies were not needed in this case, as MRI confirmed the diagnosis unequivocally [9].

Bleeding or compression from mass effect are the most common presenting symptoms of LMs. These vascular anomalies grow larger due to drainage outflow obstructions. Similarly, LMs contain fragile malformed veins in their walls which can bleed easily and fill the LM with blood and cause it to expand further. As the LM grows larger and begins to involve local structures (the urethra and rectum, in this case), injury to these tissues and erosion of the cystic components of the LM can occur, causing bleeding that becomes apparent to the patient. In this case, the involvement of the urethra and the rectum gave rise to the presenting symptoms: hematospermia, hematuria, and hematochezia [9].

Treatment strategies for LM depend upon the presentation, size, characteristics, and location of the lesion. For complex lesions, multi-disciplinary input is required to develop an optimal treatment strategy. Current management options include observation, medical therapy, surgery, sclerotherapy, and ablation. Surgical excision remains the gold standard for large LM with a reported persistence of disease of about 30% [2]. While surgery can be definitive treatment for LMs, it carries the highest risk complications including lymphatic leak, neurovascular injury, fistula formation, and poor cosmesis [2, 4, 5].

Medical therapy for LM is targeted at the mammalian target of rapamycin (mTOR) pathway because mTOR acts as a master switch for multiple cellular processes and is associated with lymphangiogenesis [6, 7]. Specifically, mTOR functions as a serine/threonine kinase regulated by phosphoinositide-3-kinase (PI3K). While there have been reports of somatic mutations in the catalytic subunit of PI3K in patients with LM, the exact mechanism of the effects of sirolimus on LM remains unknown [7]. In a recent study by Strychowsky et al. [8], 19 young patients with refractory cervicofacial LM were treated with sirolimus resulting in reduced LM bulk for all patients with most seeing clinically significant improvements in symptoms.

In the case presented, sirolimus had a significant impact on the bleeding diathesis from the extensive pelvic LM but did not significantly decrease the size of the lesions on repeat MRI one year later (Figures 1 & 2). The improvement in symptoms despite the significant change in size suggests that the efficacy of sirolimus might be due to cellular or microscopic changes that are not visible on conventional imaging.

Conclusion

Lymphatic malformations are a rare clinical entity that usually occur in the lymphatic-rich areas of the body, but pelvic LM should be

considered when exploring the etiology of unexplained pelvic bleeding in an adolescent. Multidisciplinary input is required to determine the best treatment options for anatomically complex lesions. For this patient, medical management with sirolimus, an mTOR inhibitor, and doxycycline sclerotherapy provided partial symptomatic relief. While sirolimus is an effective treatment for minimizing the morbidity associated with these malformations, its ability to achieve complete resolution must be further investigated. After sirolimus therapy was discontinued, doxycycline therapy proved to be a valuable treatment modality for controlling the patient's symptoms, but also failed to resolve them completely. If symptoms persist, possible definitive treatment with surgery, despite its increased risk for complication, could also be considered.

Compliance with ethical statements

Conflicts of Interest: None.

Financial disclosure: None.

Consent: All photos were taken with parental consent.

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