Case Reports in Women's Health 40 (2023) e00557

Contents lists available at ScienceDirect

Case Reports in Women's Health

journal homepage: www.elsevier.com/locate/crwh

Intravascular leiomyomatosis with cardiac and pelvic involvement in a postmenopausal woman: A case report of multidisciplinary team management

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ARTICLE INFO

Keywords:
Intravascular leiomyomatosis
Heart tumor
Inferior vena cava
Ovarian vein
Case report

ABSTRACT

Intravascular leiomyomatosis (IVL) is a rare benign condition in which a leiomyoma, originating from the uterus, propagates through the pelvic venous system and occasionally extends into the inferior vena cava (IVC), occasionally reaching the heart. Despite its low incidence and benign nature, IVL can lead to life-threatening obstructions in the right heart's outflow tract, potentially resulting in sudden death. In this article, we present a case of a 72-year-old postmenopausal patient with IVL, who initially presented with palpitations. The diagnosis was made through echocardiography and a computerized tomography (CT) scan, revealing a tumor that extended from the uterus through the IVC and into the right ventricle. The patient was managed by a multidisciplinary team of gynecologists and cardiothoracic surgeons, who performed a single-stage surgical removal of a tumor 25 cm long. The pathological report confirmed the diagnosis of IVL. Postoperative follow-up is crucial, as IVL recurs in up to 30% of cases. This article's objective is to provide a clinical illustration of this exceedingly rare condition, with fewer than 300 reported cases, and to offer a comprehensive overview of IVL, including its clinical presentation, diagnosis, treatment, and outcomes.

1. Introduction

Intravascular leiomyomatosis (IVL) is an exceptionally rare condition characterized by the intraluminal growth of benign smooth muscle tumors within the venous system [1], with fewer than 300 reported cases in the literature. It was first described by Birch-Hirschfeld in 1896. Its pathogenesis remains uncertain, with two proposed theories: one suggesting IVL originates from uterine leiomyomas infiltrating venous walls and the other proposing it arises from smooth muscle cells within uterine veins [2]. IVL predominantly affects premenopausal women with a history of uterine leiomyomas, myomectomy, or hysterectomy, usually confined to the pelvic venous system but potentially life-threatening when extending into the inferior vena cava (IVC), right atrium, and pulmonary veins [3,4].

IVL poses diagnostic challenges due to its nonspecific clinical features and variable imaging findings [6], complicating the establishment of management guidelines. Treatment strategies are contingent on the extent of venous system involvement, necessitating multidisciplinary teams, with recurrence rates reaching up to 30% [5].

This article presents a rare clinical case of IVL extending into the right ventricle while summarizing the current understanding of IVL, offering insights into its clinical manifestations, diagnostic approaches, and treatment modalities.

2. Case Presentation

A 72-year-old woman attended the cardiac surgery unit due to palpitations during physical exertion over the past three years, recently worsening, even occurring at rest, particularly in the evenings. Physical examination showed no specific symptoms, and the electrocardiogram (ECG) revealed no abnormalities or heart murmurs. Further investigation with transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) unveiled a free-floating tumor within the right atrium, originating from the IVC and causing mild tricuspid regurgitation. A contrast computerized tomography (CT) scan detailed an elongated mass originating from the left ovarian vein, traversing the left renal vein, and reaching the right atrium and ventricle (Fig. 1). Differential diagnosis included thrombus or IVL. Discussions between

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https://doi.org/10.1016/j.crwh.2023.e00557
Received 10 October 2023; Received in revised form 18 October 2023; Accepted 24 October 2023
Available online 25 October 2023

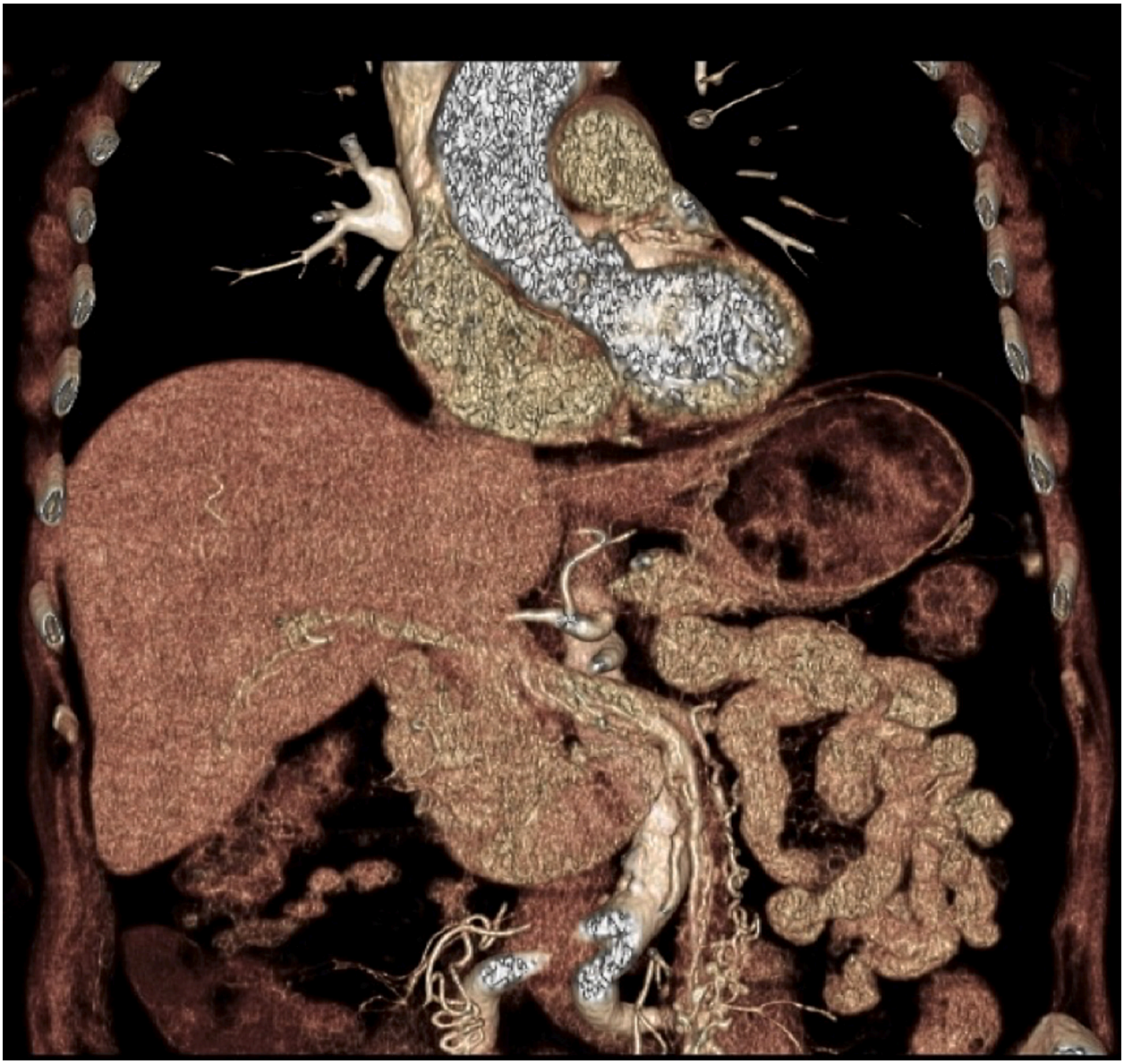

Fig. 1. Volume-rendering coronal reconstructions showing the extension of tumor-thrombus from the left ovarian vein through the left renal vein and inferior vena cava to the right heart atrium.

cardiothoracic and gynecological teams led to the selection of a single-stage procedure to remove the mass.

The gynecological team performed a midline laparotomy, and discovered an intraligamentary fibroid (FIGO 6) measuring 8 cm in diameter adjacent to the left adnexa. Examination of the left infundibulopelvic ligament revealed an enlarged and thickened ovarian vein with a normal ovarian artery running alongside. After coagulating and severing the ovarian artery, they ligated and excised the ovarian vein, along with the enclosed mass, cranially at its entry into the renal vein. The left tube, left utero-ovarian ligament, left adnexa, and the tumor were all coagulated and removed. The excised mass exhibited the characteristic firm and elastic consistency of leiomyomas. The intraligamentary leiomyoma was also excised.

The cardiothoracic team performed a sternotomy, gaining access to the pericardium and the heart. Total cardiopulmonary bypass (CPB) was initiated after cannulating the ascending aorta and the right atrium. An elongated tumor within the right atrium was discovered, entering through the IVC and extending into the right ventricle. Fine adhesions were identified between the mass and the right atrium, necessitating adhesiolysis. The mass, measuring 25 cm in length and 2 cm in width, with the characteristic pale white color of leiomyomas, was carefully extracted (Fig. 2, Fig. 3).

The postoperative period progressed without complications, and the patient was discharged ten days later. Pathological analysis confirmed the presence of a SMA-positive smooth muscle tumor, with abundant vascular structures, confirming the diagnosis of IVL (Fig. 4).

3. Discussion

Intravascular leiomyomatosis (IVL) remains an enigmatic and rare disease, often challenging to diagnose due to its nonspecific clinical manifestations and low incidence. Predominantly affecting premenopausal women in their 40s, it can also occur in individuals ranging from 24 to 76 years old [6]. Surprisingly, a history of hysterectomy increases the risk of IVL [7]. Symptoms vary from none to palpitations, symptoms of right heart failure like dyspnea, ascites, jugular vein distension, lower limb edema, syncope, and even sudden death [8], with symptom severity corresponding to the extent of leiomyoma involvement in the

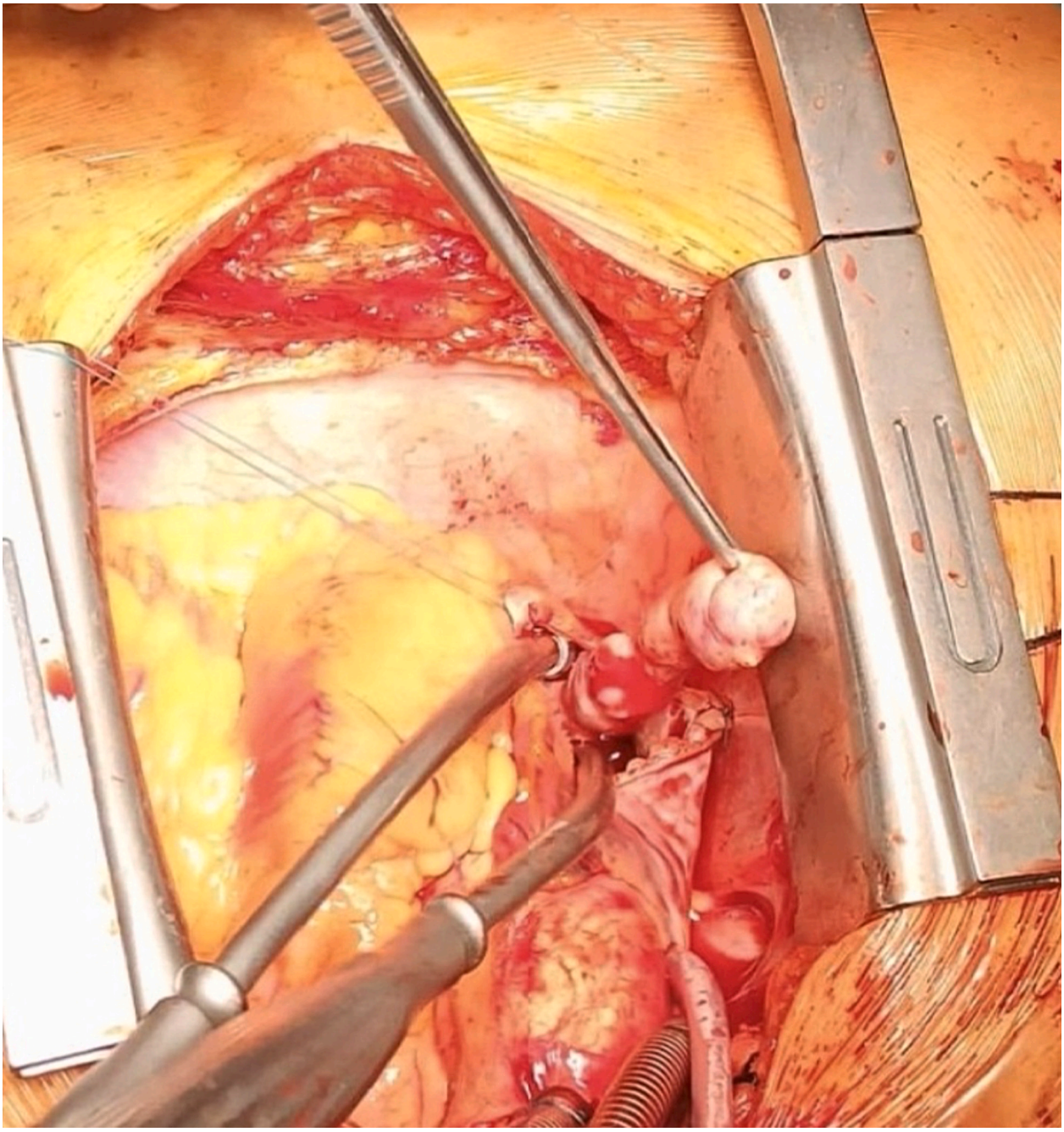

Fig. 2. Intraoperative finding with a pincer removing the intracaval part of the tumor from the right heart atrium.

venous system.

IVL has been associated with genetic alterations in several genes, most commonly found on chromosomes 1p, 22q, 2q, 1q, 13q, and 14q [9]. Contrary to this finding, the most common genetic alterations found in standard uterine leiomyomas are the MED12 and HMGA2 genes, located on the X and 12q chromosomes, respectively, which are responsible for 90% of all uterine fibroids [9]. Another study identified HOXA13 as a distinctly upregulated gene found in typical uterine leiomyomas when compared with IVL [10]. The authors of that study suggest that IVL may be a subtype of conventional uterine myoma, and HOXA13 status may serve as a biomarker to distinguish these conditions.

IVL spreads through two primary venous routes: one involving the ovarian vein directly to the IVC (if originating from the right adnexa) or via the left renal vein before reaching the IVC, and the other utilizing the internal iliac vein system, ultimately reaching the IVC through the common iliac vein [11]. IVL extending to the heart, referred to as intracardiac leiomyomatosis or ICL, is exceptionally rare [1]. Ma et al. proposed a classification system categorizing IVL into four stages based on its venous propagation to guide surgical management [12]. In stage I, the tumor is confined to the pelvic cavity. Stage II denotes extension into the abdominal cavity without reaching the renal vein. Stage III encompasses cases where IVL reaches the renal vein, IVC, or the right atrium but does not invade the pulmonary arteries. Finally, stage IV involves lung metastases or pulmonary artery invasion [13].

Accurate preoperative workup and staging rely on comprehensive imaging techniques, combining echocardiography (transthoracic or transesophageal), venography, abdominal and pelvic CT scans, magnetic resonance venography, or CT angiography (CTA). Echocardiography plays a crucial role, particularly in stages III and IV, identifying

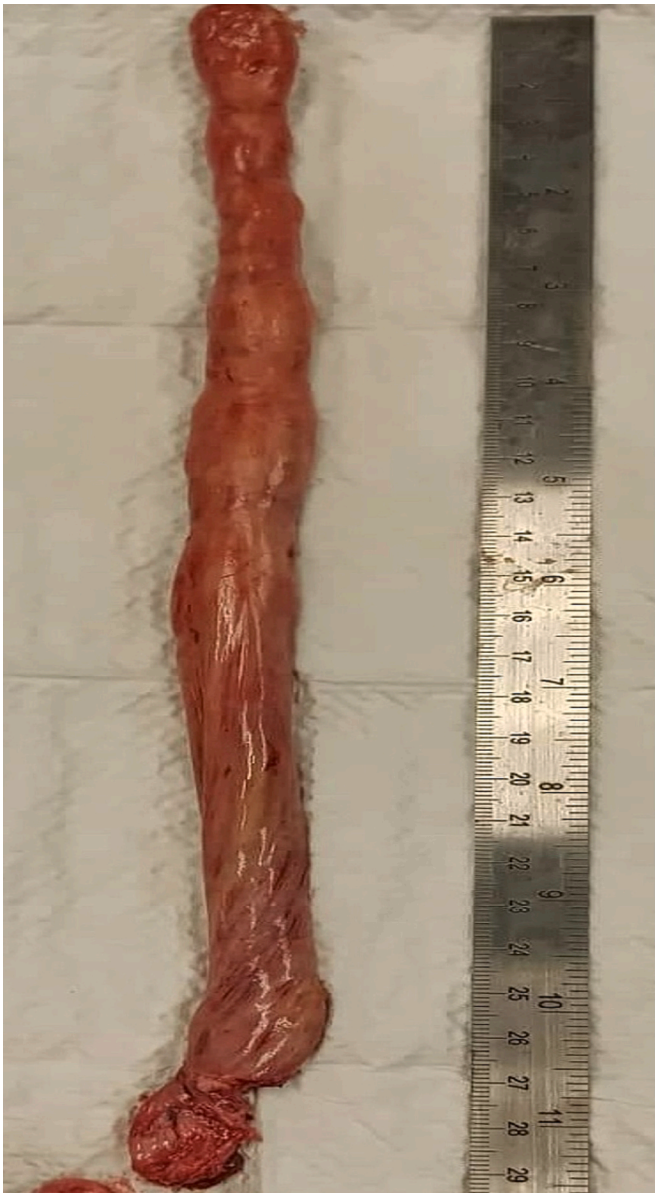

Fig. 3. Postoperative specimen - intravascular leiomyoma.

long and serpentine masses resembling "walking-stick heads" or "snakeheads," freely mobile in the IVC, right atrium, and ventricle, without attachment to vessel surfaces or endocardium [6]. TEE is better than transthoracic echocardiography in evaluating atrial masses and may reduce vascular injury during surgery [3]. Tricuspid regurgitation is characteristic of IVL due to tumor propagation through the tricuspid valve. Contrast CT and magnetic resonance imaging (MRI) assist in identifying the tumor's origin and tracing it back to the uterus or pelvic cavity, especially in cases of prior hysterectomy. Some authors argue that contrast CT is superior to MRI for mapping the tumor's full length [14].

Differential diagnoses include thrombus, atrial myxoma, and neoplasms leading to intravascular thrombi such as renal cell carcinoma, Wilms' tumor, and adrenal carcinoma [3]. Suspicions of IVL should arise in cases involving women with histories of hysterectomy or uterine leiomyoma and the presence of a right-sided cardiac mass originating from the IVC as seen on echocardiography. IVL is definitively diagnosed when the mass lacks a stalk and moves freely within the IVC and right-sided cardiac chambers without attachment to the endothelial surface or endocardium [15].

Prompt management is crucial, as IVL can abruptly transition from asymptomatic to life-threatening. Surgery remains the cornerstone of IVL treatment, aiming for complete tumor removal to minimize the risk of recurrence [8]. The choice between single-stage and two-stage procedures depends on the disease stage and individual patient considerations. In stage I, a gynecological team suffices for surgery, given the pelvic confinement of the tumor [16]. Many advocate a radical approach involving total hysterectomy and bilateral salpingo-oophorectomy in this context, considering the high recurrence rate, especially concerning premenopausal patients desiring future fertility [12]. Stage II necessitates collaboration between gynecological and vascular surgeons, as the procedure entails IVC incision but does not require cardiopulmonary bypass (CPB). For stage III and IV cases, which involve the heart, a cardiothoracic surgeon is imperative, with CPB employed to prevent massive hemorrhage during tumor resection. Surgery may be executed as a single- or a two-stage procedure, with the latter being reserved for patients in poor health or when extensive tumor removal is challenging [8]. Single-stage procedures confer better patient prognosis, reducing the risk of tumor embolization between surgeries and lowering recurrence rates [13].

Recurrence remains a pressing concern, as the condition can manifest decades after primary IVL removal [16]. To mitigate this risk, gynecologists often recommend the removal of the uterus and both adnexa, as intravascular leiomyomas frequently express estrogen and progesterone receptors, and cessation of ovarian hormone production may reduce recurrence [17]. Some authors advocate adjuvant hormonal therapy post-surgery, employing GnRH analogs, aromatase inhibitors, and SPRMs [18]. However, the efficacy of hormonal treatment in preventing recurrence remains controversial [1,16]. The risk factors for recurrence include premenopausal age, incomplete tumor resection, and large initial tumor size, and hormonal therapy may be considered in such patients [14]. Preoperative GnRH analogs may be used to reduce tumor size and facilitate surgery in hormone-dependent IVL cases [19]. In the present case, menopause and the resulting cessation of ovarian estrogen production influenced the decision to perform left adnexectomy while preserving the uterus to minimize surgical trauma.

Regarding postoperative follow-up, no consensus exists. Most studies recommend CT scans at 3, 6, and 12 months after surgery, followed by annual scans to monitor recurrence risk [17]. Vigilant follow-up imaging is essential, given the persistent risk of IVL recurrence. In the reported case, all imaging studies were negative for recurrence one year after surgery.

4. Conclusion

In conclusion, intravascular leiomyomatosis (IVL) is an exceedingly rare condition characterized by the intraluminal growth of benign smooth muscle tumors within the venous system. Despite its benign nature, IVL can rapidly progress to become life-threatening. Prompt and accurate diagnosis is challenging due to its nonspecific clinical presentation and low incidence. Treatment involves surgical removal of the tumor, often requiring multidisciplinary teams and, in some cases, cardiopulmonary bypass. Single-stage surgery is the preferred treatment option, whenever feasible. Recurrence remains a concern, and careful postoperative follow-up is necessary. Continued surveillance is crucial to manage this rare and enigmatic condition effectively.

Contributors

Atanas Aleksandrov contributed to patient care, conception of the case report, completion of the literature review, acquiring and interpreting the data, drafting the manuscript, and revising the manuscript for important intellectual content.

Aleksandar Lyubenov contributed to patient care, conception of the case report, and revising the article critically for important intellectual content.

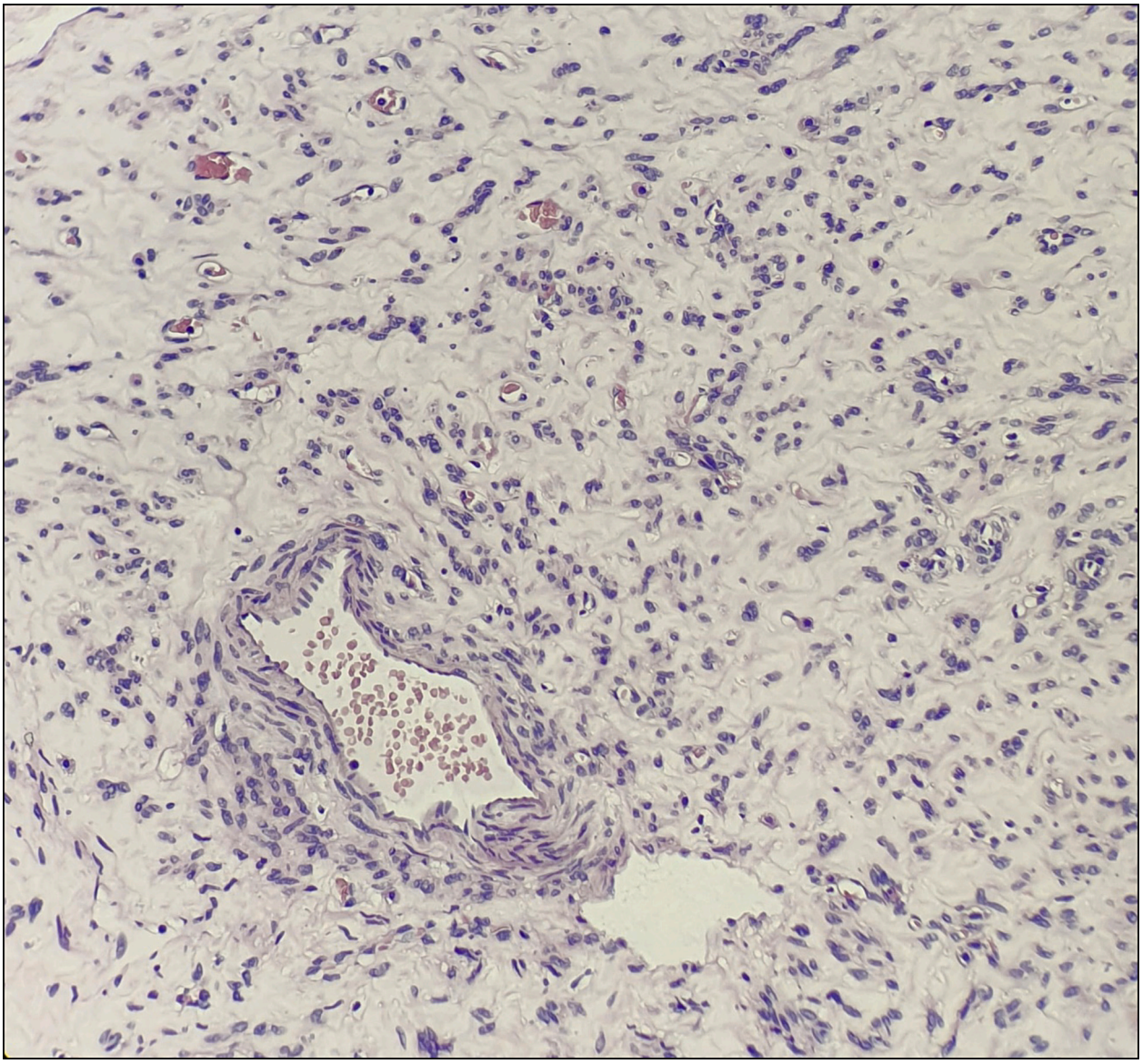

Fig. 4. Hematoxylin and eosin staining: visible blood vessels (black arrow), surrounding smooth muscle cells (red arrow) and fibrosis (red stars); magnification x200. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Polina Damyanova provided the images and histopathological examinations included in this case report and contributed to revising the article critically for important intellectual content.

All authors provided final approval of the submitted manuscript.

Funding

No funding was received to prepare this report.

Patient consent

We received the patient's written consent to submit her case for publication.

Provenance and peer review

This article was not commissioned and was peer reviewed.

Acknowledgements

We would like to thank the patient for her confidence in our team and to share her case with the scientific community.

Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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