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Case report

Gonadal vein leiomyosarcoma, from clinical practice to a literature review: surgical, oncological and histopathologic correlation

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Abstract. Vascular leiomyosarcomas are rare and generally originate from the muscular wall of the inferior vena cava. Leiomyosarcomas originating from the wall of the gonadal veins are rare and just about ten cases are described in literature. In the present paper, we have described a case of a LMS originating from the left gonadal vein. A 44-year-old woman presented in March 2020 pain symptoms at the level of the left renal lodge. The subsequent CT and the biopsy confirmed the diagnosis of G2 grade LMS. The mass was then removed en bloc from the posterior and inferior pancreatic plane, from the aortic plane and from the retroperitoneal plane, post chemoteraphy. Pathologic report revealed a typical leiomyosarcoma, moderately differentiated G2 with minor dedifferentiated areas of pleomorphic leiomyosarcoma. The LMSs originating from gonadal veins represent an uncommon oncologic challenge. The radical en bloc excision represents the therapeutic gold standard. (www.actabiomedica.it)

Key words: leiomyosarcoma, retroperitoneal space, tumor of gonadal vein

Introduction

Malignant soft tissue tumors account for less than 1% of adult malignant tumors. Leiomyosarcoma (LMS) represents a malignant mesenchymal tumor arising from smooth muscle tissue and it accounts for less than 5% of total soft tissue neoplasms (1). LMSs originating from smooth muscle vessels are very rare and they account for less than 2% of all LMSs (2). About 75% of vascular LMSs generally develop from the smooth muscle wall of the inferior cava vein along its retroperitoneal course. The growth of this rare tumor can be assessed as intraluminal or extraluminal. When an extraluminal expansion can be identified at the level of the retroperitoneum, LMS can often be erroneously classified as a primitive form resulting from retroperitoneal smooth muscle. In addition to LMSs originating from the inferior cava vein wall, LMSs originating from the renal vein, the great saphenous vein, the pulmonary veins and the femoral veins are more frequently described in literature (3,4). Conversely, LMSs of the gonadal veins (right or left) are extremely rare and only ten cases have been reported in literature (4).

Case report

A 44-year-old woman presented in March 2020 pain symptoms at the level of the left renal lodge, resistant to common painkillers. In May 2020 she entered the emergency room for the worsening of symptoms: the clinical exam and the subsequential preliminary diagnosis revealed the presence of an abdominal mass and left hydronephrosis. Therefore, abdominal CT with and without contrast medium enhancement was performed, which showed at the level of the left hypochondrium and left flank, at the retroperitoneal level, a voluminous polylobulate neoformation of 11x9x11 cm, characterized by mixed density, not clearly dissociable from the left kidney and the psoas muscle (Fig. 1).

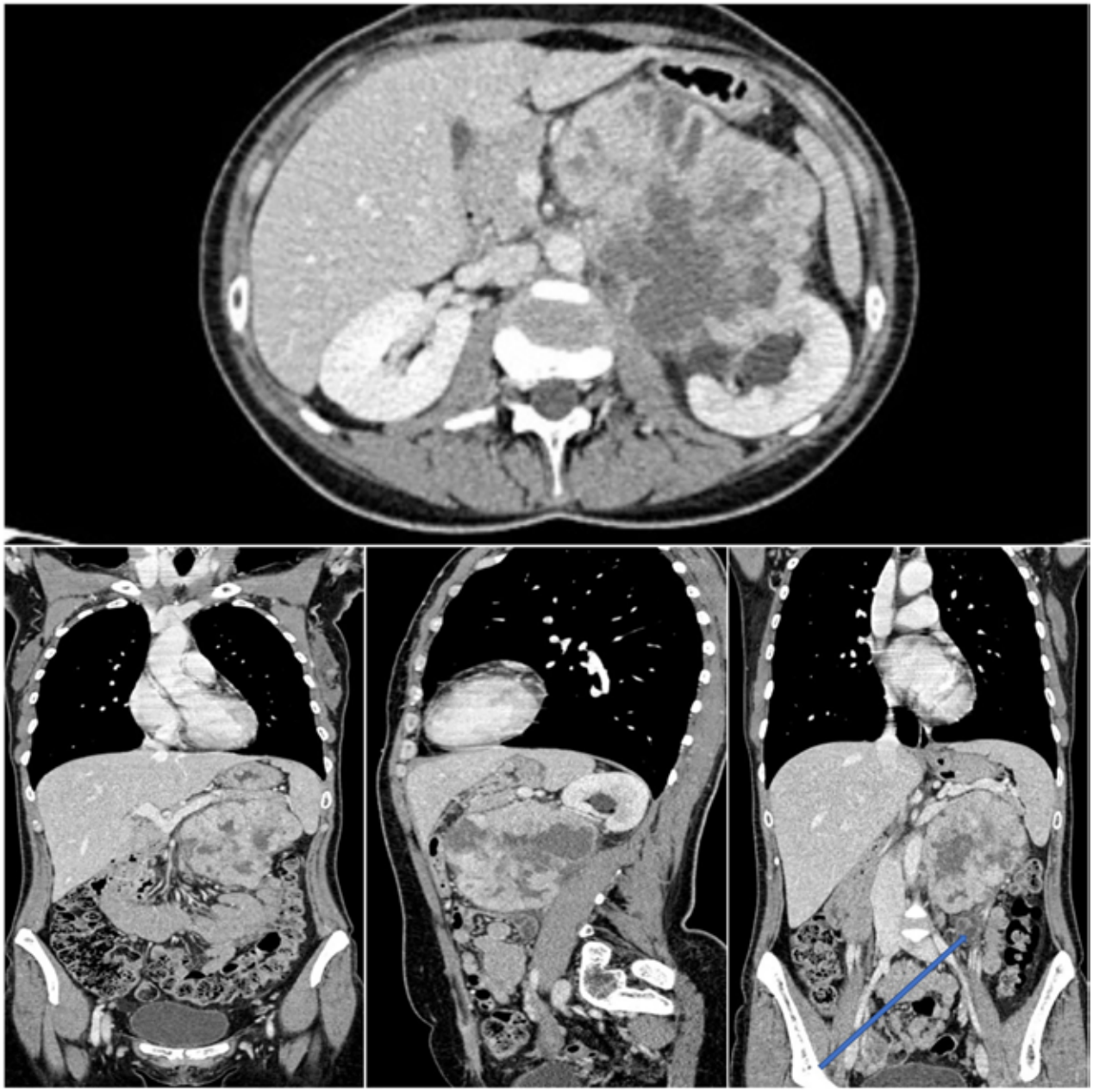

Figure 1. LMS originating from the left gonadal vein (blue arrow) – CT scans before chemotherapy.

The neoformation presented as encompassed the left ureter with upstream hydroureteronephrosis and displaced the pancreatic body and tail superiorly. At the same time, biopsy of the mass was performed, which showed the presence of moderately cellulated mesenchymal proliferation with frank cytological atypia, occasional mitosis compatible with moderately differentiated G2 grade LMS, with the following immunohistochemical profile: Vimentin +, actin 1A4 +, MYGENIN -, PgR-, DESMINE +, S100-, CD117-, ki67 of 10%, absent MDM2 mutation. The histopathological preparation has been submitted for review to another center specialized in the clinical treatment of sarcomas, with the subsequent confirmation of the original diagnosis (5). In June 2020 an ureteral stent was placed and subsequently the patient was subjected to 6 chemotherapy cycles with epirubicin and dacarbazine, as prescribed by the last NCCN Guidelines for soft tissues sarcomas (5). At the end of the chemotherapy treatment, the patient underwent a new total body CT with and without contrast medium enhancement, which showed the presence of the well-known retroperitoneal mass in the abdominal area and unaltered dimensions since the first CT scan.

The mass presented as lobulated on its margins, characterized by a rich and inhomogeneous enhancement, and several colliquative necrotic central areas. The neoformation also seemed to present a strong anatomical continuity, appearing as indissociable from the proximal section of the ureter and from the left renal pelvis, causing a marked degree IV pyelocaliectasis. Furthermore, the lesion compressed the ipsilateral psoas muscle and the left renal artery, in some points without a clear cleavage plane, which in the middle terminal segment presented a moderate reduction in caliber. It determined a moderate reduction of the parenchyma-nephrographic effect of the left kidney, with delay of elimination of iodinated urine compared to the right kidney. No alteration affecting other organs or tissues was found. On January 2021 the patient underwent surgery. The patient was placed in position before the induction of general anesthesia. The entire abdominal-pelvic cavity was carefully explored in order to detect the presence of any peritoneal metastases, even if not detected in preoperative CT. The surgical procedure began with the section of the gastrocolic ligament starting from the middle of the transverse colon in correspondence with the translucent Bouchet area, and it continued with the opening of the aforementioned ligament from right to left, until the splenocolic and frenocolic ligament were dissected. Subsequently, mobilization of the left colon was performed by detaching the Toldt fascia, superiorly from the lamina of Gerota and inferiorly from the pseudocapsule of the polyilobular leiomyosarcoma. During the aforementioned maneuvers, the artery and the inferior mesenteric vein were carefully preserved.

The mass was removed *en bloc* from the posterior and inferior pancreatic plane, from the aortic plane and from the posterior retroperitoneal plane (Fig. 2).

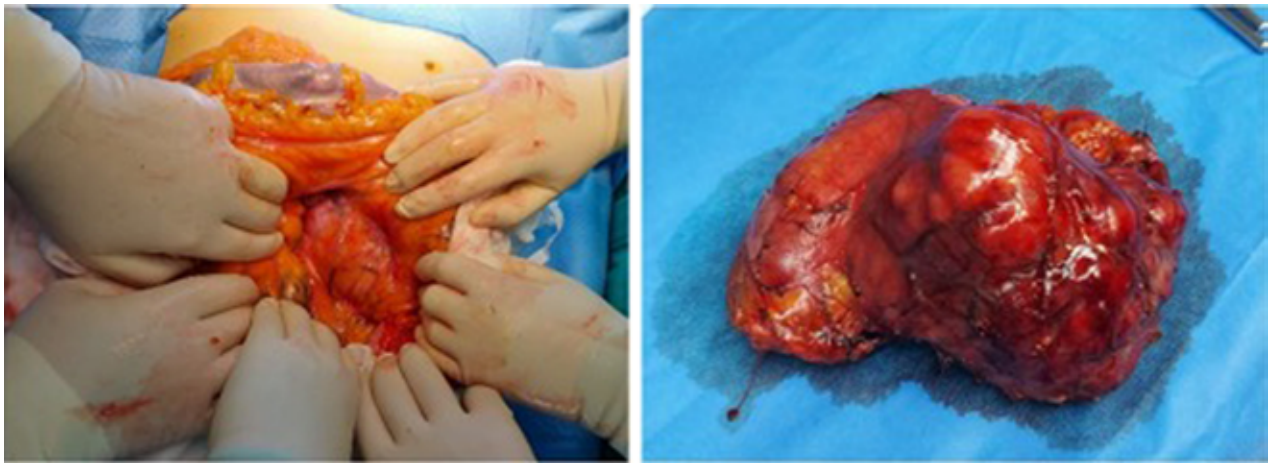

Figure 2. LMS originating from the left gonadal vein – intraoperative views.

The surgery also consisted of a radical removal of the left kidney, the gonadal vessels and the left ureter. The polylobulated tumor was removed by dissociating the pseudocapsule which surrounded it from the posterior and inferior pancreatic planes, the aortic and retroperitoneal planes, removing *en bloc* the mass and the left kidney after ligation of both renal venous and arterial vessels as well as the gonadal vessels and the left ureter, about 13 cm from the renal pelvis, after extraction of the previously placed ureteral stent. The left psoas muscle presented as limitedly infiltrated and its infiltrated portion was removed too, along with the mass and the left kidney. The postoperative course was regular and the patient was discharged after 8 days. The definitive histological examination performed on the sent specimen confirmed the supposed diagnosis (Figs. 3,4).

Pathologic report revealed a typical leiomyosarcoma (sec. WHO 2020), moderately differentiated G2 (score 4 sec. FNCLCC histologic grading system) with minor dedifferentiated areas of pleomorphic leiomyosarcoma. Postoperative pathological examination showed a well delimitated tumor developed around the gonadic vein. Renal vessels, ureter and renal pelvi was in close relationship but outside the encapsulated tumor which showed no evidence of invasion of surrounding structures or retroperitoneal adipose tissue. Microscopic analysis revealed a typical leiomyosarcoma (LMS) well circumscribed by a fibrous pseudocapsule arised from the smooth muscle cells of the muscular component of a large vein wall. LMS consisted in spindle-shaped cells with focal nuclear pleomorphism set in parallel and perpendicular fascicles in a storiform pattern without transcapsular invasion.

Discussion

Vascular leiomyosarcoma represents a rare mesenchymal tumor that develops from the vessel wall. The vessel from which the neoplasm most frequently originates is represented by the inferior vena cava, even

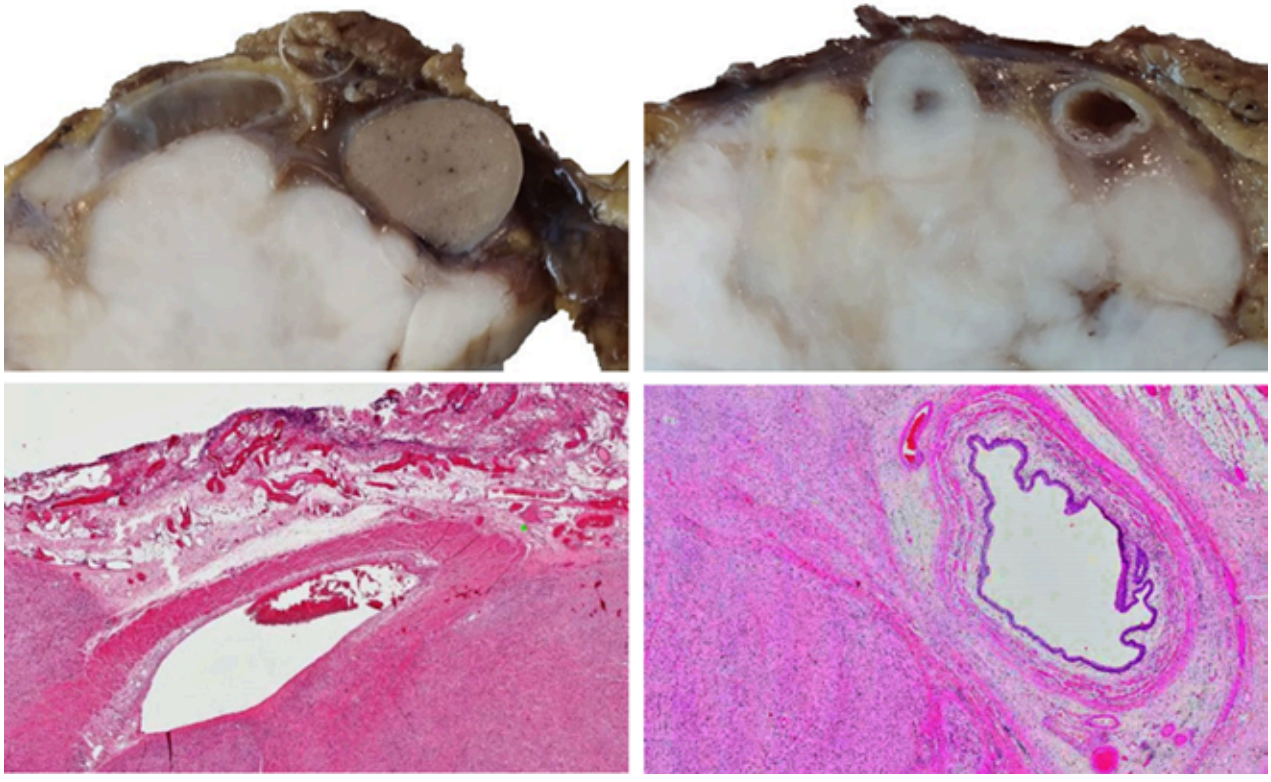

Figure 3. Macroscopic and microscopic appearance of the well-demarcated leyomiosarcoma arised from the vessel wall without ureter or kidney invasion.

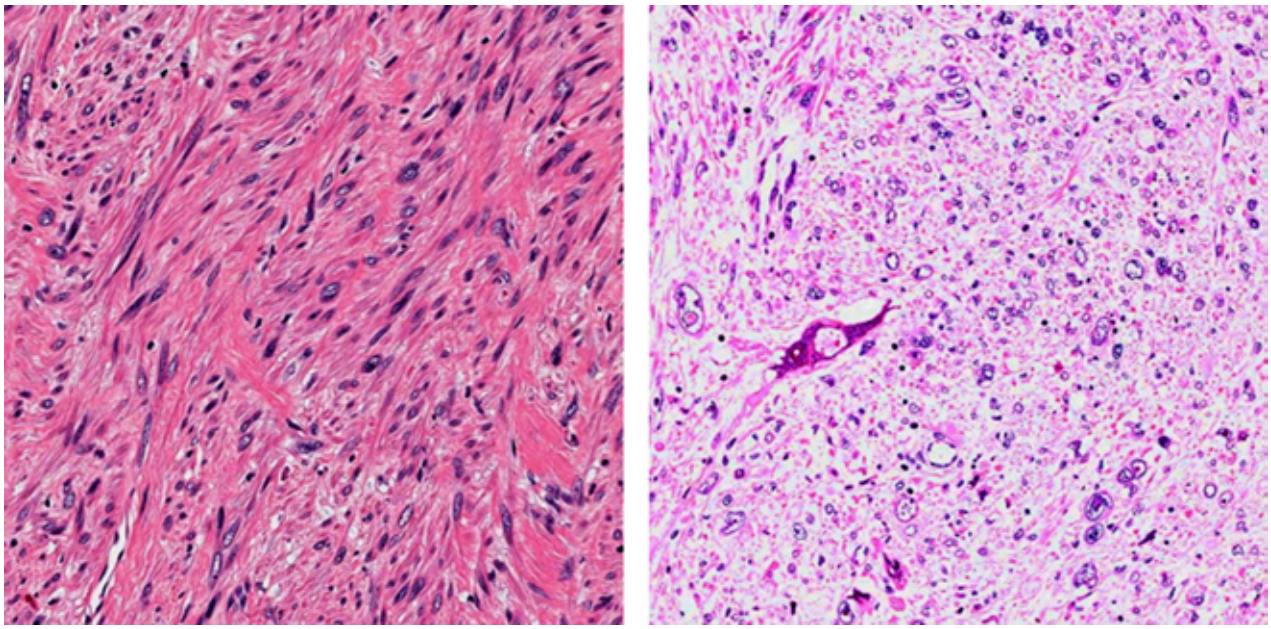

Figure 4. Spindle-shaped cells with mild nuclear atypia (left) and focal poorly differentiated areas with high nuclear pleomorphism (right).

if vascular leiomyosarcomas not originating from the vena cava wall are described in literature (6,7).

Leiomyosarcomas originating from the gonadal vein are particularly rare: only 16 cases were previously described beyond the one reported by us (8).

All women presenting with leiomyosarcomas originating from the ovarian vein wall, including our patient, were between 37 and 71 years old.

The tumors were predominantly T2 or T3, although a case of about 3 cm was described in literature. In fact, as reported, leiomyosarcomas originating from the smaller gonadal vein had a diameter of about 3 cm while the larger 28 cm (9). Our patient presented with a vascular leiomyosarcoma originating from the left gonadal vein of approximately 11 cm. The other leiomyosarcomas originating from the left gonadal vein reported in the literature are 9, while those originating from the right gonadal vein are 7. Therefore, including our patient in 59% of patients the sarcoma developed from the left ovarian vein and 41% from the right ovarian vein. Including our patient, 81% of the 17 women suffering from vascular leiomyosarcomas of the ovarian vein wall presented non-specific symptoms such as abdominal pain, abdominal mass, abdominal distension, pyelonephritis.

The gold standard radiological examination for the study of retroperitoneal neoplasms is represented by CT with and without contrast medium enhancement. Obviously, the differential diagnosis at the time of identification of a retroperitoneal mass must be placed with other sarcomas, but also with neoplasms originating of kidney and urinary system.

Due to the rarity of leiomyosarcomas originating from the gonadal vein, on CT with and without contrast medium enhancement these tumors are described as heterogeneous retroperitoneal masses with ipsilateral hydronephrosis. The standard treatment, potentially curative, for patients suffering from all retroperitoneal sarcomas, including leiomyosarcoma of vascular origin, is surgical *en bloc* resection, sometimes with the removal of organs adjacent to the tumor, with negative resection margins. The state of the margins, in fact, is the most important factor related to disease-free survival. Furthermore, surgical therapy with negative margins achieves a better prognosis with 5-year survival rates ranging between 33% and 68% of cases (10). Because these tumors are often silent or asymptomatic, diagnosis is late and surgical resection, although the best treatment, is often difficult or impossible, as these tumors are often unresectable.

Unresectable retroperitoneum tumors are defined as tumors involving vital structures or those tumors whose removal would cause unacceptable morbidity.

Neoadjuvant chemotherapy in retroperitoneal leiomyosarcomas may be indicated to render an initially inoperable mass operable, to reduce the need for a large resection or, above all, to achieve histologically negative (R0) margins, which are associated with a reduced risk of local recurrence and to a lesser extent better survival (11,12). Furthermore, neoadjuvant chemotherapy could play an important role in the eradication of micrometastatic disease. Finally, the response to preoperative chemotherapy treatment could guide the choices on chemotherapeutic agents to be used later in adjuvant chemotherapy.

Cases of metastases from leiomyosarcoma originating from the gonadal vein are not described in the literature. However, referring to leiomyosarcoma originating from the cava wall, it is possible to state that metastases develop in 12% of cases in leiomyosarcomas of caval origin, mainly in the lung and liver. There could be many risk factors for the development of local recurrence and metastases such as the high grade, the presence of positive surgical margins, the young age and the size of the neoplasm. To demonstrate this, it would be necessary to carry out studies on large numbers, which is not currently possible due to the rarity of the neoplasm.

There are not many data for assessing the benefit of systemic therapy in the management of Retroperitoneal Sarcoma (RPS). Most published studies have explored systemic therapy in the setting of unresectable and metastatic disease, and they often have included patients with RPS within a large group of patients with soft-tissue sarcomas (STS) at other anatomic sites (eg, an extremity) (13).

Anyway, systemic therapy given before surgery (neoadjuvant) has several hypothetical advantages in the management of RPS (14). For patients who respond to therapy, a decrease in tumor size may facilitate resection and, in exceptional cases, convert an unresectable situation into a resectable one. For RPS patients with high-risk disease, systemic therapy may reduce or eliminate both local and distant microscopic disease, and this could lead to improved clinical outcomes. Because of the frequently challenging nature of RPS surgery and the potential for a prolonged recovery, which may delay or even preclude adjuvant therapy, the neoadjuvant approach seems ideal.

The optimal regimen or regimens of systemic therapy in RPS need to be defined; however, there are very little data in the published literature in this regard (15).

For liposarcoma, combination therapy with an anthracycline (eg, doxorubicin) plus ifosfamide (A + I) is commonly given as first-line therapy: the tumor response rate specifically for retroperitoneal disease has been reported to vary from 0% for WD (well-differentiated) disease to up to 21% for DD (dedifferentiated) disease (16-19).

The LMSs originating from gonadial veins represent an uncommon oncologic challenge both for the surgeon, both for the clinical practitioner. A radical *en bloc* excision represents the therapeutic gold standard. The role of imaging and pathology has to be considered essential for the correct staging and the postoperative follow-up.

Ethic Committee: IRCCS CROB – S3T722021 – Rionero in Vulture (PZ)

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Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: All of authors from original idea to final realization.

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