Vascular Involvement in Primary Retroperitoneal Tumors

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The retroperitoneum can host a wide variety of pathologies, including benign and malignant tumors. Primary retroperitoneal tumors are rare, usually large in size, more than half of them being larger than 20 cm at the time of diagnosis, due to their silent growth. They often present several therapeutic challenges because of their rarity, relatively late presentation and anatomical location, often in close relationship with several important structures in the retroperitoneal space. Extensive surgery is often required because of the intimate relationships with vital organs in the retroperitoneum. Retroperitoneal sarcomas frequently involve major vessels, originating from them or secondarily encase or invade them, requiring major vascular resections, with increasing morbidity. The main intervention that can increase the survival of patients with retroperitoneal tumors is radical resection. The involvement of large retroperitoneal vessels often makes impossible a radical intervention, usually because of the lack of an adequate material for ample and laborious vascular reconstruction. In this paper, a thorough search of the PubMed database was performed, to bring into the light the implications of vascular involvement in primary retroperitoneal tumors and the need of a strong cooperation between the urological or general surgeon and the vascular surgeon.

Keywords: primary retroperitoneal tumors, vascular involvement, vascular reconstruction

The retroperitoneum is one of the vastest spaces in the body. This space is limited towards posterior by the lumbar muscles, by the peritoneum towards anterior and by the diaphragm superiorly. The inferior part of retroperitoneal space reaches the pelvic floor and the outer borders of the lumbar muscles [1]. Connective tissue, kidneys, adrenals, ureters, aorta with its emerging branches, inferior vena cava and other important vessels, lymph nodes, the pancreas as well as segments of the duodenum and colon (both ascending and descending colon) are all part of the retroperitoneum.

Being so vast, this space can host a wide spectrum of pathologies. Primary retroperitoneal tumors are a rare group of neoplasms, with an incidence of 0.3-3.0% [2,3]. More than half of the retroperitoneal masses are malignant (70-85%), and only 15-25% are benign [2,3]. Primary retroperitoneal tumors do not originate from any retroperitoneal organ (parenchymatous or not), but develop from the retroperitoneal tissues (lymphatic, nervous, vascular, muscle, connective or fibroareolar tissue) or from embryonic rests of the urogenital ridge (wolfian or müllerian ducts, germ cells, primitive notochord). The majority of the tumors have mesenchymal origin (75%), followed by the neural origin (24%), and last from embryonic rests (less than 1%) [2,3].

The two most frequent histological subtypes of sarcomas are liposarcomas (70%) and leiomyosarcomas (15%), tumors that present as hard abdominal masses with an irregular surface, surrounded by a capsule that is rapidly outgrown by tumor growth and infiltrate the peritoneum and the intra-abdominal viscera attached to it, thus becoming directly intraperitoneal, and not by metastatic invasion [4,5]. Benign tumors are often an incidental finding during investigations for unrelated symptoms. The most common primary benign pathologies encountered in the retroperitoneum include benign neurogenic tumours (schwannomas, neurofibromas), paragangliomas (functional or non-functional), fibromatosis and retroperitoneal lipomas [4,5].

Due to the inaccessibility of this area, as well as to the fact that these tumors often give no symptoms or have non-specific symptoms, they are usually discovered in advanced stages, when the tumor has reached considerable dimensions and has various local or systemic complications, making the perioperative management difficult [6-9].

Tumors located in the retroperitoneal area are discovered more frequently in patients aged between 50 and 70 years old. In terms of gender-based incidence, it has been reported that female patients have a greater risk for this type of tumors compared to male patients [10,11]. Abdominal swelling and pain, early satiety, abdominal discomfort, palpable abdominal mass are the most frequent clinical signs that usually dominate the clinical picture and due to the general manifestation, they can mislead the diagnosis for a period of time, mimicking other diseases [12-14]. The intensity of the pain is variable, as well as its severity; it can be located in the lumbar, inguinal

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or gluteal region and there is an increased need for multimodal analgesia [15,16]. Asthenia, anorexia, weight loss or prolonged fever may be present.

Recently, more than half (75%) of retroperitoneal sarcoma-related deaths were shown to be caused by recurrence localized at the tumors initial site, without concomitant metastasis. Thus, the local control is very important when managing retroperitoneal soft tissue sarcoma. Complete tumor resection, as well as of the nearby organs and tissues, is the treatment of choice for these tumors. Frequently, the tumor may involve major venous or arterial blood vessels, either by histologically proven vascular infiltration or by vascular encasement, representing a challenge for the treatment [17-19]. In the retroperitoneal space, vascular sarcomas originating from the walls of the vessels co-exist with retroperitoneal soft tissue sarcomas with secondary vascular involvement. This is why the differential diagnosis is important.

Planned vascular resection is essential to meet the standards of a complete oncological tumor excision, with microscopically negative margins.

In terms of imaging assessment, contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) are essential in the evaluation process of the retroperitoneal masses, as well as in the staging process. CT scan can differentiate between different densities, guiding the physician towards the nature of the tumor, it defines the shape and size of the mass, it detects suspect enlarged lymph nodes and it may also show adjacent organ invasion. The diagnosis of a primary sarcoma arising from the major vessels is suspected when a large mass is centered within major vessels, usually being leiomyosarcomas. If a mass secondarily encases or invades major vessels, it usually grows in front and behind the vessels, leading to horseshoe shaped surroundings. It can also be used to perform CT-guided biopsies to confirm the diagnosis of sarcoma. Image-guided biopsies are strongly recommended, unless the image is pathognomonic and no preoperative treatment is planned [20-23]. When the tumor does not contain fat, sarcoma is the correct final diagnosis in more than 50% of cases, but the rest of the patients may need a different therapeutic protocol. CT scan can detect the presence of pulmonary, bone, hepatic or peritoneal metastases, as well as the local or regional recurrence in patients who have already been treated [24-29].

**Tumor vascular invasion and its management**

The extent of inferior vena cava (IVC) involvement in tumors originating from it (more frequently leiomyosarcomas, in 95% of cases) is described based on anatomical landmarks (suprarenal and renal veins), as follows: type I (originating below the renal veins), type II (arising from the renal veins to the hepatic veins) and type III (originating above the suprarenal veins) [29]. Tumors of the middle segment of the IVC have a better prognosis than those of the upper segment, due to the fact that the rich innervation of the organs adjacent to the middle segment causes earlier abdominal pain, which brings the patient faster to hospital. Also, tumor growth from the media of the vessel has a better prognosis compared to those originating from the intima. In all the above-mentioned types of IVC tumor invasion, the next step is to evaluate the degree of caval obstruction, as well as the presence of collateral veins, on which a reconstructing surgery decision is made. For masses involving the IVC, partial resection and primary cavoplasty with a patch may be used, complete resection with synthetic materials (Dacron, polytetrafluoroethylene PTFE) vascular graft, a banked vena cava homograft, tubularized bovine pericardium or a stapled peritoneal fascial graft) and ligation [30]. Inferior vena cava ligation, without any vascular reconstruction, is well-tolerated only if previously partial or complete obstruction is present. The appearance and disappearance of leg edema is a strong indicator of a strong collateral system. Gonadic, azygo-lumbar, adrenal and diaphragmatic vessels are classic auxiliaries. Preserving the collateral venous system during surgery is very important.

The major advantages of not reconstructing the IVC are that graft infections are prevented, as well as pulmonary embolism due to prosthetic materials thrombosis, likewise the risk of anticoagulation complications [31].

In case of iliac vessels involvement, for example as in psoas muscle sarcomas, because of the proximity of the vein and artery, both venous and arterial resections are required in order to achieve a good oncological outcome [32]. Because of the thrombosis risk, the need of vein replacement is controversial.

Primary sarcomas of the aorta are very rare. On the other hand, secondary invasion of the aorta wall or of the iliac arteries is much more common [33]. The prognosis of primary aortic sarcoma is very poor, because of thromboembolic complications, mesenteric and cerebral infarctions secondary to ostial occlusions and multi-site metastatic lesions. Usually, the overall survival rate in such cases is estimated to be less than 12 months [34,35].

Primary vascular anastomosis may prove to be not feasible in patients for whom extensive resection is needed. In these patients, the use of sintetic prosthesis (Dacron, PTFE grafts) can be a successful option. In cases with concomitant iliac artery and colic resection, a femoral bypass may be taken into consideration, to avoid the proximity and the possible contact between the vascular and the digestive anastomoses, that may lead to a fistula. The involvement of the superior mesenteric artery in the majority of its length can be considered a non-resectability criteria [36].

**Discussions**

Poultsides et al, in a matched case-control study, have compared 50 patients with sarcoma, in whom they have performed tumor resection and vascular reconstruction, with 100 cases where vascular reconstruction was not needed [37]. They have reported that the rate of complications was significantly higher in the first group, as well as the need for transfusion. The overall survival rate was 59% in the first group, versus 53% in the second one, and the recurrence rates at 5 years did not differ significantly (51% versus 54%). The rates of mortality at thirty-days and ninety-days following the procedure were not significantly higher in the first group of patients. The study identified that the high tumor grade and synchronous metastases were the only independent predictors of overall survival. In this study, the morbidity doubled after vascular reconstruction, but there was no oncologic penalty in terms of the local recurrence and overall survival. The authors concluded that the need for vascular resection and reconstruction should not be a deterrent to resection for patients with sarcoma, as the oncologic outcome (overall and local recurrence-free survival) seems to be similar to that encountered in the cases where the vascular invasion is absent [37,38].

The overall incidence of distant metastasis, after vascular resection as part of an excision of a soft tissue sarcoma, is more than 50% at a median of 3 years from surgery [39,40].
Vascular involvement by direct invasion could be seen as an indirect sign of biological aggressiveness. In some cases, the tumor only pushes against major vessels and resecting them only to obtain clear margins is probably a risk that exceeds the potential benefits [39,40]. There is no data that an extensive vascular resection would increase the local control and, ultimately, the patients survival, thus the decision for the resection of an adjacent main vessel should be made when the dissection of the vessel is not possible, because of its infiltration, or when their dissection would have risks.

In their case report, Miao et al presented a case of a 61-year-old female diagnosed with a large retroperitoneal tumor [41]. After biopsies, the histopathological examination revealed a well-differentiated liposarcoma. Abdominal CT angiography showed that the mass was adherent and consticted the main trunk and branch of the supero mesenteric vein (SMV). The preferred treatment of choice was surgical removal of the liposarcoma and of the invaded SMV. The authors noticed that the patient’s liver did not showed any significant damage, giving the long compression of the SMV. During surgery, they haven’t noticed any changes of the venous blood flow towards the liver (using Doppler and B-mode ultrasound). They did not noticed any signs of bowel ischemia after the SMV was clamped, leading to the conclusion of a good collateral circulation. Finally, the SMV and liposarcoma were resected simultaneously, without graft substitutes [41].

Venous blood vessels are the most common encased or invaded by the retroperitoneal masses. Schwarzbach et al have reported in their study that, out of the 25 patients with vascular involvement by retroperitoneal sarcomas, 64% have had venous involvement [42]. 16% of the patients had arterial and vein involvement and arterial-only involvement was observed in 20% of the cases. Tumors originating from the vessels walls were less common (8 patients), compared to those that were secondarily invaded (17 patients). In their paper, 22 patients have had vascular reconstruction. Aortic replacement by Dacron or PTFE grafts, iliaca repair with Dacron and trunk reimplantation were used in patients with arterial involvement. The inferior vena cava (PTFE tube grafts, PTFE patches, venoplasties), iliaca vein (PTFE bypass, Dacron bypass, venous patch), and superior mesenteric vein (anastomosis, Dacron bypass) were reconstructed in patients with venous blood vessels involvement. The patients had good local control, as well as 2 and 5 year overall survival rates, concluding that complete resection with clear margins is important for long-term survival and the extent of vascular resection and appropriate vascular repair have to be assessed in each individual patient [42].

Bertrand et al performed reconstructions using three types of prosthetics: standard (PTFE or Dacron), externally supported (PTFE) for reconstructions of large veins, or silver-coated, to minimize the risk of infection in case of concomitant digestive anastomosis [43]. Except for the internal iliaca artery and vein, all the major vessels were reconstructed. For arterial repair, primary anastomoses, reinsertion, or synthetic prostheses were used, considering the length of the excised segment. Veins with no evidence of thrombosis on the preoperative scan were repaired without exception, in contrast with those with vein thrombosis, with collateral circulation, that were only ligated, supporting the idea that ligation without any vascular reconstruction is well-tolerated in patients with good collateral venous system [43]. However, this may raise problems in patients with concomitant morbidities and vascular calcifications [44,45].

In a study regarding resection of retroperitoneal sarcoma en-bloc with inferior vena cava, 32 patients underwent en-bloc IVC resection [46]. Multiple vascular reconstructions were performed: a graft (synthetic in most cases) was used most frequently (59% of cases), followed by primary repair in 19%, patch repair in 13% and no reconstruction in 9% of patients, due to a strong collateral venous system. By matching 1:3 retroperitoneal sarcomas resection involving the IVC by age and histology to retroperitoneal masses without IVC resection, they have concluded that en-bloc resection including the IVC can be performed safely, with disease-free and overall survival rates similar to those encountered in patients without IVC involvement [46,47].

A strong collaboration with a specialised vascular surgeon is needed [48]. Grotemeyer et al concluded that after the resection of the IVC, a PTFE graft should be interposed in combination with an AV fistula, due to the fact that, in their study, the only patients that developed graft thrombosis were those without an AV fistula [49].

In a paper regarding the surgical technique, morbidity, and outcomes of primary retroperitoneal sarcoma involving inferior vena cava, Fiore and his colleagues have reported that they have used PTFE prosthesis or banked venous homografts for major venous reconstruction. In four patients IVC reconstruction was not necessary, due to the presence of efficient collaterals. They have reached the conclusion that IVC resection is safe and well tolerated in patients with retroperitoneal masses invading the nearby vessels and that the need for vascular reconstruction has to be assessed according to preoperative imaging, intraoperative findings and to the extent of resection [50,51].

**Conclusions**

Primary retroperitoneal tumors are a rare group of tumors, frequently malignant, the most frequent histological types being liposarcoma and leiomyosarcoma. The most common symptoms that make the patient seek medical help are abdominal swelling and pain, early satiety, abdominal discomfort, a palpable abdominal mass. The imaging test of choice for the diagnosis is contrast-enhanced CT scan. In patients with vascular involvement, planned vascular resection with en-bloc excision of the tumor mass is mandatory, in order to achieve a good local control and high overall survival rates. According to literature, there are a multitude of surgical options and techniques that can be used when managing such patients. In case of venous vessels involvement, partial resection and primary venoplasty with a patch may be used, complete resection with interposition of Dacron, or PTFE vascular graft, a banked vena cava homograft, tubularized bovine pericardium or a stapled peritoneal fascial graft and ligation (in cases of strong collateral venous system). For arterial repair synthetic grafts, reimplantation, or primary anastomosis can be used, depending on the length of the excised segment. As stated in many studies, vascular resection is safe and well tolerated in patients with retroperitoneal masses with vascular involvement, if done in a strong collaboration with a vascular surgeon and in a planned manner, using the appropriate vascular repair.

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