Leiomyosarcoma of the inferior vena cava
Report of two cases and review of the literature

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INTRODUCTION: *Leiomyosarcoma (LMS) occurs most frequently in the inferior vena cav (IVC). Since Perl's first description in 1871, about 300 cases of IVX have been reported in English literature. The Authors present their personal experience of two case of IVC leiomyosarcoma treated in their Institution.*
PATIENTS AND METHODS: *Clinical and pathologic data, surgical management , ourcomes and follow-up of two patients admitted nb the Authors' Division respectively on February and November 2004 were collected.*
RESULTS: *There were a 49-years-old female with rare epigastric pain and a 42-years-old female with one-month history of abdominal discomfort and weight loss. After preoperative evaluation, both of the patients had localised and resectable tumors and underwent radical surgical excision, with prosthetic replacement of the IVC in the first patient and ligation of the IVC in the other one. The first patient is still alive but in an advanced disease. The second patient died of recurrence at seven months.*
DISCUSSION: *LMS of IVC is a rare tumor. The diagnosis is often delayed because of non-specificic symptoms. Radical resection with surgical margins free of tumor is the treatment of choice. The extent of venous resection does not seem to affect the survival. The type of IVC reconstruction is based on the extent of venal wall involvement. The prognosis is often poor because of tumor recurrence and/or metastatic disease. The role of chemo and radio therapy is not clear yet*
CONCLUSION: *Long term survival is related to an extensive surgery, being surgical margins free of tumor the only prognostic factor with significant influence on patient's survival.*

KEY WORDS: Inferior vena cava leiomyosarcoma, Prosthetic replacement, Mesencymal tumor.

Introduzione

Leiomyosarcoma (LMS) is a mesenchymal tumor that originates from the smooth cells of vessel wall; it accounts for 6% of all sarcomas and 15% of sarcomas of the soft retroperitoneal tissue. It is the most frequent mesenchymal tumor of the large vessels, occurring in among 50% of cases in the inferior vena cava (IVC). Pulmonary artery and thoracic aorta are following frequent location[1].
More than 80% of cases are females, most of them between fifth and sixth decades, while males are rarely and lately affected (seventh decade).
IVC leiomyosarcoma are classified anatomically according to their relationship to the liver and renal vessels: lower or segment 1 (below the renal vessels), middle or segment 2 (from renal vessels to retrohepatic IVC) and upper or segment 3 (suprahepatic IVC).
Since Perl's first description of a LMS of the IVC in 1871[2], little more than 300 cases have been reported in English literature. The first successful operation was reported by Melchior in 1928[3].
Surgical "en bloc" resection of tumor and vein is the mainstay of treatment.

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Case Reports

CASE 1
On February 2004 a 49-years-old female presented to

our division with rare epigastric pain. Anamnestic findings were negative. An abdominal ultrasonography (US) revealed a nodular, hypoechogenic, peri-cephalopancreatic mass, (10x6x6 cm in size), compromising the IVC. Abdominal and thoracic CT (Fig. 1) showed a 6x7 cm retroperitoneal mass, extended behind the pancreatic head and involving the left renal vein and the middle segment of the IVC. There was no evidence of distant metastatic disease. US-guided fine-needle aspiration biopsies were interpreted as probable LMS. The patient was submitted to surgery. An esofitic tumor was resected "en bloc" with the IVC and the left renal vein performing a temporary IVC occlusion to prevent pulmonary embolization. Complete occlusion time of the IVC was 70 minutes while venous outflow of the left kidney was compromised for about 35 minutes. The reconstruction was made by a synthetic expanded polytetrafluoroethylene (PTFE) prosthesis (16 cm x 8 mm in diameter) anastomized end to end to the IVC, while the left renal vein was reconstructed using an end-to-side anastomosis to the prosthetic graft (Fig. 2).
Histopathological examination revealed a moderately differentiated LMS arising from the IVC with clear surgical margins. The mitotic index was 13 mitoses/10 per high power fields (HPF). Immunohistochemical reactions were positive for vimentin, desmin, smooth muscle actin antibodies and negative for S-100.

Case 2
On November 2004 a 42-years-old female was admitted to our division with one-month history of abdominal discomfort and weight loss of 10 kg. Abdominal US revealed an echogenic mass, 10 cm in diameter, located between liver segment I and the head of the pancreas. CT showed a 10x8x5 cm retroperitoneal mass, adjacent to the caudate lobe without direct infiltration, extending into the pelvis and compromising the IVC that had already developed a collateral circulation. At surgery was found a well-circumscribed tumor originating from the lower segment of IVC with an esofitic growth; no direct infiltration of other organs nor metastatic disease was found during laparotomy. The neoplasm was resected "en bloc" with the IVC that was closed below the origin of the renal veins. (Fig. 3). A diagnosis of a moderately differentiated LMS arising from the IVC with clear surgical margin and 12 mitoses/10 HPF was established histologically.

Results

In case 1, the postoperative course was uneventful without clinical signs of lower extremity edema, renal dysfunction or graft infection. Doppler US did not find any occlusion of the implanted left renal vein. The patient was discharged on eleventh day with anticoagulant therapy. Fifteen months after surgery, abdominal CT showed multiple liver metastases and an asymptomatic

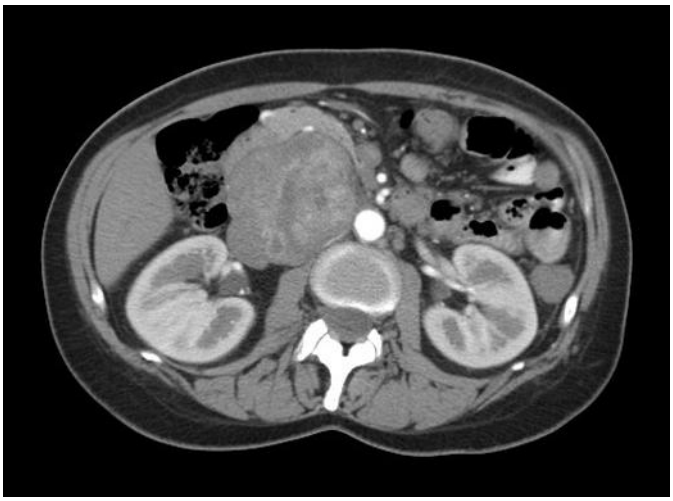

Fig. 1: Computed tomography (CT) illustrating tumor compromising the inferior vena cava (case 1).

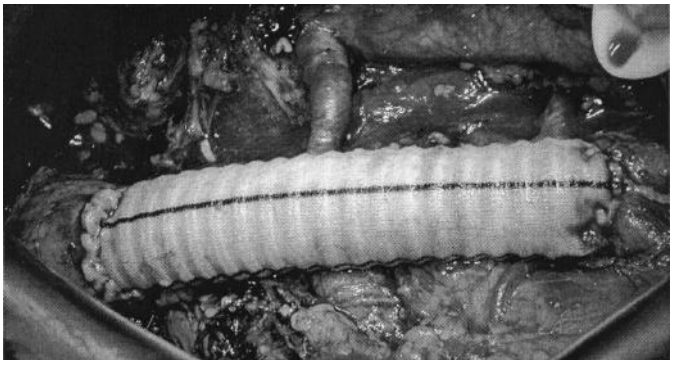

Fig. 2: Intraoperative image showing the prosthetic graft recostruction and the end-to-side anastomosis with the left renal vein (case 1).

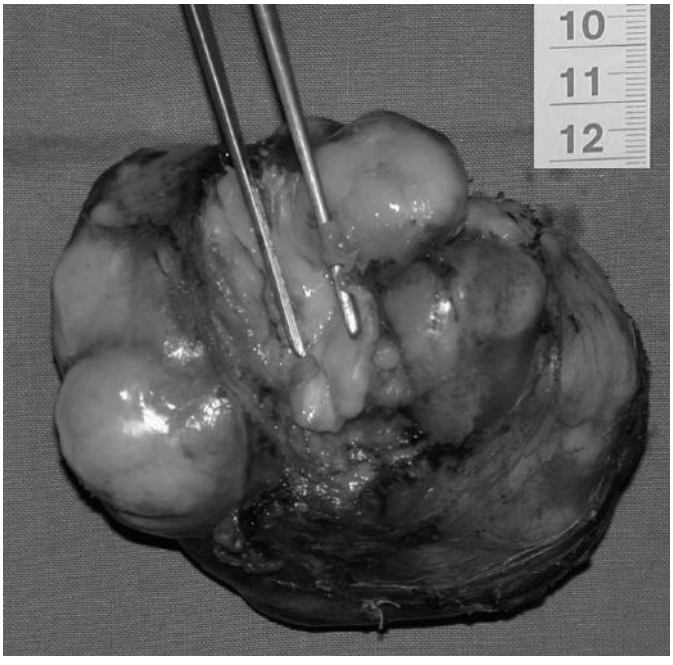

Fig. 3: Resected leiomyosarcoma of the inferior vena cava (case 2).

partial occlusion of the IVC without surgical options. The patient was commenced on adjuvant radio and chemotherapy and she is still alive but in an advanced tumor stage.
In case 2, the patient was discharged 8 days after surgery with anticoagulant therapy. Four months later multiple hepatic metastases were detected and the patient was submitted to chemotherapy but died three months later.

Discussion

LMS of IVC is considered a rare, slow-growing tumor with three possible growth patterns: extraluminal (about 73% of cases), intraluminal or both [4].
Early detection of IVC leiomyosarcoma is usually difficult, because symptoms are relatively unspecific and variuos, a reliable tumor marker does not exist, so that the diagnosis is often delayed. Presenting symptoms include epigastric or right hypocondrial pain (66% of cases), weight loss (22-31%), fever (10%), weakness (12-15%), nausea (12-15%) and emesis (9-10%). Abdominal palpable mass can be detected in 43-48% of cases. Clinical patterns depend also on the segment of IVC involved and the growth pattern[5].
Laboratory tests are generally unremarkable for diagnosis. US is useful to rule out hepatobiliary and pancreatic pathology, to confirm the presence of the tumor and provide additional information on the extent of the tumor. Doppler US gives information about the patency of the portal or systemic venous system. CT and Magnetic Resonance (MR) help to define the pattern of growth of the tumor, the relationship to the surrounding structures and enable the differentiation between tumor and intraluminal thrombus[6]. Vascular invasion is well documented with phlebo-/cavography, but angio-MR is considered the gold standard for pre-operative evaluation of IVC involvement. Percutaneous needle biopsy can provide histologic diagnosis without information about the organ of origin [7].
Radical resection of tumor and vein with surgical margins free of tumor is the mainstay of treatment and the only potentially curative treatment.
One report suggests that the extent of venous resection does not affect long term outcome, being survival rates similar between tangential caval wall with primary closure and prosthetic replacement of IVC. Caval wall radical resection may be limited to 1 cm around macroscopic evidence of the tumor to reduce technical difficulties and postoperative complications without an increased risk for local recurrence [8].
When the tumor origins below the renal vessels, ligation of the IVC after tumor resection seems best tolerated in patients with preoperative IVC thrombosis, because an adeguate collateral circulation has already developed without lower extremity edema [9].
When the tumor is located in the middle segment, the option is a tangential resection with primary closure of IVC, otherwise large defects (more than 50% of the diameter of IVC) can be repaired with synthetic patch or PTFE or Dacron prosthesis anastomised end to end to the IVC.
Prosthetic replacement of IVC is usually performed with ring-reinforced PTFE because it theorically resists to respiratory compression without collapse. The graft is generally smaller than the surrounding native cava, promoting a higher blood velocity through the graft and minimizing blood-prosthesis interaction [10].
When the tumor involves the left renal vein, its resection may be carried out without nephrectomy because of the adequate collateral circulation via adrenal, gonadal and lumbar branches. When the resection of the right renal vein is necessary, the kidney is often removed en bloc with the tumor [11].
Resection of tumors originating from the upper segment of the IVC may require extracorporeal techniques. Similarly, tumors of the upper IVC caval segment occluding hepatic veins can be treated by an extracorporeal resection of the caval segment with liver transplantation. The IVC should be managed with temporary occlusion during manipulation of the tumor to prevent pulmonary embolization from the dislodged mass [12].
The most common intraoperative complication is hemorrhage. The postoperative morbidity ranges between 15%, the most common being occlusion of the IVC and deep vein thrombosis. The reported perioperative mortality for resection of primary LMS of the IVC ranges from 0% to 15%, according to the series[13].
Late graft occlusion has been reported with and without tumor recurrence[14], but routine postoperative anticoagulant therapy is not accepted by all authors. Some reports suggest the use of short-term anticoagulation when a known risk factor for venous thrombosis develops in a patient with a prior IVC prosthetic graft[15].
Metastatic disease is initially present at diagnosis in 35-50% of cases[16]. There is a report of surgical treatment in cases of synchronous hepatic and omental nodes without apparent more post operative complications. So in case of advanced neoplastic stage, debulking may be considered for a good palliation and, in these cases, the presence of synchronous resectable metastases may not represent a controindication to surgery[17]. Metastases are initially spread haematogenously to liver and lung and lately through the lymphatics. Other sites of metastases reported in literature are skin, brain and bones.
In case of radical surgery five-year survival rates arrives to 49,4%, while 10-year result is about of 29,5%. However recurrence rates are about as 50%[18].
The role of the neoadjuvant therapy is not clear yet, but they may be administered to downsize the tumor and increase the rectability rate, mostly in high risk LMSs.
The impact of adjuvant chemotherapy and radiotherapy can not be ascertained yet, because of the small number of cases treated and the variability of agents, doses

and duration of administration used. They may be indicated in high risk tumors and in case of uncompleted resection [19].

Conclusions

IVC leiomyosarcoma is a rare tumor and the diagnosis is often delayed because of the absence of specific signs. Long term survival depends on performing an extensive surgery with surgical margins free of tumor. The type of IVC reconstruction does not influence survival. The role of CT and RT is not demonstrated. The main prognostic factors investigated in Literature as predictive of long survival are tumor grade and size, lymphonode status, mitotic activity, the pattern of growth but the only prognostic factor with proved significant influence on patient's survival is the presence of surgical margins free of tumor.

Riassunto

Gli autori riportano l'esperienza di due casi di leiomiosarcoma della vena cava inferiore (VCI): due donne, rispettivamente di 49 e 42 anni giunsero alla loro osservazione nei mesi di febbraio e novembre 2004 con sintomatologia aspecifica, caratterizzata la prima da saltuari episodi di epigastralgia, la seconda da un fastidio addominale diffuso accompagnato da un calo ponderale di 10 Kg nell'ultimo mese. Dopo stadiazione preoperatoria si procedette alla resezione "en bloc" del tratto di VCI interessato dalla neoplasia, nella prima paziente con impiego di protesi in PTFE, nella seconda con chiusura diretta della VCI al di sotto dell'origine delle vene renali. L'esame anatomopatologico dimostrò un leiomiosaroma della VCI moderatamente differenziato, con margini indenni da neoplasia. La prima paziente è ancora viva, ma in progressione di malattia dopo radio-chemioterapia. La seconda paziente è deceduta dopo 7 mesi, per ripresa di malattia a livello epatico a 4 mesi dall'intervento. I leiomiosarcomi della vena cava sono relativamente rari. La diagnosi è spesso tardiva per l'assenza di segni e sintomi specifici. L'opzione chirurgica con intento "R0", ovvero margini di resezione indenni da tumore, rappresenta dal punto di vista oncologico la migliore strategia terapeutica. La prognosi è scarsa a causa dell'alto tasso di recidiva locale o a distanza che contraddistingue queste neoplasie e al ruolo ancora limitato della chemio- e radioterapia.

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