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clinical practice

Retroperitoneal or mesenteric primary liposarcoma: clinical and prognostic evaluations on five cases

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SUMMARY: **Retroperitoneal or Mesenteric Primary Liposarcoma: clinical and prognostic evaluations on five cases.**

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Background. *Retroperitoneal or mesenteric primary liposarcoma is a malignant neoplasia whose prognosis depends on the biological variants, the radical resection surgery and the histological subtypes, as well as on local and remote recurrences. Liposarcoma is the most common variant of this tumour among tumours of soft retroperitoneal tissue. The purpose of this study is to evaluate whether the treatment of this disease, carried out at the Ivrea Hospital for urgent reasons, may be considered in line with the experience of high-volume Centres.*

Patients and methods. *Between 1982 and 2016 five patients were hospitalized with a diagnosis of acute abdomen due to retroperitoneal or mesenteric primary liposarcoma: one myxoid of the mesentery, one well-differentiated of lesser epiploon, one well-differentiated of mesentery, and two dedifferentiates of the retroperitoneum.*

Results. *The five patients, all males, had a average age of 59 years (range 48-86) and were all subjected to general anaesthesia and open technique for total tumour removal. Only the patient with the myxoid liposarcoma had two recurrences. All are alive and healthy after a follow-up of 177 months (range 9-420).*

Conclusion. *These tumours should be removed radically, if necessary in conjunction with contiguous organs. Rarity and therapeutic complexity require a treatment, sometimes even multimodal, in high-volume centres.*

Patients admitted in General Surgery Unit for unpostponable urgency should be operated by surgeons experienced in the treatment of abdominal disease to achieve survival results in line to those achievable in Hub Centres.

KEY WORDS: Retroperitoneal liposarcoma - Mesenteric liposarcoma - Soft tissue sarcoma.

Introduction

The ventral body cavity is divided into the thoracic cavity and abdominal cavity by the diaphragm. During embryonic development, a large part of the anatomical structures located in the abdominal cavity are wrapped in a complex way by peritoneum, as if they were floating inside a semi-deflated balloon. The peritoneum, therefore, covers these organs with a visceral and a parietal membrane. In the retroperitoneal space and in the mesentery there is a connective tissue containing organs and structures defined as extra peritoneal (1, 2). Retroperitoneal or mesenteric primary sarcomas (RPMPS) show some peculiar characteristics:

- they are very rare: they represent 0.2% of all cancers and 15% of all soft tissue sarcomas (3);
- they account for a third of retroperitoneal tumours (4);
- they may belong to different histological types, but liposarcomas (70%) and leiomiosarcomas (15%) are the most common forms (4);
- they originate in the retroperitoneal space, although neither from the retroperitoneal (RP) organs nor the digestive tract;
- as a consequence of their location and slow growth, diagnosis is often late and they may therefore grow to an important size before being discovered (about 40-50% exceed 20 cm) (3);
- after surgical removal they tend to have a high local recurrence (60-80%);
- their long-term prognosis depends on histological features, resectability of the tumour, local recurrence and presence, albeit rare, of metastasis

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(5-year survival rates: 65-70% for complete resection (CR); but 4%, 14%, 20-29% for incomplete resection (IR), local recurrence (LR) and distant metastasis (DM), respectively) (5-9).

The purpose of this study is to evaluate whether the treatment of this disease, carried out at the Ivrea Hospital as urgent cases, may be considered in line with the experience of high-volume specialist Centres.

Patients and methods

From 1982 to 2016 five patients were hospitalized with a diagnosis of acute abdomen due to retroperitoneal or mesenteric primary liposarcoma.

- **Case 1**, 55-years-old man, farmer. Nothing to point out on the familial and pathological anamnesis.
  - In 1982, hospitalized with steady abdominal pain, constipation, nausea, vomiting, and weight loss. To the clinical examination: good general conditions, abdomen swelling, and painful especially in the right quadrants where there is a massive indistinct margins tumefaction. Ultrasound and CT abdomen do not provide any clarify. Laparotomy with massive cystic mucosal mass feedback. It occupies much of the abdominal cavity, contains 7.5 litres of hematic serum liquid, and has adhesions with gastrocolic ligament, ileal and transverse colon mesentery, round ligament of liver and parietal peritoneum, but not with the intestine. The major vascular peduncle originates from the right mesocolon. Surgery duration: 140 minutes.
  - Pathological anatomy description: multi-lobate mass with a residual weight of 1.3 Kg and dimensions 30x24x15 cm. Histologic diagnosis: myxoid liposarcoma.
  - 24 hours after surgery: postoperatively haemorrhagic shock. Laparotomy with evidence of about two litres of free partly coagulated blood in the abdomen. Haemostasis. Discharge on eleventh day.
  - In 1987, 5 years after the first surgery (60 years old), recurrence with sub-occlusive syndrome. Laparotomy shows a voluminous subhepatic, partly cystic-mass, two smaller contiguous neoformations, and one more of the peritoneal wall in the pelvis. Histologic diagnosis: epithelioid leiomiosarcoma.
  - In 1996, 14 years after the first surgery (69 years old) and 9 from the first recurrence, second recurrence manifested with sub-occlusive syndrome. Laparotomy with evidence of bulky mass submesocolic consisting of multiple lardaceous nodules. Histologic diagnosis: epithelioid leiomiosarcoma.
  - In 1999, plastic surgery for inguinal hernia.

The patient since 1982 has never wanted to be followed up and went to the hospital only for abdominal acute disease.

In 2017, the patient is alive and has reached 90 years of age. Disease Free Interval (DFI): 252 months.

- **Case 2**, 52-years-old man, prison guard. Positive anamnesis for oncological pathology (deceased father for gastric carcinoma).
  - In 1997, hospitalized with severe abdominal pain, decreased appetite, nausea, and constipation. Clinical examination: good general conditions, abdominal swelling, pain located in upper abdomen especially in the epigastric and hypochondriac right region where there is a massive indistinct margins tumefaction. The ultrasound and abdomen CT showed a subhepatic mass of 10x6x6 cm. Laparotomy with massive cystic mucosal mass feedback. This occupied the subhepatic space and was inserted into the lesser epiploon. Surgery duration: 60 minutes.
  - Pathological description: multi-lobate mass. Histologic diagnosis: well-differentiated liposarcoma (previously classified as liposarcoma not otherwise specified). Oncological Follow-up.
  - In 2007, 10 years after the first surgery (62 years old), Hartmann's operation for complicated diverticulitis.
  - In 2008, 11 years after the first surgery (63 years old), colon recanalization after Hartmann's procedure.
  - In 2010, 13 years after the first surgery (65 years old), incisional hernioplasty.
  - In 2015, 18 years after the first surgery (70 years old), total thyroidectomy for multinodular goiter.

In 2017, the patient reached 72 years of age, is healthy and has no recurrence of liposarcoma. DFI: 240 months.

- **Case 3**, 55-years-old man, office worker. Anamnesis: acute myocardial infarction in 2001; aorto-bifemoral bypass in 2002.
  - In 2005, hospitalized with acute abdomen, pain in the lower right part of the abdomen, nausea and vomiting, fever, diarrhea. To the clinical examination: general sick feeling, abdomen slightly distended and tender in all four quadrants, with maximum tenderness elicited in the right lower quadrant on palpation. Bowel sounds were decreased, and no masses were palpable. The computed tomography (CT) scan showed a mesenteric mass of 5x6x6 cm. Laparotomy revealed a mesenteric suppurative adenitis and a mass of mesenterial intestine. Surgery duration: 95 minutes.

Pathological anatomy description: multi-lobate mass of 5x5x6 cm and mesenteric suppurative adenitis. Histologic diagnosis: Well-differentiated liposarcoma (previously classified as liposarcoma not otherwise specified). Oncological Follow-up.
In 2017, the patient is 67 years old and has discrete health status without signs of recurrence of liposarcoma. DFI: 144 months.

- **Case 4**, 48-years-old man, blue collar worker. Familial and pathological negative anamnesis.
  - In 2011, hospitalized with acute abdominal pain, constipation, nausea, vomiting, and weight loss. To the clinical examination: good general conditions but distressing, asymmetrical and swelling abdomen, painful especially in the right quadrants, where there is a massive indistinct margins swelling. CT and magnetic resonance imaging (MRI) revealed bulky expansive mass of right abdominal quadrants of 19x20x13 cm, inseparable from the ascending colon and posteriorly from the kidney and adrenal gland. Laparotomy shows the massive and bumpy formation of retroperitoneum. This dislocates the right colon at the front and compresses the kidney and adrenal gland, infiltrating them. Removal of the mass with ascending colon, kidney and right adrenal gland. Duration of surgery: 255 minutes.

Pathological description: multi-lobate mass of 21x22x11 cm and 2476 grams, including kidney, adrenal gland, and right colon. Histologic diagnosis: dedifferentiated liposarcoma. Marked infiltration of the capsule and renal parenchyma.
Adjuvant chemotherapy (aChT) with six cycles of infusional Epirubicin and Ifosfamide.
In 2017, the patient is 54-years-old and is fine. TC and MRI controls show a persistent complete response according to the RECIST criteria. DFI: 72 months.

- **Case 5**, 86-years-old man, retired farmer. Familial and pathological negative anamnesis.
  - In 2016, hospitalized with acute abdominal pain, abdominal cramps, inability to pass gas or stool, nausea and vomiting, severe bloating, decreased appetite, weight loss, and oedema of the inferior limbs.
  - Clinical examination: compromised clinical conditions; asymmetrical and swelling abdomen, painful especially in the right quadrants where there is a massive indistinct margins swelling. CT and MRI revealed voluminous expanded cystic formation of mesentery - retroperitoneum in iliac right fossa of 30x20 cm. Laparotomy shows the massive and bumpy formation of retroperitoneum. This dislocates the right colon and mesenterial intestine anteriorly and medially. Duration of surgery: 130 minutes.

Pathological anatomy description: multi-lobate mass of 25x17x10 cm and 1540 grams. Histologic diagnosis: dedifferentiated liposarcoma. Fluorescent in situ hybridization (FISH): Co-presence of amplification of the centromeric sequences of chromosome 12.
Because of advanced age and general clinical conditions, there are not indications of adjuvant chemotherapy. Oncological follow-up.
In 2017, the patient is 88 years old and has poor health conditions. TC and MRI controls show a persistent complete response according to the RECIST criteria. DFI: 9 months.

Results

The retrospective observational study concerns five patients who have been operated urgently for a retroperitoneal or mesenteric primary liposarcomas, with acute abdominal symptoms. Our patients were all males and at the time of acute disease the average age was 59 years (range 48 - 86).

Diagnosis was performed with CT and MRI in all cases, except for the first one which performed CT only. In one of the cases fine needle aspiration

biopsy (FNAB) of the lesion was performed, taking into consideration acute symptomatology.

Surgery was performed in general anaesthesia and with open technique. All patients were subjected to total resection of mass. Evaluation of healthy margins was performed during surgery. After being cut, the soft tissues retract themselves and the pathological evaluation on the margins is not always reliable. Careful attention was paid to keeping the neoplasm capsule untouched. The duration of surgery was 136 minutes on average (range: 60-255).

Case 1 had two recurrences: the first after 5 years and the second after 14 years from the first procedure. The only complication involved was significant post-operative bleeding after 24 hours from the first procedure, which required a re-surgery.

After surgery, the patients were assisted in the Intensive Care Unit in order to monitor their general conditions. Heart and respiratory rate, peripheral O_2 saturation, invasive blood pressure, urine output, temperature, and numeric rate scale for pain have been evaluated every 2 hours. Blood electrolytes were maintained within normal range, Serum glucose level was also periodically checked and insulin infusion was carried out when necessary. All patients were hydrated and an echocardiogram confirmed that they had been administered the appropriate quantity of infusions; in the first 24 hours, blood cell count was strictly monitored. Antibiotic prophylaxis was continued for 48 hours. Only the first patient needed vasoconstrictors and intubation with mechanical ventilation for 96 hours, while in all the other cases extubation was performed within 48 hours.

The average follow-up was 177 months (range 9-420). The five patients are alive and have no clinical signs of recurrence (Table 1).

TABLE 1 - CLINICAL RECORDS.

CASE	Age	Gender	Location	Size in cm	Weight in grams	Resection	Surgical duration in minutes	Histology	Recur	aChT	Follow-up in month	Living
1	55	male	mesentery	30x24x15	8800	total	140	Myxoid	2		420	yes
2	52	male	lesser epiploon	10x6x6		total	60	Well-differentiated	0		240	yes
3	55	male	mesentery	5x5x6		total	95	Well-differentiated	0		144	yes
4	48	male	retroperitoneum	21x22x11	2476	total	255	Dedifferentiated	0	yes	72	yes
5	86	male	retroperitoneum	25x17x10	1540	total	130	Dedifferentiated	0		9	yes

Discussion

All patients electively admitted to the Ivrea Hospital who present intraabdominal neoformations, intra - or extra - peritoneal, are subjected to the clinical evaluation of our interdisciplinary care group (GIC). The team includes specialists in surgery, oncology, radiotherapy, radiodiagnostics, and pathological anatomy. Having evaluated both the diagnostic examinations and the proven or suspected diagnosis of retroperitoneal or mesenteric primary tumour, the patient is directed to the reference centre (Hub) of the Oncologic Network of Piedmont and Valle d'Aosta.

The five patients in our study arrived at our Emergency Department for acute abdominal disease and were hospitalized and operated urgently in our hospital between 1982 and 2016.

Retroperitoneal or mesenteric primary liposarcoma is a typical adult disease. It happens more frequently around the age of 50, but it has been described as occurring at all ages. In our small series the average age was 59, but in the first four cases it was 52.5 years (range 48-55) and the fifth patient was 86 years old.

This is an insidious disease because it develops slowly in the retroperitoneal space or in the thickness of the mesentery until it reaches a considerable size. For this reason, sometimes it shows up with a clinical picture of acute abdominal bulking or intestinal obstruction, requiring urgent surgical treatment.

In 2013, the WHO published the revised soft tissue tumours classification - 4th edition (10). Based on this classification, depending on their biological behaviour, soft tissue tumours are classified as:

- benign: lipoma (usually does not recur);
- intermediate - locally aggressive: well-differentiated liposarcoma (it recurs often but does not metastasize);
- intermediate - rarely metastasizing: solitary fibrous tumour (it recurs often and may metastasize in < 2% cases);
- malignant: dedifferentiated liposarcoma (it is common and has high risk of metastases) (10-12).

The major liposarcoma subtypes are:

- Well-differentiated (8850/3). This is the most common liposarcoma. Previously, it was classified as Liposarcoma not otherwise specified;
- Dedifferentiated (8858/3). They are mainly found in the retroperitoneum and very voluminous. Typically they have both a fluid and a solid component and they recur very frequently;
- Myxoid (8852/3). They recur very frequently. In 2013 the WHO removed the standalone "round cell liposarcoma" classification (8853/3), and included it in the category of high quality - worse prognosis - myxoid liposarcoma;
- Pleomorphic (8854/3). This is the least frequent and most aggressive liposarcoma. Prognosis is unfavourable and worsened by the presence of metastases (10, 13, 14).

The 2013 WHO classification also eliminated the definition of Mixed-type liposarcoma (8855/3), likely to avoid equivocal histological interpretations.

The classification of soft tissue tumours and the various therapeutic options can have relevant implications for the radiologist, especially in relation to the treatment response based on the Response Evaluation Criteria in Solid Tumours (RECIST) (13, 15).

Diagnostic tests are performed with CT, MRI and Fine Needle Aspiration Biopsy (FNAB).

The cornerstone of curative intent treatment of soft-tissue liposarcomas is surgery with free margins. Sometimes it is necessary to resect adjacent intra-abdominal organs. Moreover, obtaining clean resection margins may be difficult because of the complex anatomical condition that can occur.

Prior to surgery, it may be useful to evaluate the option to perform the combination of high-dose long-infusion Ifosfamide (HLI) and External Beam Radiotherapy (EBRT), with the aim of reducing the mass and performing a full resection (16, 17). The combination of preoperative EBRT and chemotherapy (ChT) with surgery and Intraoperative Radiotherapy (IORT) seems to be superior to surgery alone or surgery with EBRT in local control. According to some authors, it even improves the overall survival rate (18).

After surgery, the EBRT gives no advantage and it should be applied exclusively to rare, selected cases only. The same applies to ChT, which seems to provide limited benefits in a very low number of patients (17).

The prognosis is affected both by the histological subtype and by the clinical and pathological characteristics of this tumour. This prevents from identifying meaningful prognostic cohorts (19). Well-differentiated liposarcomas subjected to radical surgical treatment usually exhibit a low incidence of local recurrences (<10%) and remote metastasis (close to 0%). Complete resection, which often includes adjacent organs, offers the only reasonable chance of long-term survival, with overall average rates between 23% and 59%. These outcomes are worse in patients with myxoid, pleomorphic, and dedifferentiated liposarcoma as well as in the recurrences (5, 7, 9).

In an attempt to improve outcomes, a multidisciplinary approach with integration of neo-adjuvant or adjuvant therapies can be proposed, sometimes with some advantage. Unfortunately, the results are not particularly promising because of the complications often associated with these treatments (20).

The surgical complexity and the absolute necessity of radicality lead to carry out these interventions with open technique through a suitable laparotomy. While laparoscopic excision may be considered for mesenteric

benign cysts, it is certainly not appropriate for the removal of these retroperitoneal or mesenteric neoplasms (21, 22).

In our small series, all patients are still alive. Case 1, which was first operated at the age of 55 for myxoid liposarcoma and again for recurrence after 5 and 14 years, is currently disease-free from 252 months and has reached 90 years of age.

All patients were operated radically, with average surgery duration of 136 minutes (range: 60-255).

Postoperative patients were treated in Intensive Care Unit. Here, in addition to the vital parameters, the risk of bleeding was closely monitored and an appropriate infusion of hydration therapy was performed.

Conclusions

The rarity and therapeutic complexity of retroperitoneal or mesenteric primary liposarcomas require treatment, sometimes also multimodal, to carry out in reference high-volume Centres (Hub). In presenting our small series of cases, we aim to demonstrate that patients with this rare neoplastic disease, hospitalized in the Unit of General Surgery for reasons of unpostponable urgency, if operated by surgeons well experienced in abdominal surgery and if treated with an adequate management and care, can achieve survival and quality of life equivalent to those of the Hub Centres.

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