Well-Differentiated Liposarcoma of the Retroperitoneum with Dedifferentiation and Multiple Recurrences: Case Report

doi: https://doi.org/10.32635/2176-9745.RBC.2023v69n3.3626

Lipossarcoma Bem Diferenciado do Retroperitônio com Desdiferenciação e Múltiplas Recidivas: Relato de Caso

Liposarcoma Bien Diferenciado de Retroperitoneo con Desdiferenciación y Múltiples Recurrencias: Informe de Caso

Ivna Silva Gonçalves[1]; Davi Teixeira de Macêdo[2]; Iasmin Maria Rodrigues Saldanha[3]; Lívia Fernandes e Silva[4]; Paulo Henrique Silva Nunes[5]; Gunter Gerson[6]; Marcelo Leite Vieira Costa[7]; Irapuan Teles de Araújo Filho[8]

ABSTRACT

Introduction: Retroperitoneal liposarcomas are rare mesenchymal neoplasms, with well-differentiated and dedifferentiated liposarcomas being most common. The well differentiated subtype can undergo dedifferentiation to higher grade tumors. These are difficult neoplasms to treat surgically because they have high rates of local recurrence, some subtypes can metastasize, and are poorly responsive to radiotherapy and chemotherapy. **Case report:** Female patient, 45 years old, presented abdominal pain and palpable abdominal mass in 2017. She underwent resection of well-differentiated liposarcoma of the retroperitoneum, without intercurrences. In 2020, she manifested abdominal pain and weight loss. Tomography showed multiple voluminous abdominal masses, with biopsy suggestive of dedifferentiated liposarcoma. The patient was submitted to neoadjuvant radiotherapy, followed by surgical resection of the masses and right ileocolectomy. In 2022, she presented symptoms suggestive of intestinal obstruction, and underwent laparotomy that revealed intense blockage of intestinal loops, duodenal fistula, retroperitoneal tumor, and fecal peritonitis. Retroperitoneal neoplasm resection, ileostomy and fistula closure were performed. Histopathology showed relapsed dedifferentiated liposarcoma. The patient evolved with operative and infectious complications, requiring intensive care and antibiotic therapy. After clinical improvement, the patient was discharged with enteral diet and continues under outpatient follow-up. **Conclusion:** Retroperitoneal liposarcoma may undergo multifocal dedifferentiation and recurrence, requiring several surgical approaches, increasing morbidity and the risk of complications. Wide margin surgery remains the main therapeutic modality.

Key words: liposarcoma; retroperitoneal neoplasms; recurrence; cell dedifferentiation; surgical oncology.

RESUMO

Introdução: Os lipossarcomas retroperitoneais são neoplasias mesenquimais raras, sendo mais comuns os bem diferenciados e os desdiferenciados. O subtipo bem diferenciado pode sofrer desdiferenciação para tumores de maior grau. São neoplasias difíceis de tratar cirurgicamente, pois apresentam altas taxas de recorrência local, alguns subtipos podem metastizar e são pouco sensíveis à radioterapia e à quimioterapia. **Relato do caso:** Paciente feminina, 45 anos, apresentou dor abdominal e massa abdominal palpável em 2017. Foi submetida à ressecção de lipossarcoma bem diferenciado de retroperitônio, sem intercorrências. Em 2020, manifestou dor abdominal e perda ponderal. A tomografia mostrou múltiplas massas volumosas abdominais, com biópsia sugestiva de lipossarcoma desdiferenciado. Foi submetida à radioterapia neoadjuvante e, em seguida, à ressecção cirúrgica das massas e ileocolectomia direita. Em 2022, apresentou quadro sugestivo de obstrução intestinal, sendo submetida à laparotomia que evidenciou intenso bloqueio de alças intestinais, fístula duodenal, tumor retroperitonial e peritonite fecal. Procedeu-se à ressecção de neoplasia retroperitoneal, ileostomia e rafia de fístula. O histopatológico mostrou lipossarcoma desdiferenciado recidivado. A paciente evoluiu com complicações operatórias e infecciosas, necessitando de cuidados intensivos e antibioticoterapia. Após melhora clínica, recebeu alta com dieta enteral e segue em acompanhamento ambulatorial. **Conclusão:** O lipossarcoma de retroperitônio pode sofrer desdiferenciação, recidivas multifocais e múltiplas recorrências, necessitando de várias abordagens cirúrgicas, o que aumenta a morbidade e o risco de complicações. A cirurgia com margens amplas continua sendo a principal modalidade terapêutica.

Palavras-chave: lipossarcoma; neoplasias retroperitoneais; recidiva; desdiferenciação celular; oncologia cirúrgica.

RESUMEN

Introducción: Los liposarcomas retroperitoneales son neoplasias mesenquimatosas raras, siendo los más comunes los liposarcomas bien diferenciados y desdiferenciados. El subtipo bien diferenciado puede sufrir desdiferenciación hacia tumores de mayor grado. Estas neoplasias son difíciles de tratar quirúrgicamente porque presentan altas tasas de recidiva local, algunos subtipos pueden hacer metástasis y responden mal a la radioterapia y la quimioterapia. **Informe del caso:** Mujer de 45 años, en 2017 presenta dolor abdominal y masa abdominal palpable. Fue sometida a la resección de un liposarcoma bien diferenciado del retroperitoneo, sin intercurrencias. En 2020, manifestó dolor abdominal y pérdida de peso. La tomografía mostró múltiples masas abdominales voluminosas, con biopsia sugestiva de liposarcoma desdiferenciado. Fue sometida a radioterapia neoadyuvante y luego a resección quirúrgica de las masas y a ileocolectomía derecha. En 2022, presentó síntomas de obstrucción intestinal y fue sometida a una laparotomía que reveló obstrucción de las asas intestinales, fístula duodenal, tumor retroperitoneal y peritonitis fecal. Se realizó la resección de la neoplasia retroperitoneal, la ileostomía y la fistulización. La histopatología mostró un liposarcoma desdiferenciado. La paciente evolucionó con complicaciones operatorias e infecciosas, requiriendo cuidados intensivos y terapia antibiótica. Tras la mejora clínica, la paciente fue dada de alta con dieta enteral y está en seguimiento. **Conclusión:** El liposarcoma retroperitoneal puede sufrir desdiferenciación multifocal y recurrencia, requiriendo varios a tratamientos quirúrgicos, aumentando la morbilidad y el riesgo de complicaciones. La cirugía con márgenes amplios sigue siendo la terapia principal.

Palabras clave: liposarcoma; neoplasias retroperitoneales; recurrencia; desdiferenciación celular; oncología quirúrgica.

[1]Instituto do Câncer do Ceará (ICC), Hospital Haroldo Juaçaba (HHJ). Fortaleza (CE), Brazil. E-mail: ivnasg@gmail.com. Orcid iD: https://orcid.org/0000-0002-1144-4614
[2-5]Universidade Federal do Ceará (UFC), Faculdade de Medicina. Fortaleza (CE), Brazil. E-mails: davitm23@gmail.com; iasminsaldanha14@gmail.com; fernandesliviam25@alu.ufc.br; henriquedepalhano@gmail.com. Orcid iD: https://orcid.org/0000-0002-4193-7700; Orcid iD: https://orcid.org/0000-0002-3719-8175; Orcid iD: https://orcid.org/0000-0002-2035-2287; Orcid iD: https://orcid.org/0000-0002-9591-1012
[6-8]UFC, Hospital Universitário Walter Cantídio. Fortaleza (CE), Brazil. E-mails: gunter_gerson@yahoo.com.br; marcelolvcosta@gmail.com; irapuan42@gmail.com. Orcid iD: https://orcid.org/0000-0001-9054-253X; Orcid iD: https://orcid.org/0000-0002-1343-4292; Orcid iD: https://orcid.org/0000-0001-8935-7994
Corresponding author: Ivna Silva Gonçalves. Rua Papi Júnior, 1222 – Rodolfo Teófilo. Fortaleza (CE), Brazil. CEP 60430-230. E-mail: ivnasg@gmail.com

INTRODUCTION

Soft tissue sarcomas (MPs) are rare mesenchymal neoplasms and represent approximately 1% of all malignancies diagnosed in adults[1]. About 10-15% of PMS arise in the retroperitoneum, with liposarcoma being the most common variant, equivalent to 20% of all PMS and more than 50% of retroperitoneal sarcomas[2]. With an approximate incidence of 0.6 cases per 100,000 people each year, liposarcomas are tumors originating from primitive multipotent mesenchymal precursors and can arise anywhere in the body. The retroperitoneum is the second most common site, after only the extremities[3-5].

Histologically, liposarcomas are classified into five types: 1) well-differentiated; 2) dedifferentiated; 3) myxoid; 4) round cells; and 5) pleomorphic. In addition, they can be classified according to the grade – high, intermediate and low –, which has a strong relationship with the natural history of the tumor, and with the response to chemotherapy in advanced disease. Each subtype has different clinical behavior and natural history, requiring an individualized approach[3].

Retroperitoneal liposarcomas are difficult tumors to treat surgically, as they have high rates of local recurrence, some subtypes can metastasize and are little sensitive to radiotherapy and chemotherapy[4,6]. Between 60-80% of patients have a palpable abdominal mass, and half have abdominal pain. Because the retroperitoneum is a deep and expandable space, slow-growing tumors, such as liposarcoma, usually do not cause symptoms quickly and can grow for long periods, being diagnosed late when they exert compressive effects on abdominal organs. At diagnosis, 94% of these tumors have a diameter greater than 5 cm and 60% greater than 10 cm[2].

This study aims to report a case of well-differentiated liposarcoma (LBD) of retroperitoneum with dedifferentiation and multiple relapses, being approved by the Research Ethics Committee of the Walter Cantídio University Hospital under opinion number: 5,771,820 (CAAE: 64639122.5.0000.5045) in compliance with Resolution 466/127 of the National Health Council for research with human beings.

CASE REPORT

Female patient, 45 years old, black, farmer. In 2017, she presented moderate intensity pain in the left hypochondrium, in colic and intermittent. After five months, she noticed a palpable mass in the left hypochondrium and flank, and a change in the pattern of pain to "stabbing". Computed tomography (CT) of the abdomen showed a heterogeneous mass, measuring 18 x 15 x 13 cm, with gross calcifications. In November 2017, a laparotomy was performed, which showed a large retroperitoneal tumor on the left, medially displacing the left colon and posteromedially the left kidney. Absence of sarcomatosis or liver metastasis. The tumor and the anterior fascia of the renal capsule were resected, with preservation of the left colon, kidney and ureter. Biopsy revealed low-grade LBD of the retroperitoneum (Figure 1).

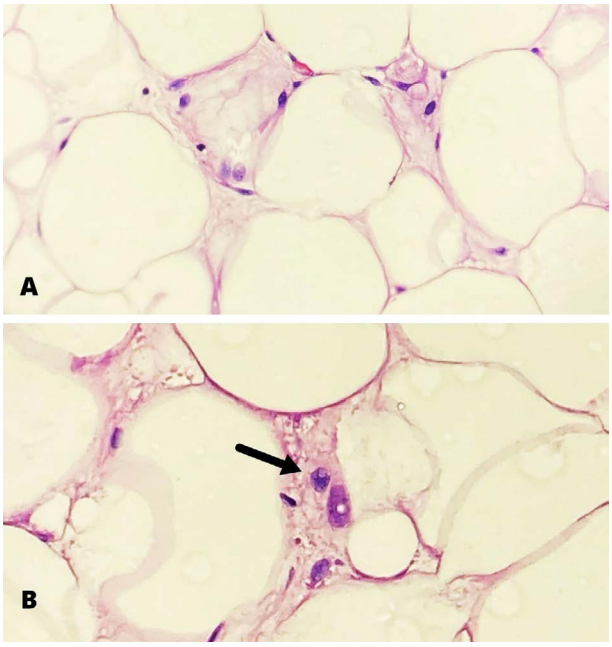

Figura 1. (A) Well-differentiated liposarcoma that exhibits adipocytic differentiation with eventual atypical cells of hyperchromic nuclei, in addition to associated lipoblasts. Hematoxylin and eosin, 200× increase; (B) Well-differentiated liposarcoma with emphasis on the presence of lipoblasts (arrow). Hematoxylin and eosin, 200× increase

In May 2020, after loss of outpatient follow-up for two years, the patient presented with left abdominal pain, epigastric pain, constipation, adynamia and weight loss of 8 kg. On examination, he showed an extensive and large hardened abdominal mass that occupied practically all quadrants of the abdomen. Abdominal CT showed a large heterogeneous cystic formation with solid areas, septations and calcifications located in the pelvic cavity, with a median and left paramedian predominance, extending to the projection of the epigastrium. She underwent laparotomy for incisional biopsy in June 2020 with histopathology compatible with myxoid liposarcoma (grade I). However, in view of the clinical history, the dedifferentiation of the previous LBD was considered as the main hypothesis. The patient was referred to clinical oncology, which indicated neoadjuvant radiotherapy to maximize the possibility of local control.

In September 2020, after completing the cycles of radiotherapy, the patient presented a considerable

reduction in the tumor mass, which became four tumors, two in the peritoneal cavity and two in the retroperitoneum. Subsequently, she underwent surgical resection of large solid-cystic masses: the first measuring 12 x 12 cm, located below the stomach and adhered to the transverse colon mesocolon; the second, a 6 x 6 cm lesion adjacent to the left kidney, without adhesions to noble structures; the third, about 14 x 14 cm, affecting a slender loop; and the largest lesion, in retroperitoneum, posterior to the retrocavity of the epiplons, measuring approximately 20 x 20 cm, adhered to the inferior mesenteric vein.

Biopsy of the retroperitoneal lesions showed dedifferentiated liposarcoma (LDD) (Figure 2). CT scan performed one week after surgery revealed a large expansive solid-cystic lesion near the right adnexal region, which was not seen in the previous laparotomy. She then underwent a right ileocolectomy procedure to resect the lesion, which measured 15 x 15 cm, in addition to implantation in the abdominal wall. Biopsy of the surgical specimen showed relapsed LDD in the mesentery.

In August 2022, after another loss of follow-up, the patient presented fever, vomiting, distension and abdominal pain, evolving with intestinal obstruction. Abdominal CT showed distension of the slender loops with expansive lesion in the right hypochondrium. She underwent laparotomy, which showed intense blockage of intestinal loops, transverse ileocolon fistula with duodenum, retroperitoneal tumor in the area of previous anastomosis and intense fecal peritonitis. Retroperitoneal neoplasia, ileostomy and fistula raffia were resected. Histopathology showed relapsed LDD (Figure 3). A week later, she evolved with ileostomy collapse and infection without improvement with antibiotic therapy.

She underwent laparotomy again, which showed a large amount of enteric/purulent fluid and adhesions throughout the abdomen, ileostomy collapse, fistulous path in the duodenum and multiple abdominal collections. A new ileostomy was performed. Ten days after the procedure, the patient presented decreased ileostomy output, associated with the contaminated surgical wound and the large amount of enteric secretion drained from the cavity.

A new laparotomy was performed, which identified intense blockages between loops without possibilities of surgical access, pelvic collection with enteric aspect and ileostomy without signs of collapse. Cavity washing, drainage apposition in the topography of the pelvic collection and antibiotic therapy were performed.

The patient evolved with septic shock, requiring intensive care and antibiotic therapy. After clinical improvement, an attempt was made to start an enteral diet, as she had been on total parenteral nutrition since the last surgery. There was good acceptance of the diet, however, when it was tried to start it orally, there were successive episodes of vomiting, suggestive of gastroparesis. She was discharged with a full enteral diet after 87 days of hospitalization and remains in outpatient follow-up.

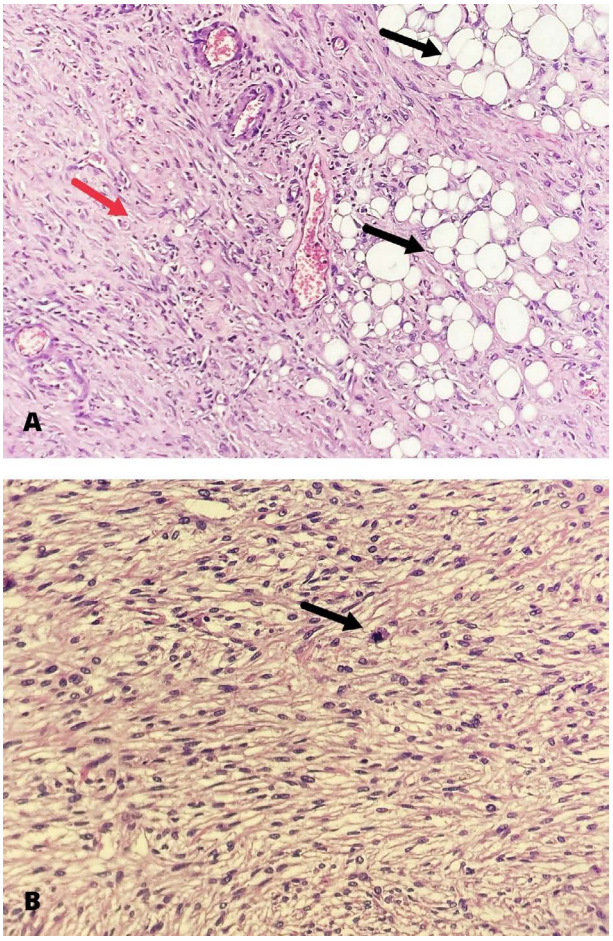

Figura 2. (A) Dedifferentiated liposarcoma with emphasis on the transition between well-differentiated adipocytic areas (black arrows) and areas of sarcomatous appearance (red arrow). Hematoxylin and eosin, 100× increase; (B) Dedifferentiated liposarcoma highlighting sarcomatous area with anaplastic cells, bundle arrangement and frequent mitosis figures (black arrow). Hematoxylin and eosin, 200× increase

DISCUSSION

In the present study, the histopathological result of the 2020 incisional biopsy showed myxoid liposarcoma, however, primary myxoid liposarcomas occur mostly in the lower limbs and are extremely rare in the retroperitoneum, and can be considered "non-existent" in this space. Thus, diagnoses of retroperitoneal myxoid liposarcoma should be considered suspicious, as most of these cases are metastatic myxoid liposarcomas or LBD/LDD with myxoidstromal changes[2].

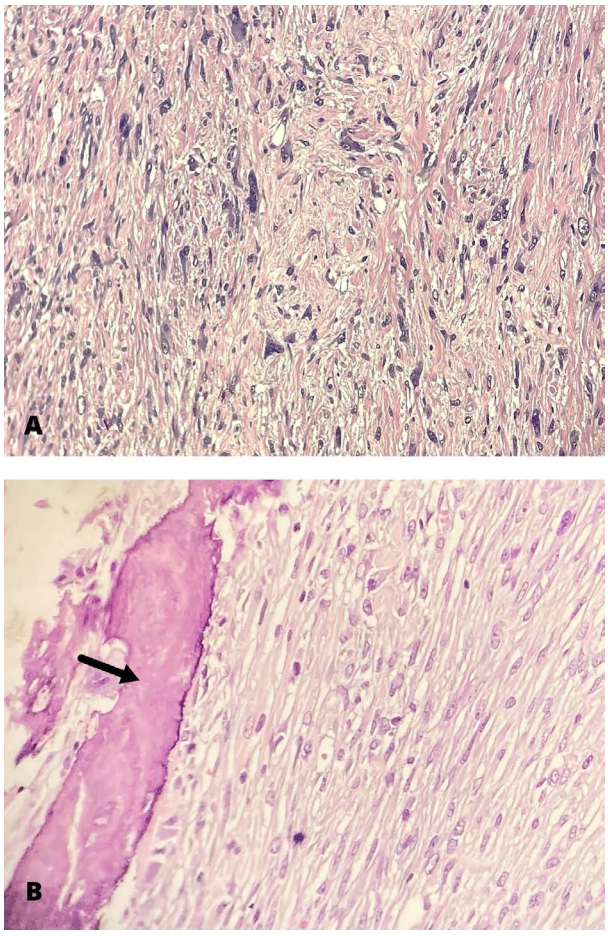

Figura 3. (A) Dedifferentiated liposarcoma of high degree of diffuse sarcomatous aspect. Hematoxylin and eosin, 200× increase; (B) High-grade dedifferentiated liposarcoma with emphasis on the presence of heterologous immature osteoid element (black arrow). Hematoxylin and eosin, 200× increase

In the retroperitoneum, the most common subtypes of liposarcomas are LBD and LDD[2,8]. LBD is a low-grade, locally aggressive adipocyte tumor that rarely causes metastasis, however, it has repeated local recurrences between 40-60% even with complete surgical resections. Disease-specific mortality is secondary to uncontrolled local disease. Overall survival rates are 80% at five years and 50% at ten years[6,8]. In addition, 20% of LBD undergo dedifferentiation to higher grade tumors on average in eight years[4].

LDD is a more aggressive high-grade sarcoma with metastatic capacity. Generally, it shows an abrupt transition between well-differentiated and de-differentiated areas in histology[9], but can be seen without any identifiable well-differentiated components[5]. Approximately 90% of LDD arise again and 10% develop as recurrence of a previously resected LDD or LBD, as in the present study. In 5-10% of cases, LDD undergoes heterogeneous differentiation with myogenic, osteosarcomatous and chondrosarcomatous elements. Its annual incidence is less than 0.1 per million[9]. And local recurrence and distant metastasis rates range from 40-80% and 15-20%, respectively. The lungs are the most common site of metastasis. Disease-free survival rates of LDD are lower than those of LBD and range from 44-53%[6].

The mechanisms responsible for progression from LBD to LDD are complex and not fully known[2]. Both subtypes arise from a 12q chromosome fragmentation event causing genomic rearrangements that lead to the formation of supernumerary ring chromosomes and amplification of the 12q13-15 segment and, consequently, of the MDM2, FRS2, CDK4, HMGA2, YEATS2 and NAV3[1] genes. In the dedifferentiation process, continuous DNA damage leads to the accumulation of more complex chromosomal aberrations, causing an increase in the degree, cellularity and aggressiveness of tumors, which completely changes their original histological appearance[4]. Thus, the term "tumor dedifferentiation" characterizes "the morphological progression of a low-grade tumor to a less differentiated neoplasm with more aggressive behavior" [2].

Surgery is the basis of treatment of non-metastatic retroperitoneal liposarcoma. Whenever possible, macroscopically complete resection should be chosen, often requiring en bloc removal of adjacent structures[2]. Preservation of specific organs should be considered individually based on tumor and patient characteristics, weighing locoregional control against dysfunction in the long term[8].

The number of locally recurrent tumors may also affect management. The first recurrence of the disease may be multifocal in up to 47-57% of patients. Five-year overall survival rates were 58-20% for unifocal and multifocal disease, respectively[6]. In this context, it is imperative to perform rigorous inspection and palpation of all abdominal organs intraoperatively to avoid not visualizing possible foci of disease, as occurred in the September 2020 surgery of the present case.

Recurrent disease is rarely curable, and surgery should be seen as temporary and reserved for cases where significant control of the disease is anticipated. Patients with more than seven lesions had overall five-year survival of only 7%. This result was similar to that of patients undergoing incomplete coarse resection. Patients with tumors that have grown faster than 0.9 cm per month since previous complete macroscopic resection had median disease-specific survival of only 13 months. Patients with rapid recurrence and multifocal disease are generally considered for systemic therapies, and surgical intervention is reserved for symptom palliation[10]. Even with multiple relapses, the lesions described in this report were considered surgically approachable. Systemic therapy was reserved for a possible need for palliation in future unresectable lesions.

Liposarcoma is moderately chemosensitive. Neoadjuvant therapies are more applicable in the advanced disease setting, especially if an LDD component is present[8]. First-line treatment for advanced LDD is anthracycline9-based. In patients with resistant disease, gemcitabine, docetaxel, trabectedin, and pazopanib were established as second- and third-line options[2]. The role of radiotherapy for primary retroperitoneal liposarcomas is controversial.

Studies show improvement in local control rate, but this impact is not necessarily seen in disease-free survival[6]. The STRASS[1] study revealed a non-significant trend in favor of preoperative radiotherapy in patients with liposarcomas. Despite this, it is important to remember that this study was not designed to detect differences in the subgroup of liposarcomas. Therefore, the use of radiotherapy should be an individualized decision[1]. In the present report, preoperative radiotherapy presented relevant results, allowing a better surgical approach to initial recurrences.

CONCLUSION

Conclusion: Retroperitoneal liposarcoma can undergo dedifferentiation, multifocal relapses and multiple recurrences, requiring several surgical approaches, which increases morbidity and the risk of complications. Surgery with wide margins remains the main therapeutic modality, as the role of radiotherapy and chemotherapy is not entirely clear.

CONTRIBUTIONS

All authors contributed substantially in the design and/or planning of the study; in the collection, analysis and interpretation of data; in the writing and critical review; and approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

FUNDING SOURCES

None.

REFERENCES

1. Haddox CL, Riedel RF. Recent advances in the understanding and management of liposarcoma. Fac Rev. 2021;10:1. doi: https://doi.org/10.12703/r/10-1
2. Matthyssens LE, Creytens D, Ceelen WP. Retroperitoneal liposarcoma: current insights in diagnosis and treatment. Front Surg. 2015;2:4. doi: https://doi.org/10.3389/fsurg.2015.00004
3. Chamberlain F, Benson C, Thway K, et al. Pharmacotherapy for liposarcoma: current and emerging synthetic treatments. Future Oncol. 2021;17(20):2659-70. doi: https://doi.org/10.2217/fon-2020-1092
4. Tyler R, Wanigasooriya K, Taniere P, et al. A review of retroperitoneal liposarcoma genomics. Cancer Treat Rev. 2020;86:102013. doi: https://doi.org/10.1016/j.ctrv.2020.102013
5. Mack T, Purgina B. Updates in pathology for retroperitoneal soft tissue sarcoma. Curr Oncol. 2022;29(9):6400-18. doi: https://doi.org/10.3390/curroncol29090504
6. Bagaria SP, Gabriel E, Mann GN. Multiply recurrent retroperitoneal liposarcoma. J Surg Oncol. 2018;117(1):62-8. doi: https://doi.org/10.1002/jso.24929
7. Conselho Nacional de Saúde (BR). Resolução nº 466, de 12 de dezembro de 2012. Aprova as diretrizes e normas regulamentadoras de pesquisas envolvendo seres humanos. Diário Oficial da União, Brasília, DF. 2013 jun 13; Seção 1:59.
8. Mansfield SA, Pollock RE, Grignol VP. Surgery for abdominal well-differentiated liposarcoma. Curr Treat Options Oncol. 2018;19(1):1. doi: https://doi.org/10.1007/s11864-018-0520-6
9. Nishio J, Nakayama S, Nabeshima K, et al. Biology and management of dedifferentiated liposarcoma: state of the art and perspectives. J Clin Med. 2021;10(15):3230. doi: https://doi.org/10.3390/jcm10153230
10. Crago AM, Dickson MA. Liposarcoma: multimodality management and future targeted therapies. Surg Oncol Clin N Am. 2016;25(4):761-73. doi: https://doi.org/10.1016/j.soc.2016.05.007

Recebido em 10/1/2023
Aprovado em 26/6/2023

Scientific-editor: Anke Bergmann. Orcid iD: https://orcid.org/0000-0002-1972-8777