European Journal of Clinical Pharmacy
PrintISSN:2385-409X**OnlineISSN**:3105-0409
Website: https://farmclin.com/

The Notch-Crossing Liposarcoma: A Rare MDM2/CDK4-Amplified Giant

Article History:

Name of Author:
Dr Aishwarya Sharma[1], Dr Ganesh Guru[2], Dr. V. Ramalakshmi[3]

Affiliation: *[1]POST GRADUATE , DEPARTMENT OF GENERAL SURGERY, SREE BALAJI MEDICAL COLLEGE AND HOSPITAL, CHROMEPET, CHENNAI, TAMIL NADU.*
[2]ASSISTANT PROFESSOR, DEPARTMENT OF GENERAL SURGERY, SREE BALAJI MEDICAL COLLEGE AND HOSPITAL, CHROMEPET, CHENNAI, TAMIL NADU
[3] PROFESSOR, DEPARTMENT OF GENERAL SURGERY, SREE BALAJI MEDICAL COLLEGE AND HOSPITAL, CHROMEPET,CHENNAI, TAMIL NADU

Corresponding Author:
Dr Ganesh Guru

Received: 02-05-2025
Revised: 20-05-2025
Accepted: 05-06-2025
Published: 15-06-2025

Abstract: ***Background:*** Retroperitoneal liposarcomas are rare malignant adipocytic neoplasms that may grow to massive sizes before detection due to the capacious nature of the retroperitoneal space. Dedifferentiated variants often show heterogeneous radiologic patterns and require combined clinicoradiologic, histopathologic, and immunohistochemical evaluation for accurate characterization. Overexpression of MDM2 and CDK4 is a key diagnostic feature, allowing reliable distinction from benign adipocytic lesions and other sarcomas ***Case Presentation:*** A 60-year-old male presented with a six-month history of progressive abdominal distension after incidentally noting a right iliac fossa mass while lying down. He had no abdominal pain, vomiting, altered bowel habits, weight loss, or constitutional symptoms. Examination revealed a firm, ill-defined, non-tender mass extending from the right iliac fossa toward the umbilical region, with no organomegaly or ascites. Contrast-enhanced CT demonstrated a large heterogeneous fat-attenuating retroperitoneal mass measuring 20.6 × 13.1 cm, abutting the aorta, inferior vena cava, and right psoas muscle, with displacement of bowel loops. A second similar lesion (11.6 × 6.5 cm) extended from the pelvis into the left gluteal region through the greater sciatic notch. No lymphadenopathy or visceral invasion was observed. Ultrasound-guided core biopsy revealed atypical spindle-cell proliferation within myxoid stroma. Immunohistochemistry showed strong nuclear positivity for MDM2 and CDK4, with a Ki-67 index of approximately 40%, favouring a diagnosis within the liposarcoma spectrum. The patient underwent open surgical excision, achieving en bloc removal of the mass. Postoperative recovery was stable, and he was discharged with plans for histologic subtyping and close oncologic follow-up. ***Conclusion:*** This case highlights the silent but progressive nature of giant retroperitoneal liposarcomas and the pivotal role of multimodal evaluation—imaging, core biopsy, and molecula immunohistochemistry—in establishing diagnosis. Complete surgical excision remains the cornerstone of management, and vigilant postoperative surveillance is crucial due to the high risk of recurrence associated with dedifferentiated variants

Keywords: Liposarcoma , Retroperitoneal Neoplasms , Sarcoma , Immunohistochemistry , MDM2 Protein , CDK4 Protein , Soft Tissue Neoplasms , Abdominal Neoplasms.

INTRODUCTION

Liposarcomas constitute a major subtype of malignant adipocytic sarcomas and frequently arise in deep anatomic compartments such as the retroperitoneum, where slow expansion and late symptomatology often delay clinical detection. Their diverse radiologic morphology and histologic variability demand combined radiologic–pathologic assessment for accurate characterization, especially in determining the presence and extent of dedifferentiated tumour components [1]. Molecular studies have further highlighted the biologic heterogeneity of retroperitoneal liposarcomas, with genomic profiling offering deeper insights into tumour behaviour and supporting the refinement of diagnostic strategies [2]. A defining molecular feature of well-differentiated and dedifferentiated liposarcomas is amplification of the 12q13–q22 region, particularly involving MDM2

and CDK4, which serves as a diagnostic hallmark and reliably differentiates these neoplasms from benign adipocytic proliferations [3]. Because morphologic overlap is common, routine immunohistochemistry for these amplified oncogenes, along with selected ancillary markers, substantially improves diagnostic accuracy in borderline cases. Additional markers such as p16 and CD34 have been evaluated to enhance interpretive clarity in adipocytic tumours, particularly in settings where molecular analysis is limited, although their diagnostic performance varies and remains inferior to MDM2 and CDK4 in distinguishing malignant entities [4].

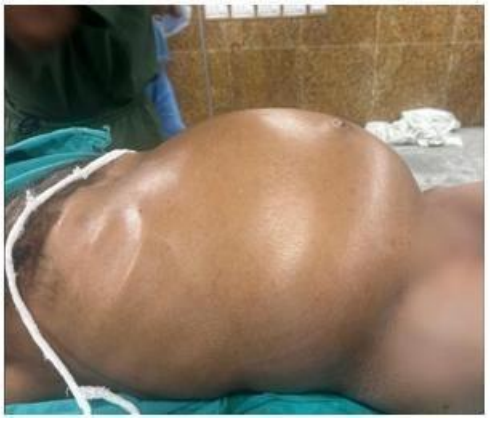
The superiority of MDM2 and CDK4 immunohistochemistry in differentiating dedifferentiated liposarcomas from histologic mimics—especially within the retroperitoneum—has been consistently demonstrated across multiple studies [5]. Combined panels incorporating p16 with MDM2 and CDK4 have shown added value, particularly in differentiating atypical lipomatous tumours from benign adipocytic lesions, supporting a multiparametric immunohistochemical approach [6]. Advances such as automated dual- colour in situ hybridization for MDM2 amplification have further strengthened diagnostic precision in difficult cases by enhancing detection reliability and reducing interpretive subjectivity [7].

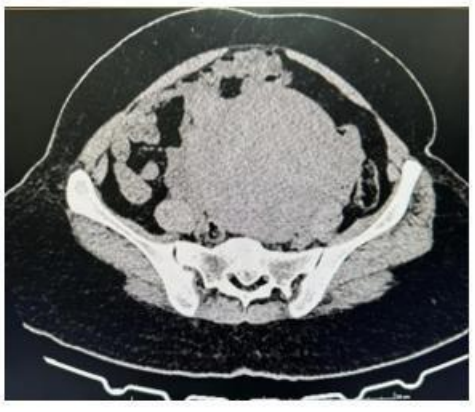
The histopathologic spectrum of dedifferentiated liposarcoma remains broad, including spindle-cell, pleomorphic, and myxoid patterns that may complicate diagnosis, especially in limited core biopsies. Detailed evaluations from tertiary oncologic referral centres have emphasized the need for careful interpretation of uncommon variants to avoid diagnostic misclassification and ensure appropriate management planning [8]. Collectively, these diagnostic refinements underscore the importance of integrating imaging, morphology, and molecular markers in evaluating retroperitoneal and pelvic liposarcomas.

CASE PRESENTATION

A 60-year-old man with no comorbidities presented with a six-month history of progressive abdominal distension after noticing a right iliac fossa mass. He had no abdominal pain, gastrointestinal symptoms, weight loss, fever, urinary complaints, or neurologic deficits.

Examination revealed a firm, ill-defined, non-tender mass in the right iliac fossa extending toward the umbilicus, with no organomegaly, ascites, or lymphadenopathy. Laboratory tests were normal





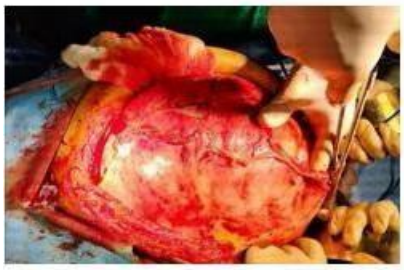
CECT of the abdomen showed a large heterogeneous retroperitoneal mass with predominant fat attenuation, measuring 20.6 × 13.1 cm, extending across the epigastric, lumbar, umbilical, and iliac regions. It abutted the aorta, IVC, and right psoas and displaced bowel loops without obstruction. A second fat-attenuating lesion (11.6 × 6.5 cm) extended from the pelvis into the

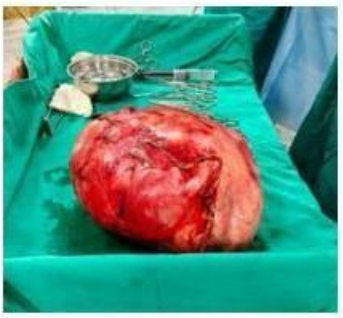
left gluteal region via the greater sciatic notch. No calcification, lymphadenopathy, ascites, or visceral invasion was observed.

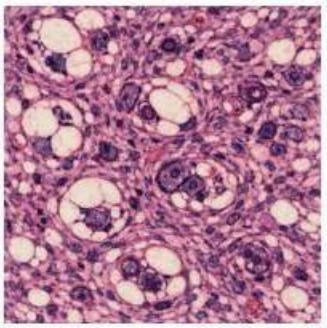
Ultrasound-guided core biopsy showed atypical spindle-cell proliferation in a myxoid stroma. Immunohistochemistry revealed strong nuclear MDM2 and CDK4 positivity with a Ki-67 index of ~40%, and SMA negativity—findings consistent with a malignant adipocytic tumour within the liposarcoma spectrum. Given potential tumour heterogeneity, complete excision was recommended.

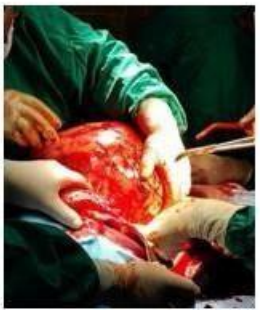
Correlation of imaging and pathology supported a diagnosis of retroperitoneal and pelvic liposarcoma with extension through the greater sciatic notch.
Intervention

The patient underwent open surgical excision following multidisciplinary evaluation. Intraoperatively, a large retroperitoneal mass occupying most of the abdominal cavity was identified and removed en bloc. The specimen was submitted for complete histopathological and immunohistochemical assessment.









Outcome and Follow-Up

Postoperative recovery was uneventful, and the patient was discharged in stable condition. Final histologic subtyping of the resected tumour is awaited to guide decisions regarding adjuvant therapy. He continues on scheduled oncologic follow-up for surveillance of recurrence.

This case highlights the silent progression of giant retroperitoneal liposarcomas and emphasizes the importance of multimodal diagnosis—imaging, biopsy, and immunohistochemistry—along with complete surgical excision and vigilant long-term monitoring.
Histopathology report

Well-differentiated Liposarcoma Histologic Grade (FNCLCC Grade): 2 pTNM classification: pT4NxMx (Retroperitoneum).

Table 1. Radiologic and Pathologic Correlation in the Diagnosis of Retroperitoneal Liposarcoma

Domain	Findings	Correlation / Interpretation
Radiologic Features (CECT)	• Large heterogeneous retroperitoneal mass with fat attenuation	
• Size 20.6 × 13.1 cm		
• Pelvic extension (11.6 × 6.5 cm) through greater sciatic notch		
• Abutting aorta, IVC, psoas; bowel displacement		
• No calcification or visceral invasion	Fat-dense mass with solid nodular areas strongly suggests liposarcoma; large size	

	and mixed density indicate possible dedifferentiation.	
Histopathology (Core Biopsy)	• Atypical spindle-cell proliferation	
• Myxoid stroma	Spindle-cell morphology compatible with dedifferentiated component; correlates with solid regions on imaging.	
Immunohistochemistry	• MDM2: Positive	
• CDK4: Positive		
• SMA: Negative		
• Ki-67 ≈ 40%	MDM2/CDK4 positivity confirms liposarcoma lineage; high Ki-67 supports aggressive/dedifferentiated behaviour.	
Final Integrated Impression	—	Concordant radiologic and pathologic features strongly favour dedifferentiated retroperitoneal liposarcoma with pelvic extension.

DISCUSSION

This case highlights a giant retroperitoneal liposarcoma with pelvic and gluteal extension, showing classic radiologic features and biopsy-proven dedifferentiation supported by spindle- cell morphology and MDM2/CDK4 positivity. Such tumours commonly present late due to their deep location and slow expansion, consistent with patterns described in the literature.

Tateishi et al. reported that large size, heterogeneous enhancement, and non-lipomatous solid areas predict poorer outcomes in dedifferentiated retroperitoneal liposarcomas [9]. Our tumour similarly demonstrated extensive retroperitoneal involvement, vascular abutment, and mixed-density components, aligning with these prognostic imaging markers. In contrast, Silverstein et al. emphasised the diagnostic difficulty of MDM2/CDK4-negative fatty tumours [10]; the strong positivity in our case allowed confident classification and avoided the ambiguity encountered in their cohort.

The high proliferative index and dedifferentiated morphology place this tumour in a higher- risk category, comparable to the recurrence patterns described by Matsui et al., who identified grade and completeness of resection as key determinants of prognosis [11]. Khan et al. also noted that dedifferentiated variants frequently arise in the retroperitoneum and behave more aggressively than superficial lesions [12], a profile mirrored in our patient. Zhang et al. showed that non-fatty enhancing regions on imaging often correspond to high- grade dedifferentiated tissue [13]. The inhomogeneous soft-tissue areas in our case matched these observations, reinforcing the importance of targeted biopsy. Imaging characteristics also paralleled those described by Francis et al., who outlined large size, predominant fat, and thickened septa as suggestive features of liposarcoma rather than benign lipomas [14].

Management in our case—comprising cross-sectional imaging, guided biopsy, immunohistochemistry, and en bloc resection—is consistent with contemporary recommendations highlighted by Schmitz and Nessim, who emphasized MDT-based care and histology-directed strategies for retroperitoneal sarcomas [15]. Despite complete excision, recurrence risk remains substantial, as noted by Hogg et al. [16], underscoring the need for long-term surveillance.
The presentation also reflects the challenges described in Indian series, such as delayed diagnosis and large tumour burden at presentation, particularly noted by Kumar et al. [17]. The extension through the greater sciatic notch adds a distinctive anatomic complexity, though the overall behaviour and morphology remain characteristic of dedifferentiated retroperitoneal liposarcoma.

Overall, the findings in this case align closely with established literature, highlighting the importance of integrating imaging, histopathology, and molecular markers for accurate diagnosis and guiding definitive

surgical management in high-risk retroperitoneal liposarcomas.

CONCLUSION

This case illustrates the silent but progressive nature of retroperitoneal liposarcomas, which may reach enormous sizes before detection. Accurate diagnosis was achieved through integrated imaging, targeted biopsy, and immunohistochemistry, with MDM2/CDK4

positivity confirming a liposarcoma spectrum tumour. The tumour's mixed fat and solid components and its extension through the greater sciatic notch paralleled typical features of dedifferentiated retroperitoneal liposarcoma reported in the literature.

Complete surgical excision remains the primary treatment, and the successful en bloc resection here highlights the importance of multidisciplinary planning. Given the high recurrence risk associated with dedifferentiated subtypes, structured long-term surveillance is essential. This case underscores the need for early recognition, comprehensive evaluation, and coordinated care in managing complex retroperitoneal liposarcomas.

BIBLIOGRAPHY

1. Murphey MD, Arcara LK, Fanburg-Smith J. From the archives of the AFIP: imaging of musculoskeletal liposarcoma with radiologic-pathologic correlation. Radiographics. 2005 Sep-Oct;25(5):1371-95. doi: 10.1148/rg.255055106. PMID: 16160117.
2. Tyler R, Wanigasooriya K, Taniere P, Almond M, Ford S, Desai A, Beggs A. A review of retroperitoneal liposarcoma genomics. Cancer Treat Rev. 2020 Jun;86:102013. doi: 10.1016/j.ctrv.2020.102013. Epub 2020 Mar 28. PMID: 32278233.
3. Pilotti S, Della Torre G, Lavarino C, Sozzi G, Minoletti F, Vergani B, Azzarelli A, Rilke F, Pierotti MA. Molecular abnormalities in liposarcoma: role of MDM2 and CDK4-containing amplicons at 12q13-22. J Pathol. 1998 Jun;185(2):188-90. doi: 10.1002/(SICI)1096-9896(199806)185:2<188::AID-PATH53>3.0.CO;2-2. PMID:
4. 9713346.
5. Altun E, Yüksel S, Kaygusuz G, Yıldız HY. Diagnostic importance of clinicopathologic features and p16, CD34, MDM2 expression in differential diagnosis of adipocytic tumors. Acta Orthop Traumatol Turc. 2020 Jan;54(1):59-65. doi: 10.5152/j.aott.2020.01.445. PMID: 32175898; PMCID: PMC7243699.
6. Kang Y, Horvai AE. p16 Immunohistochemistry is Less Useful Than MDM2 and CDK4 to Distinguish Dedifferentiated Liposarcomas From Other Retroperitoneal Mimics. Appl Immunohistochem Mol Morphol. 2017 Jan;25(1):58-63. doi: 10.1097/PAI.0000000000000270. PMID: 26509911.
7. Kammerer-Jacquet SF, Thierry S, Cabillic F, Lannes M, Burtin F, Henno S, Dugay F, Bouzillé G, Rioux-Leclercq N, Belaud-Rotureau MA, Stock N. Differential diagnosis
8. of atypical lipomatous tumor/well-differentiated liposarcoma and dedifferentiated liposarcoma: utility of p16 in combination with MDM2 and CDK4 immunohistochemistry. Hum Pathol. 2017 Jan;59:34-40. doi: 10.1016/j.humpath.2016.08.009. Epub 2016 Sep 3. PMID: 27597521.
9. Kobayashi A, Sakuma T, Fujimoto M, Jimbo N, Hirose T. Diagnostic Utility and Limitations of Immunohistochemistry of p16, CDK4, and MDM2 and Automated Dual-color In Situ Hybridization of MDM2 for the Diagnosis of Challenging Cases of Dedifferentiated Liposarcoma. Appl Immunohistochem Mol Morphol. 2019 Nov/Dec;27(10):758-763. doi: 10.1097/PAI.0000000000000677. PMID: 31145104.
10. Rekhi B, Navale P, Jambhekar NA. Critical histopathological analysis of 25 dedifferentiated liposarcomas, including uncommon variants, reviewed at a Tertiary Cancer Referral Center. Indian J Pathol Microbiol. 2012 Jul-Sep;55(3):294-302. doi: 10.4103/0377-4929.101733. PMID: 23032820.
11. Tateishi U, Hasegawa T, Beppu Y, Satake M, Moriyama N. Primary dedifferentiated liposarcoma of the retroperitoneum. Prognostic significance of computed tomography and magnetic resonance imaging features. J Comput Assist Tomogr. 2003 Sep- Oct;27(5):799-804. doi: 10.1097/00004728-200309000-00019. PMID: 14501373.
12. Silverstein ML, Kalof AN, Kurchena KC, Harlow SP, Lemos DF, Cintolo-Gonzalez JA. Diagnostic and management challenges for MDM2-, CDK4-negative fatty tumors of the retroperitoneum. J Cancer Res Clin Oncol. 2021 Apr;147(4):1137-1144. doi: 10.1007/s00432-021-03512-x. Epub 2021 Feb 6. PMID: 33550433; PMCID: PMC11802130.
13. Matsui Y, Iwata S, Moritani K, Maejima A, Nara S, Yamagata Y, Komiyama M, Kamio S, Yonemori K, Kawai A, Fujimoto H. The prognostic factors and treatment patterns of the first recurrence of retroperitoneal liposarcoma. Int J Clin Oncol. 2025 Aug;30(8):1641-1649. doi: 10.1007/s10147-025-02790-6. Epub 2025 May 28. PMID: 40434510.
14. Khan N, Ud Din H, Hashmi SN, Muhammad I,

Atique M, Khadim T, Akhtar F. Spectrum of liposarcomas-a study of 106 cases. J Ayub Med Coll Abbottabad. 2014 Jul-Sep;26(3):320-2. PMID: 25671937.

15. Zhang JY, Yu XD, Song Y, Zhang HT, Chen Y, Ouyang H, Zhao XM. [Comparison of Imaging and Pathologic Findings of Retroperitoneal Dedifferentiated Liposarcoma]. Zhonghua Zhong Liu Za Zhi. 2019 Mar 23;41(3):223-228. Chinese. doi: 10.3760/cma.j.issn.0253-3766.2019.03.013. PMID: 30917460.
16. Francis IR, Cohan RH, Varma DG, Sondak VK. Retroperitoneal sarcomas. Cancer Imaging. 2005 Aug 23;5(1):89-94. doi: 10.1102/1470-7330.2005.0019. PMID: 16154826; PMCID: PMC1665230.
17. Schmitz E, Nessim C. Retroperitoneal Sarcoma Care in 2021. Cancers (Basel). 2022 Mar 2;14(5):1293. doi: 10.3390/cancers14051293. PMID: 35267600; PMCID: PMC8909774.
18. Hogg HD, Manas DM, Lee D, Dildey P, Scott J, Lunec J, French JJ. Surgical outcome and patterns of recurrence for retroperitoneal sarcoma at a single centre. Ann R Coll Surg Engl. 2016 Mar;98(3):192-7. doi: 10.1308/rcsann.2016.0057. Epub 2016 Feb 14. PMID: 26876538; PMCID: PMC5226156.
19. Kumar V, Misra S, Chaturvedi A. Retroperitoneal sarcomas- a challenging problem. Indian J Surg Oncol. 2012 Sep;3(3):215-21. doi: 10.1007/s13193-012-0152-4. Epub 2012 May 30. PMID: 23997509; PMCID: PMC3444574.