Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Pathology

Fibrolamellar Carcinoma, A Rare Tumor with Distinctive Features: A Case Report

Sara El Ghaffouli[1,2*], Hanae Benabdenbi[1,2], Alaaeddine Boujeddaine Tsouli[2,3], Hafsa Chahdi[1,2], Mohamed Amine Essaoudi[1,2], Mohamed Oukabli[1,2]

[1]Department of Pathology, Mohammed V Military Teaching Hospital, 10045 Rabat, Morocco
[2]Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, 10100 Rabat, Morocco
[3]Department of Visceral Surgery I, Mohammed V Military Teaching Hospital, 10045 Rabat, Morocco

DOI: https://doi.org/10.36347/sjmcr.2025.v13i08.032 | **Received:** 09.06.2025 | **Accepted:** 12.08.2025 | **Published:** 18.08.2025

***Corresponding author:** Sara El Ghaffouli
Department of Pathology, Mohammed V Military Teaching Hospital, 10045 Rabat, Morocco

Abstract | **Case Report**

Fibrolamellar carcinoma (FLC) is a rare and aggressive tumor. FLC typically occurs in children and young adults and is known to be associated with a unique gene mutation. Unlike conventional hepatocellular carcinoma, it presents with unique clinical and histologic features and poses significant diagnostic and therapeutic challenges. Its pathogenesis remains poorly understood. Currently, both histopathologic and biomolecular studies contribute to its characterization. Herein, we report the case of a 43-year-old patient with diabetes mellitus and two previous hepatic resections, who presented with a newly identified lesion in segment IVa of the liver. Imaging, including MRI and PET-CT, revealed a metabolically active mass in close contact with the diaphragm. The patient underwent exploratory laparoscopy and subsequent surgical resection. Histopathologic and immunohistochemical studies (positive for CK7, CD68, and AE1/AE3) supported the diagnosis of fibrolamellar carcinoma.

Keywords: Fibrolamellar carcinoma – surgery – Histopathology – Immunohistochemistry -molecular pathogenesis– case report.

INTRODUCTION

Fibrolamellar carcinoma (FLC) was first described by Edmondson in 1956 as "a rare, distinct form of primary hepatocellular carcinoma" [1]. While previous editions of the WHO Classification of Tumors regarded FLC as a histological variant, it was only in the 2010 edition that FLC was assigned its own classification code, reflecting its unique clinical, histopathologic, and molecular profile and justifying its consideration as a separate entity from conventional hepatocellular carcinoma (HCC) [2].

FLC is a rare neoplasm, accounting for less than 1% of all primary liver tumors, in contrast to classical HCC, which comprises 60–80% of cases [3,4]. It predominantly occurs in children and young adults and, unlike classical HCC, is not associated with underlying chronic liver disease or cirrhosis. Nevertheless, FLC is by no means an indolent tumor; it frequently demonstrates aggressive behavior and a propensity for recurrence [2]. A definitive diagnosis ultimately relies on histopathologic examination.

Herein, we report a case of recurrent fibrolamellar carcinoma in a 43-year-old patient, which was incidentally detected during routine radiologic follow-up after initial surgical resection. This case underscores the rarity of FLC and the diagnostic challenges related to its recurrence.

CASE REPORT

We report the case of a 43-year-old female patient with a history of insulin-dependent diabetes mellitus and recurrent fibrolamellar carcinoma, who had previously undergone two hepatic resections: a segmental hepatectomy involving segments IVb, V, and part of VI in February 2022, followed by a segment III resection for tumor recurrence in February 2024.

During routine imaging surveillance, follow-up MRI in October 2024 revealed a newly developed extra-capsular nodule adjacent to segment IVa. PET-CT further characterized this lesion as metabolically active and in close contact with the diaphragmatic dome, raising suspicion of recurrence. The patient subsequently

underwent exploratory laparoscopy and was scheduled for tumor excision in December 2024.

Histopathological examination of the resected specimen revealed a poorly circumscribed, whitish hepatic lesion measuring 2.8 cm at its greatest dimension, located less than 0.1 cm from the liver surface. Microscopically, the tumor was composed of malignant epithelial cells arranged in trabecular and lobular patterns, with abundant eosinophilic cytoplasm, hyperchromatic nuclei, and marked cytologic atypia, within a fibrous and inflammatory stroma , no vascular invasion was identified (figure 1 A-B-C).

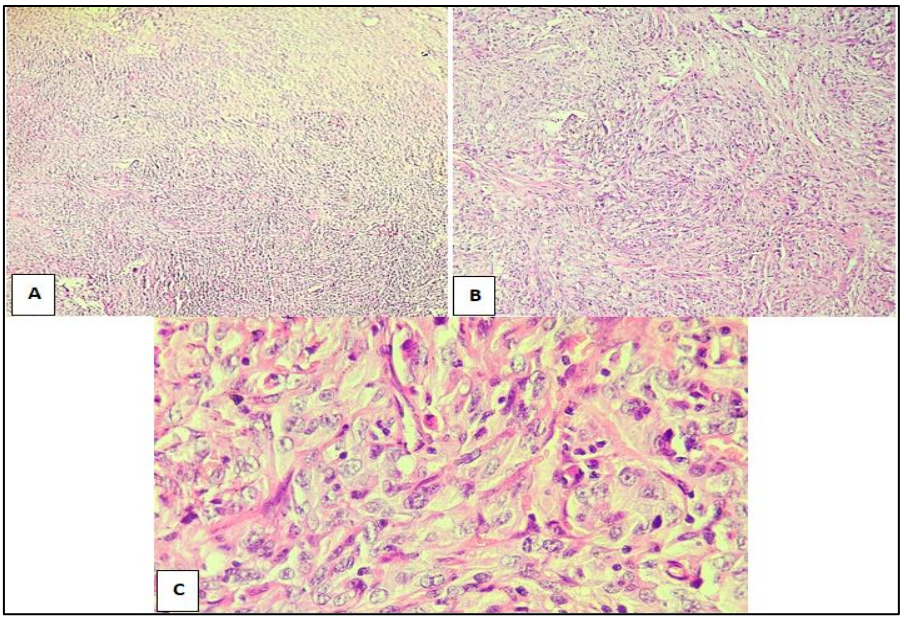

Figure 1: Histological analysis demonstrated large polygonal cells characterized by abundant eosinophilic cytoplasm, hyperchromatic nuclei, and marked cytologic atypia within a fibrous and inflammatory stroma (hematoxylin and eosin stain); representative images are shown at magnifications of ×4 (A), ×10 (B), and ×40 (C)

Immunohistochemical analysis showed positive staining for AE1/AE3, CK7 and CD68 (figure2 A-B-C) and negativity for hepatocyte-specific antigen, CK19, alpha-fetoprotein, synaptophysin, and chromogranin. These features supported the diagnosis of fibrolamellar variant hepatocellular carcinoma.

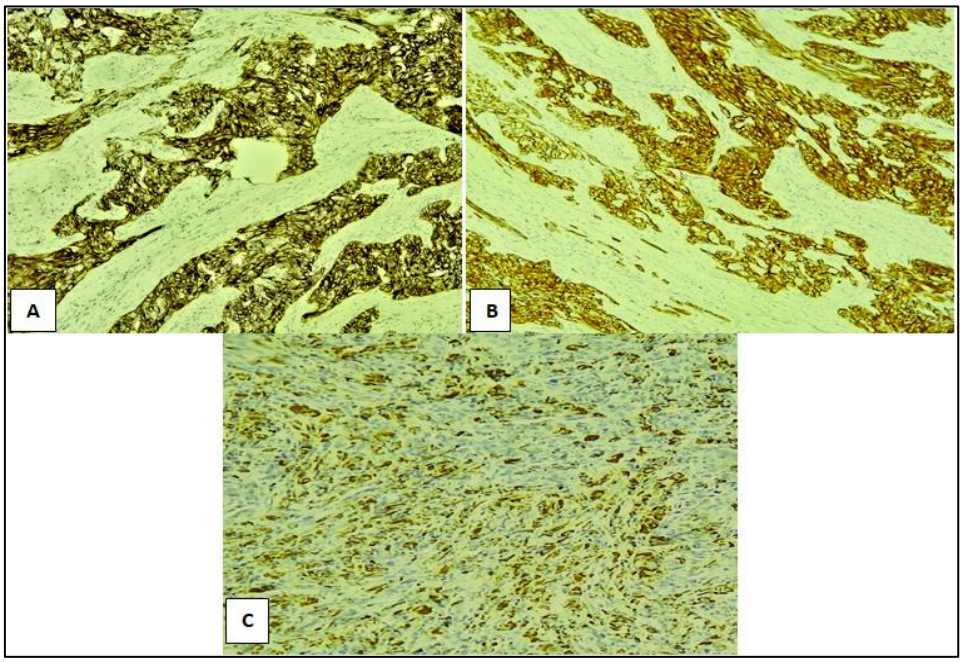

Figure 2: Immunohistochemistry of fibrolamellar carcinoma shows strong diffuse cytoplasmic staining for CK7 (A) and AE1/AE3 (B), with weak to moderate granular cytoplasmic staining for CD68 (C) (original magnification ×40)

DISCUSSION

Fibrolamellar carcinoma (FLC), also referred to as fibrolamellar hepatocellular carcinoma (FL-HCC), is a rare primary liver tumor, accounting for less than 1% of all liver cancers and approximately 13.4% of liver tumors [5]. It predominantly affects young adults, with a mean age at diagnosis of 25 years, and shows a secondary incidence peak in the seventh decade [6]. Patients often report nonspecific symptoms such as abdominal pain, nausea, fullness, or weight loss [7]. FLC arises in a normal liver and typically shows normal alpha-fetoprotein levels [6]. On imaging, ultrasound reveals a well-defined lesion with variable echogenicity [7]. Contrast-enhanced CT shows a large, heterogeneous, lobulated mass frequently containing calcifications or necrosis, with strong arterial enhancement [7]. MRI typically demonstrates a hypointense lesion on T1, hyperintense on T2, with a central hypointense scar and enhancement patterns similar to CT [7].

Pathologic examination remains the gold standard for the diagnosis of Fibrolamellar carcinoma [8]. Macroscopically, FLC typically appears as a large, well-circumscribed, heterogeneous mass arising in a non-cirrhotic liver, frequently featuring a central scar and calcifications in approximately 70% of cases [9]. Microscopically, FLC is composed of large polygonal cells with prominent nucleoli and abundant eosinophilic cytoplasm, arranged in nests, cords, and trabeculae within a dense, lamellar fibrous stroma. This stroma frequently forms thick septa and scar-like formations [10]. Tumor cells are notably larger than normal hepatocytes and may contain cytoplasmic inclusions, although these are not diagnostically specific [11]. Importantly, bile production is frequently observed within the tumor, further supporting its hepatocellular differentiation [11]. Occasionally, FLC may show pseudoglandular formations with focal mucin production, a feature that should not be misinterpreted as cholangiocarcinoma [11].

Immunohistochemically, FLC expresses both hepatocellular and biliary markers [12]. Cytokeratin 7 (CK7) is consistently positive in FLC, while CD68, a lysosomal protein, shows high sensitivity and specificity, making it a key marker to distinguish FLC from other hepatocellular carcinomas, particularly scirrhous variants [11]. Therefore, combined assessment of CK7 and CD68 is recommended, as the absence of both markers reliably excludes an FLC diagnosis [11].

The molecular pathogenesis of FLC remains incompletely understood 4. The discovery of the DNAJB1-PRKACA fusion gene, which results in constitutive activation of protein kinase A, represents a defining molecular hallmark of FL-HCC and has facilitated molecular diagnosis [13]. However, this fusion has also been identified in select pancreatic and biliary neoplasms, and FLC cases lacking the fusion have been reported, indicating genetic heterogeneity [8] . In the present case, molecular testing was not performed; nevertheless, classic histopathological features supported the diagnosis. Further research is warranted to delineate the full spectrum of genetic alterations driving FLC tumorigenesis [8].

Despite its distinctive clinical and histopathological features, FLC can pose significant diagnostic challenges. The primary entities to consider in the differential diagnosis include conventional hepatocellular carcinoma (HCC), particularly the scirrhous variant, and intrahepatic cholangiocarcinoma, both of which may exhibit abundant fibrous stroma resembling that seen in FLC. Notably, focal areas within conventional HCC can sometimes mimic the histological patterns characteristic of FLC. In these contexts, immunohistochemical profiling and molecular studies play a crucial role in distinguishing FLC from these morphologically overlapping tumors, thereby ensuring accurate diagnosis and appropriate clinical management [8].

Surgical resection remains the primary treatment for FLC, providing the best chance for prolonged survival despite frequent recurrence [8]. Chemotherapy is generally reserved for unresectable cases but has shown limited efficacy [8]. Prognostic factors are dominated by the presence of cirrhosis and metastases at diagnosis, which are associated with poorer outcomes. In the absence of cirrhosis, patient survival rates are comparable to those observed in HCC affecting non-cirrhotic livers, regardless of tumor size or histological atypia [14].

CONCLUSION

Fibrolamellar carcinoma is defined by unique histopathological features and the DNAJB1-PRKACA fusion gene, which aids diagnosis and suggests novel therapeutic targets. However, further molecular studies are essential to fully understand its pathogenesis and improve patient outcomes.

Acknowledgements: Not applicable

Competing interests: The authors declare that they have no competing interests.

Funding: No funding source was needed

Ethics approval and consent to participate: not applicable

Consent Informed consent was obtained from the patient

Guarantor: is the corresponding author

Availability of data and materials Not applicable

Authors' contributions: All authors read and approved the final manuscript.

REFERENCES

1. Edmondson HA. Differential diagnosis of tumor and tumor-like lesions of the liver in infancy and childhood. Am J Dis Child. 1956;91(2):168-86.
2. Torbenson M. Fibrolamellar carcinoma: 2012 update. Scientifica. 2012;2012:743790. DOI: 10.6064/2012/743790.
3. Liu S, Chan KW, Wang B, Qiao L. Fibrolamellar hepatocellular carcinoma. Am J Gastroenterol. 2009;104(10):2617-24.
4. McLarney JK, Rucker PT, Bender GN, Goodman ZD, Kashitani N, Ros PR. Fibrolamellar carcinoma of the liver: radiologic/pathologic correlation. Radiographics. 1999;19(2):453-71. DOI: 10.1148/radiographics.19.2.g99mr09453.
5. Paradis V. Histopathology of hepatocellular carcinoma. Recent Results Cancer Res. 2013;190:21-32.
6. O'Neill AF, Church AJ, Perez-Atayde AR, et al. Fibrolamellar carcinoma: An entity all its own. Curr Probl Cancer. 2021. DOI: 10.1016/j.currproblcancer.2021.100770.
7. Abdelhamed W, El-Kassas M. Fibrolamellar hepatocellular carcinoma: a rare but unpleasant event. World J Gastrointest Oncol. 2022;14(6):1103-14. DOI: 10.4251/wjgo.v14.i6.1103.
8. Na SK. Fibrolamellar hepatocellular carcinoma that was successfully treated with surgical resection: a case report. J Liver Cancer. 2022 Sep;22(2):178-82. DOI: 10.17998/jlc.2022.06.10.
9. Ichikawa T, Federle MP, Grazioli L, Madariaga J, Nalesnik M, Marsh W. Fibrolamellar hepatocellular carcinoma: imaging and pathologic findings in 31 recent cases. Radiology. 1999;213(2):352-61.
10. Craig JR, Peters RL, Edmondson HA, Omata M. Fibrolamellar carcinoma of the liver: a tumor of adolescents and young adults with distinctive clinicopathologic features. Cancer. 1980;46(2):372-9.
11. Lin CC, Yang HM. Fibrolamellar Carcinoma: A Concise Review. Arch Pathol Lab Med. 2018 Sep;142(9):1141-5. DOI: 10.5858/arpa.2017-0083-RS.
12. Wennerberg AE, Nalesnik MA, Coleman WB. Hepatocyte paraffin 1: a monoclonal antibody that reacts with hepatocytes and can be used for differential diagnosis of hepatic tumors. Am J Pathol. 1993;143(4):1050-4.
13. Honeyman JN, Simon EP, Robine N, Chiaroni-Clarke R, Darcy DG, Lim II, et al. Detection of a recurrent DNAJB1-PRKACA chimeric transcript in fibrolamellar hepatocellular carcinoma. Science. 2014;343(6174):1010-4.
14. Kakar S, Burgart LJ, Batts KP, Garcia J, Jain D, Ferrell LD. Clinicopathologic features and survival in fibrolamellar carcinoma: comparison with conventional hepatocellular carcinoma with and without cirrhosis. Mod Pathol. 2005;18(11):1417-23.