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Case Report

Fibrolamellar Hepatocellular Carcinoma in Young Adult: A Case Report and Literature Review

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Abstract: Fibrolamellar carcinoma (FLC), a truly unique and uncommon variation of hepatocellular carcinoma (HCC), accounting for barely 1%–9% of all HCC cases. Fibrolamellar carcinoma, an unclear malignancy, appears to be more commonly observed in youthful individuals without any preexisting liver conditions. The nomenclature "fibrolamellar" originates from the presence of dense fibrous collagen bands enveloping the neoplastic cells. Contrary to hepatocellular carcinoma (HCC), cirrhosis and viral hepatitis infection do not serve as predisposing factors for fibrolamellar carcinoma (FLC). Additionally, FLC is not typically associated with increased levels of serum alpha-fetoprotein. Patients with FLC frequently manifest with nonspecific abdominal discomfort, queasiness, general discomfort, and decreased in body mass. Surgical intervention, specifically resection or liver transplantation, serves as the cornerstone of treatment and represents the sole potentially curative avenue. FLCs, or fibrolamellar carcinomas, have historically exhibited lower responsiveness to chemotherapy compared to conventional hepatocellular carcinomas (HCC). Nevertheless, it is important to note that in cases of advanced FLCs, the utilization of multi-modality treatments has shown promising effectiveness. The purpose of this review is to explain the clinical characteristics, diagnostic techniques, and therapeutic approaches for this uncommon tumor in order to enhance the knowledge of healthcare professionals.

Keywords: Fibrolamellar Carcinoma, Hepatocellular Carcinoma, Hepatitis, Cirrhosis, Viral Hepatitis Infection.

INTRODUCTION

Fibrolamellar carcinoma (FLC) is a very rare kind of liver cancer that exhibits distinct behavioral and clinical characteristics that set it apart from the more frequent hepatocellular carcinoma (HCC). It constitutes a range of 1% to 9% of all hepatocellular carcinomas (HCCs). In 1956, Edmonson provided the initial description of fibrolamellar carcinoma (FLC) as a kind of hepatocellular carcinoma occurring in an adolescent female patient who did not have any pre-existing liver conditions. The term "FLC" is derived from the histologically discernible intratumoral lamellar collagen bands that are visible amidst big polygonal cells exhibiting ample eosinophilic cytoplasm, prominent vesiculated nuclei, and sizable nucleoli. The condition frequently manifests in individuals aged 10 to 35 who do not have any underlying liver pathology. The presence of a specific underlying trigger in the fuzzy logic controller (FLC) is not identified. The proportion of individuals diagnosed with fibrolamellar carcinoma (FLC) exhibiting cirrhotic liver morphology is less than 10%. In contrast to hepatocellular carcinoma, the presence of cirrhosis and viral hepatitis infection does not serve as predisposing factors for fibrolamellar carcinoma (FLC). Furthermore, FLC is generally not accompanied by elevated levels of serum alpha-fetoprotein. A majority of individuals diagnosed with fibrolamellar carcinoma are of Caucasian descent, although over 80% of patients with hepatocellular carcinoma also belong to the Caucasian ethnic group. Tumor markers exhibit elevated levels in less than 10%

of individuals affected by the condition, and they do not play a significant role in the evaluation or identification of fibrolamellar carcinoma. The present primary therapeutic options, namely resection or liver transplantation, remain the only potentially curative strategies. Chemotherapy was employed as an adjunctive therapy both before and during surgical resection. There is currently no evidence to suggest that neo-adjuvant or adjuvant systemic therapy provides a survival benefit for individuals who have undergone surgical resection for fibrolamellar carcinoma (FLC). Obtaining precise estimates of the incidence of this tumor across different countries is challenging due to its rarity. Fibrolamellar carcinomas (FLCs) constitute a minority, specifically less than 1%, of primary liver tumors in the United States, but in Mexico, they account for around 5.8% of liver tumors. In contrast, incidence rates exhibit a high degree of consistency across various regions globally. Fibrolamellar carcinoma (FLC) predominantly impacts a demographic of younger individuals, with a median age of 21 years. In contrast, hepatocellular carcinoma (HCC) primarily affects individuals aged between 14 and 33 years. A significant proportion of instances (64%) are detected prior to reaching the age of 40. Additional research demonstrated a higher representation of female individuals in the FLC group compared to the typical HCC group, with proportions of 60% and 37%, respectively. This observation was similarly seen in the SEER study, when the researchers identified a higher proportion of females in the FLC group (51.5% vs. 26.3%). Moreover, a number of countries, like the United States, Mexico, Sweden, Saudi Arabia, Thailand, France, Canada, South Africa, Japan, South Korea, India, Taiwan, and the United Kingdom, have shown similar rates of fibrolamellar carcinoma. The cause of FLC remains unclear. The occurrence of this phenomenon is commonly observed in livers that do not exhibit evident liver fibrosis or cirrhosis, in contrast to hepatocellular carcinoma, which is frequently detected in the context of cirrhosis or chronic hepatitis. There have been reports of a link between fibrolamellar carcinoma and focal nodular hyperplasia (FNH), which is a benign kind of liver tumor. There appears to be a coincidental association between the use of oral contraceptives and the occurrence of fibrolamellar cancer in women.

Clinical Finding

There are no early-stage signs or symptoms of fibrolamellar carcinoma (FLC). There is a wide range of symptoms that have been documented, ranging from localized discomfort and distention in the abdomen region to more widespread ymptoms including fatigue and weight loss. The most common symptoms are a palpable lump or abdominal discomfort; nevertheless, FLC lesions are most frequently discovered by accident during tests for other clinical diseases.

RADIOLOGY

FLC is characterized by a lack of specific symptoms, so a diagnosis is typically made based on a combination of the patient's clinical presentation and diagnostic imaging testing. Ultrasound, CT scans, and MRI scans are all types of imaging investigations that may provide helpful information. FLC is seen on ultrasonography as a discrete mass with variable echogenicity. Most liver lesions, including FLC, are better characterized with cross-sectional imaging than with ultrasound. Typically, a fibrolamellar carcinoma (FLC) would manifest as a big, isolated tumor. Misdiagnosis is probable due to radiomorphological similarities with focal nodular hyperplasia (FNH), as both conditions commonly have a central scar. Some individuals present with FLC and a history of surveillance for FNH, whereas others appear with both lesions at the same time, suggesting a correlation between the two.

MRI has become the gold standard for imaging in many hospitals. MRI is a powerful tool that can help doctors identify FLC in the liver. The fibrous central scar of an FLC tumor is hypointense on both T1- and T2-weighted imaging, but the tumor itself is hyperintense on T1-weighted images. FLC can be distinguished from benign liver masses, like focal nodular hyperplasia, by the hypointensity of the central scar, which is generally mainly hyperintense on T2-weighted images. Many medical facilities employ gadolinium-enhanced magnetic resonance imaging (MRI) to better characterize liver abnormalities. During the arterial phase of gadolinium-enhanced MRI, FLC appears as a very heterogeneous enhancement, but by the portal venous phase, the enhancement has disappeared, leaving an isointense or hypointense lesion.

CASE REPORT

Patient is a woman who is 19 years old and has no significant past medical history of any significant pathology. It begins three weeks before the patient is admitted with a sudden, strong pain in the right hypochondrium of the punching type, transfictive, and it is made worse when the patient is in the decubitus supinolateral position on the right. It is then evaluated at the second level of care, where paraclinical studies are conducted, with the following findings emerging from those studies: BT 0.2, BD 0.2, BI 0; TGP 20; TGO 35; DHL 841; values are still within normal ranges. Contrasted abdominal TAC was ordered, and it was discovered that the patient had a hypotensive lesion in the right lobe of the liver measuring 215 mm by 143 mm, with highlighting zones in the peripheral, conditioned ipsilateral kidney displacement, and no obvious vascular compromise. The patient is thought to have a huge hemangioma, thus they are transferred to the third level for selective hepatic angioembolization to be conducted. The right hepatectomy was scheduled to take place. During the operation, a massive liver

tumor measuring 20 by 14 centimeters was discovered. The tumor had affected segments V, VI, VII, and VIII, and it had adhesions to the right kidney, the right renal vein, and the lower vena cava. There was no sign of metastasis observed at all. after performing a right hepatechotomy and an ipsilateral nephrectomy, transoperative colangiography can be carried out without the presence of bile leakage. Histopathology reveals a moderately differentiated hepatocarcinoma that measures at least 20 centimeters and passes into the hepatic capsule. The surgical margins are clear.

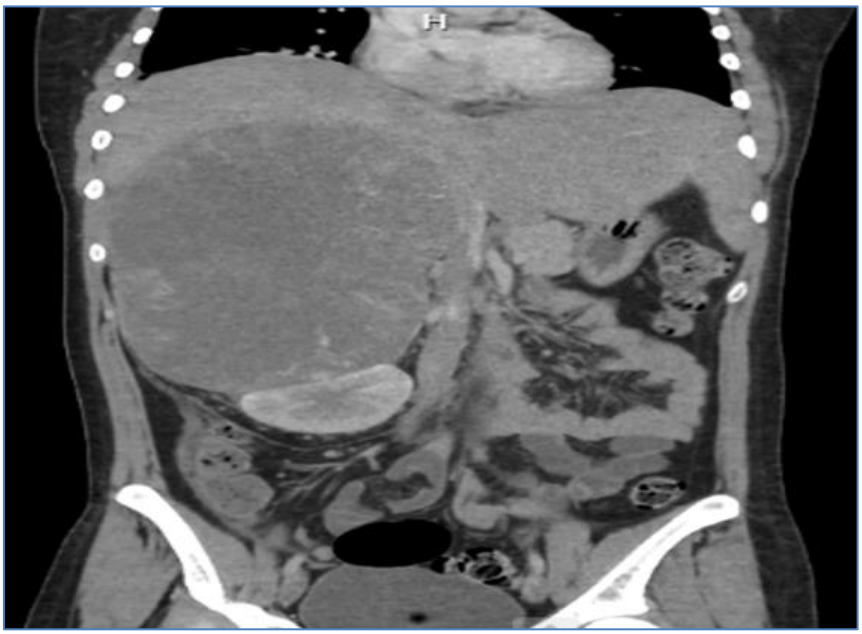
Surgical Treatment

A significant proportion of patients diagnosed with FLC often exhibit substantial tumor sizes, frequently exceeding 10 centimeters in diameter. However, it is important to note that complete surgical resection is achievable only due to the patient's young age and absence of cirrhosis, with success rates reaching up to 73% in adult patients and 84% in pediatric patients. Attaining negative resection margins is of utmost importance, hence necessitating a hemi-hepatectomy for the majority of patients. In certain specific instances, palliative surgical tumor reduction may be employed as a therapeutic intervention to mitigate symptoms such as hyperammonemic encephalopathy. However, it is important to note that this approach is not considered a conventional practice. The utilization of liver transplantation as a therapeutic approach for fibrolamellar carcinoma (FLC) is limited due to various organizational factors, including the requirement for specialized medical facilities and the insufficient availability of suitable donor grafts in some geographical areas. Additionally, the presence of nodal infiltration further contributes to the infrequent use of this treatment modality. When feasible, transplantation has demonstrated similar overall survival (OS) rates compared to surgical resection treatment, or at the very least, significantly improved OS rates compared to systemic therapy alone. The occurrence of recurrent disease is commonly documented in a significant proportion of patients following curative resection, regardless of the margins of resection. Various studies have reported recurrence rates ranging from 50% to 80%, while smaller monocentric analyses have even reported rates as high as 100%. A younger age, absence of vascular invasion, and absence of extrahepatic disease have been found to be correlated with extended periods of recurrence-free life. Although intraabdominal lymph nodes and the liver are the most frequently observed sites of recurrence, systemic illness associated with fibrolamellar carcinoma (FLC) can also manifest in the lungs and bones. In few instances, peritoneal carcinomatosis or recurrence in the duodenum has been reported.

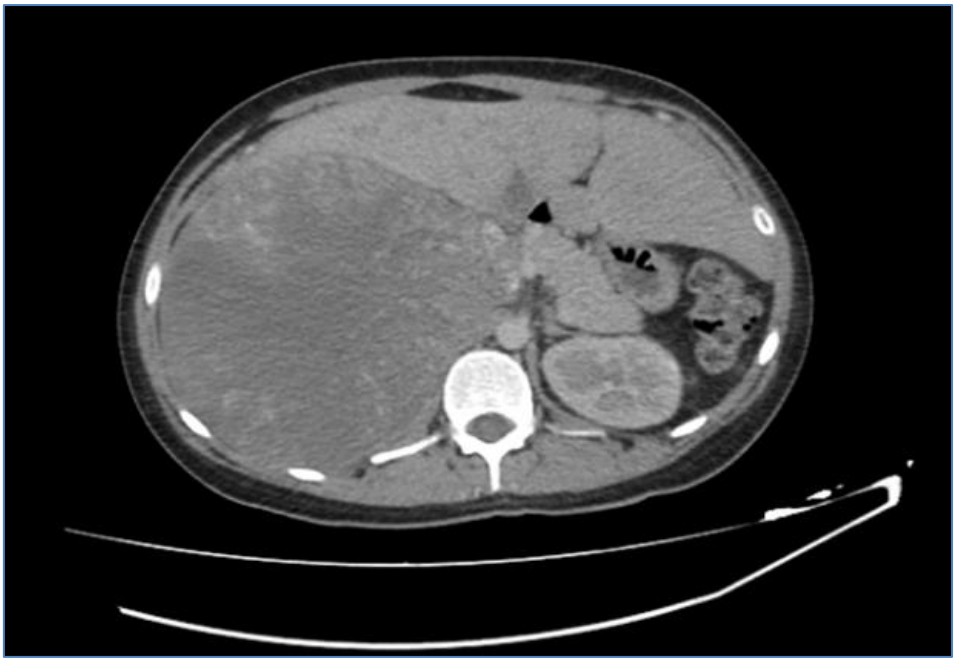
NON - SURGICAL TREATMENT

Surgery is still the gold standard treatment for FLC, as no effective systemic treatments exist at this time. The 5-year predicted overall survival rate for patients who had no surgical therapy was zero. Possibly due to confounding factors and rather advanced cancer, combined chemotherapy and surgery resulted in poorer overall survival than surgery alone. Only sporadic reports of interventional radiological procedures being used have been documented, therefore their safety and efficacy have not been determined.

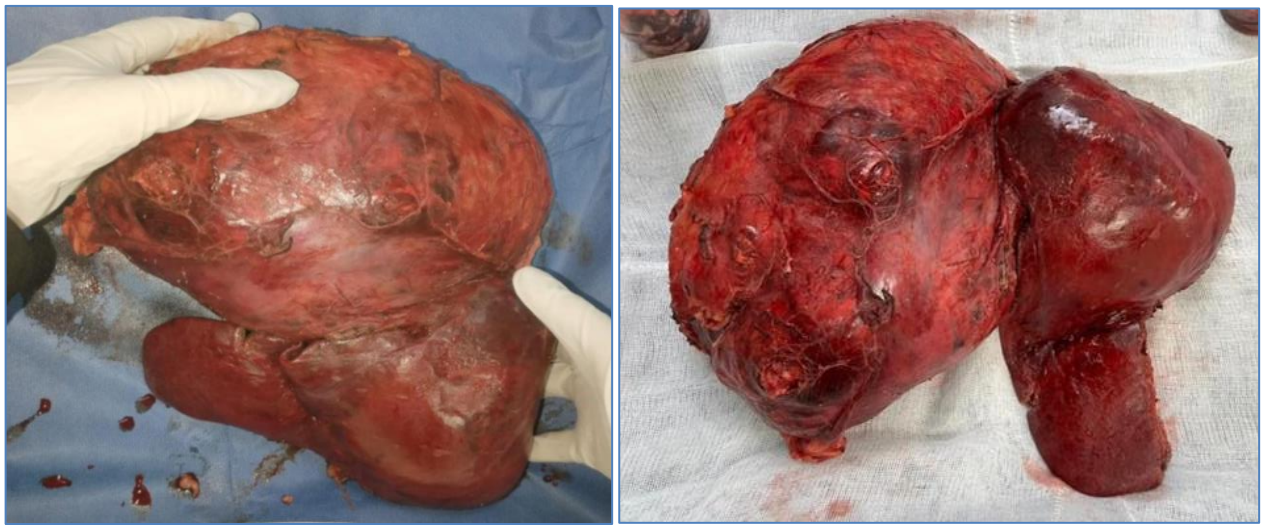
FIGURES



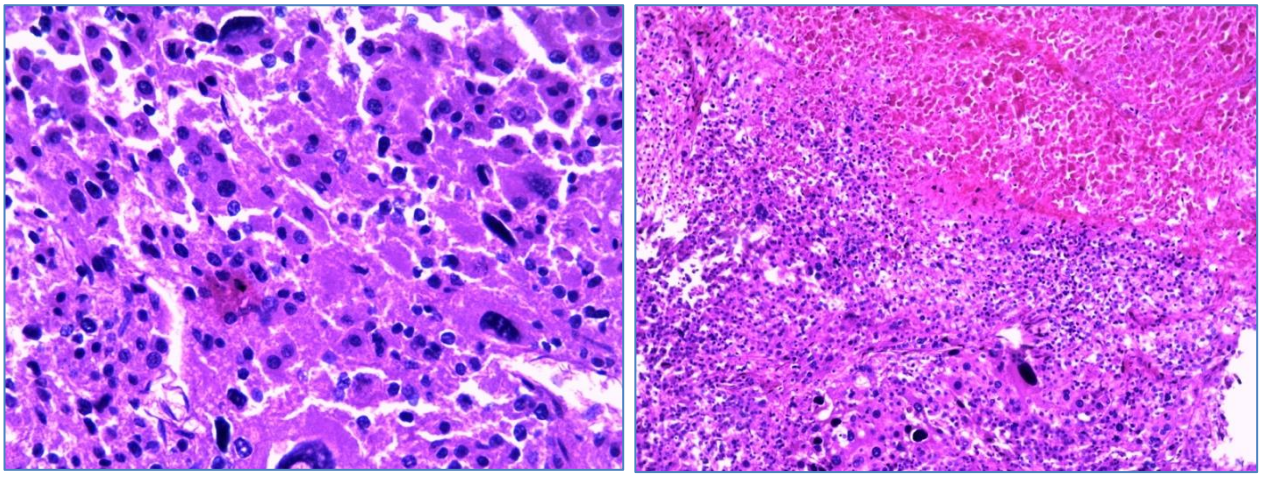
1. Non- Contrast CT- Scan Coronal View



2. Non- Contrast CT- Scan Axial view, Well- defined Liver Mass



3. Hemihepatectomy surgical piece



4. Tumoral lamellar collagen bands observed with abundant eosinophilic cytoplasm

DISCUSSION

Fibrolamellar hepatocellular carcinoma is an uncommon form of cancer, with an estimated incidence of 0.02 cases per 100,000 people in the United States when adjusted for age. FLC is one of the more common primary liver cancers in teenagers and young adults who do not have any underlying cirrhosis or hepatitis. This is despite the fact that FLC is quite uncommon. Since Edmondson's initial description of fibrolamellar hepatocellular carcinoma in 1956, very little progress has been made in either the understanding of the disease's biology foundations or its clinical manifestations. There have been no particular serum indicators discovered up until this point. In individuals with FLC, a raised AFP is found in less than 5% of cases, and there have been reports of people with an elevated vitamin B12 binding capacity. This is in contrast to the typical hepatocellular carcinomas. CD68 and cytokeratin are the immunohistochemical markers of tumor cells that are observed most frequently. Despite the fact that FLC has distinct histologic and clinical characteristics, hepatocellular carcinomas are frequently mistaken as FLC. This leads to misunderstandings regarding survival and recurrence rates. There is no unique FLC classification because of the disparities in categorization and its rarity. Instead, tumors are categorized according to the American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC) classifications for hepatocellular carcinoma.

CONCLUSION

Fibrolamellar carcinoma is a rare, highly malignant liver lesion, usually, there is no cirrhosis in the surrounding liver parenchyma, although mononuclear cells and lymphocytes imply nonspecific inflammation, FLC patients often complain of nonspecific abdominal pain, nausea, abdominal fullness, malaise, and weight loss, Alpha-fetoprotein levels are predominately normal, unlike in traditional. Most cases with FLC cases are advanced at the time of diagnosis; however, up to 70% of patients may still be treated with curative therapy. The current cornerstone therapy (resection/liver transplantation) is still the sole possibly curative approach.

CONFLICTS OF INTERESTS

The researchers have disclosed no conflicts of interest.

REFERENCES

- Abdelhamed, W., & El-Kassas, M. (2022). Fibrolamellar hepatocellular carcinoma: a rare but unpleasant event. *World Journal of Gastrointestinal Oncology*, *14*(6), 1103. https://doi.org/10.4251/wjgo.v14.i6.1103
- Kakar, S., Burgart, L. J., Batts, K. P., Garcia, J., Jain, D., & Ferrell, L. D. (2005). Clinicopathologic features and survival in fibrolamellar carcinoma: comparison with conventional hepatocellular carcinoma with and without cirrhosis. *Modern pathology*, *18*(11), 1417-1423. https://doi.org/10.1038/modpathol.3800449
- Katzenstein, H. M., Krailo, M. D., Malogolowkin, M. H., Ortega, J. A., Qu, W., Douglass, E. C., ... & Bowman, L. C. (2003). Fibrolamellar hepatocellular carcinoma in children and adolescents. *Cancer: Interdisciplinary International Journal of the American Cancer Society*, *97*(8), 2006-2012. https://doi.org/10.1002/cncr.11292
- Lafaro, K. J., & Pawlik, T. M. (2015). Fibrolamellar hepatocellular carcinoma: current clinical perspectives. *Journal of hepatocellular carcinoma*, 151-157. https://doi.org/10.2147/jhc.s75153
- Mayo, S. C., Mavros, M. N., Nathan, H., Cosgrove, D., Herman, J. M., Kamel, I., ... & Pawlik, T. M. (2014). Treatment and prognosis of patients with fibrolamellar hepatocellular carcinoma: a national perspective. *Journal of the American College of Surgeons*, *218*(2), 196-205. https://doi.org/10.1016/j.jamcollsurg.2013.10.011
- Polychronidis, G., Murtha-Lemekhova, A., Fuchs, J., Karathanasi, E., & Hoffmann, K. (2022). A multidisciplinary approach to the management of fibrolamellar carcinoma: current perspectives and future prospects. *OncoTargets and Therapy*, 1095-1103. https://doi.org/10.2147/ott.s296127
- Ward, S. C., Huang, J., Tickoo, S. K., Thung, S. N., Ladanyi, M., & Klimstra, D. S. (2010). Fibrolamellar carcinoma of the liver exhibits immunohistochemical evidence of both hepatocyte and bile duct differentiation. *Modern Pathology*, *23*(9), 1180-1190. https://doi.org/10.1038/modpathol.2010.105
- Zack, T., Losert, K. P., Maisel, S. M., Wild, J., Yaqubie, A., Herman, M., ... & Gordan, J. D. (2023). Defining incidence and complications of fibrolamellar liver cancer through tiered computational analysis of clinical data. *NPJ Precision Oncology*, *7*(1), 29. https://doi.org/10.1038/s41698-023-00371-2