CASE REPORT

Follicular dendritic cell sarcoma of the porta hepatis

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SUMMARY

Follicular dendritic cell (FDC) sarcoma is a very rare neoplasm which commonly involves the lymph nodes and less commonly involves extranodal organs such as the liver. Most cases of FDC sarcoma are idiopathic, however some cases are associated with other disease states. Management of FDC sarcoma is primarily focused on surgical resection of the mass, and secondarily focused on radiotherapy, chemotherapy and/or biologic pharmacotherapy. We report the case of a patient who was found to have FDC sarcoma presenting as an obstructing mass of the porta hepatis, a manifestation which does not appear to be reported in the literature.

BACKGROUND

B-cell zones within lymph nodes can exist as primary or secondary follicles.¹ The former is an inactive state composed primarily of naïve B-cells that await exposure to antigen.¹ The latter is an active state composed of germinal centres, with B-cell blasts undergoing affinity maturation of antibody in an effort to target the source of an unknown antigen.¹ Follicular dendritic cells (FDCs) reside within germinal centres and function to present immune complexes to B-cells, produce cytokines and chemokines, and produce factors that attract B-cells.¹ FDC sarcoma is an extremely rare neoplasm of FDCs,¹ with two-thirds of cases affecting the lymph nodes and one-third of cases involving extranodal sites such as the gastrointestinal tract, soft tissue, tonsils or skin.² Of the extranodal manifestations of FDC sarcoma, abdominopelvic involvement is the most common, followed by neck and thoracic involvement, and the rarest of this group involves the breast and skin.³ Here, we present a case of FDC sarcoma involving the hilum of the liver.

CASE PRESENTATION

A 50-year-old Hispanic man presented with worsening lower abdominal pain that began a few days prior to his presentation, and which was associated with a lack of appetite. Initial laboratory values were significant for a leucocyte count of 3.32 x10⁹ cells/L, aspartate aminotransferase of 176 U/L, alanine aminotransferase of 212 U/L, alkaline phosphatase of 115 U/L and bilirubin of 1.8 mg/dL. Values for alpha-fetoprotein, cancer antigen 19-9 and carcinoembryonic antigen were within normal limits. MRI demonstrated a 4.5x5.7 cm peripherally enhancing and centrally necrotic mass of the porta hepatis (figure 1) which exerted a compressive effect on the common bile duct. Based on CT and MRI imaging, the origin of the mass

was unable to be determined, however it did not appear to be hepatopancreaticobiliary in origin. No other intra-abdominal organs showed suspicion for malignancy, making an extrahepatic primary tumour unlikely. Within 3 days of presentation, total bilirubin rose to 7.0 mg/dL. The patient underwent endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy and biliary stent placement for relief of biliary obstruction. The patient also underwent endoscopic ultrasound (EUS) with biopsies which demonstrated neoplastic cells closely associated with vasculature, concerning for an epithelioid and spindle cell-based malignancy. There was also initial suspicion for the mass being a nerve-based or pseudopapillary tumour, and low suspicion for lymphoma which is amenable to non-operative management. Although a definitive diagnosis was not available preoperatively, given the patient's desire for quick intervention, the obstructive nature of the mass and concern for malignancy, our team decided to proceed with laparoscopic resection of the mass. On initial surgical inspection, there was marked enlargement of the mesocolon of the hepatic flexure and transverse colon, later identified as a large retroperitoneal bleed. He was also noted to have free intra-abdominal bile. Adherent omentum overlying the area of the tumour was removed, revealing significant retroperitoneal/intratumoral haemorrhage that necessitated immediate conversion to an open approach. Further inspection of the area of haemorrhage demonstrated a large, anterior opening in the tumour with erosion into the gastroduodenal artery which was located at the base of the tumour. After adequate haemostasis, the tumour was dissected off of the hepatic artery, hepatic portal vein and common bile duct. The ancillary finding of a zone II and mesentery non-expanding, retroperitoneal haematoma with free intra-abdominal bile suggests biliary injury at the time of the patient's prior ERCP and EUS with biopsies. The patient underwent a Roux-en-Y hepaticojejunostomy to the level of the bifurcation in order to remove the entirety of the tumour and bypass the biliary system. The patient's immediate postoperative course was uncomplicated. Final histopathological findings, which included second opinions from the National Institutes of Health and MD Anderson Cancer Center, demonstrated invasion into soft tissue and adipose tissue without concern for dedifferentiated liposarcoma, atypical spindle cells with focal areas of necrosis, focal haemorrhage, cellular organisation which took the form of fascicles and whorling in some areas, and the form of sheets and nodules in other areas. Nuclei were ovoid, some of which

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Figure 1 Abdominal MRI with transverse and coronal images demonstrating a peripherally enhancing and centrally necrotic mass (A) present in close association with structures of the porta hepatis.

were binucleated or multinucleated. There were >5 mitoses per 10 high power fields. A scattering of lymphocytes and neutrophils constituted the background which demonstrated acute-on-chronic inflammation. There was no lymphatic tissue suggestive of a lymph node origin of the mass, and positive immunostaining was demonstrated for CD21 and CD23 (figure 2). The histopathological findings were diagnostic of extranodal FDC sarcoma. The patient required a protracted hospitalisation due to prolonged ileus and partial bowel obstruction secondary to the large retroperitoneal and mesentery bleed which slowly improved. The patient was discharged on postoperative day 15.

INVESTIGATIONS

See the Case presentation section.

DIFFERENTIAL DIAGNOSIS

See the Case presentation section.

TREATMENT

See the Case presentation section.

OUTCOME AND FOLLOW-UP

The patient underwent genomic testing which demonstrated six gene alterations, none of which are amenable to any Food and Drug Administration-approved treatments. Chemotherapy regimen including gemcitabine and docetaxel was first initiated 14 weeks after surgery, and the patient continued to receive subsequent cycles. The use of radiotherapy was deferred. The patient was admitted and treated for cholangitis secondary to

malignant stricture of the common bile duct approximately 14 weeks after his initial discharge. Prior to this admission, he underwent biliary stent exchange after findings were consistent with a malignant stricture of the upper third of the common bile duct, and treatment of bacteraemia. During the most recent admission, he was found to have progression of FDC sarcoma involving the area around the biliary stent, additionally manifesting as peripancreatic adenopathy and liver metastases (figure 3). The treatment plan for recurrence included continued cycles of chemotherapy as haematologically tolerable, further imaging to determine the progression and spread of tumour, with possible role of pancreaticoduodenectomy should there be adequate response to chemotherapy and control of metastatic disease. On positron emission tomography CT scan performed approximately 5 weeks after, the patient was found to have mild regression of the main mass surrounding the biliary stent, with total regression of a liver metastasis, suggesting response to chemotherapy regimen. There was no evidence of disseminated malignancy.

DISCUSSION

This case of extranodal, intra-abdominal FDC sarcoma most likely arose from the biliary system, however primary hepatic and pancreatic aetiologies cannot be excluded, thus making the true origin of this mass still unknown. Most cases of FDC sarcoma are of unknown aetiology, however associations exist with Castleman's disease, myasthenia gravis and paraneoplastic pemphigus.² FDC sarcoma is a rare primary sarcoma of the liver which, in total, constitutes less than 0.1% of primary liver

Figure 2 Histopathological images of the porta hepatis mass. H&E staining (A) with diffusely positive CD 21 (B) and CD 23 (C) immunohistochemical staining, confirms the diagnosis of follicular dendritic cell sarcoma.

Figure 3 Abdominal CT performed 4 months after surgery demonstrating recurrence of the mass (A) around the biliary stent, associated hepatic metastasis (B) and metastatic peripancreatic lymphadenopathy (C).

tumours.⁴ Presenting symptoms of an intra-abdominal FDC sarcoma are non-specific and may include abdominal pain, malaise and weight loss.⁵ A subtype of FDC sarcoma called the inflammatory pseudotumour (IPT)-like subtype occurs almost exclusively in the liver and spleen⁶ and has unique histological findings including cellular growth into fascicles and sheets, vesicular nuclei, a background containing lymphocytes and plasma cells, and Reed-Sternberg-like nuclear atypia.² The IPT-like FDC sarcoma is strongly associated with Epstein-Barr virus (EBV) positivity, female gender preference^{2,4} and significant inflammatory cell infiltration.⁴ A likely culprit for the strong association of EBV with FDC sarcoma is LMP-1, an EBV onco-gene capable of exerting cellular changes, with variants found more often in persons of Asian race.⁶ An in situ hybridisation assay for EBV-encoded small RNAs should be considered in the diagnosis of IPT-like FDC sarcoma.⁷ Although the histological features present in this case raise suspicion for IPT-like FDC sarcoma, EBV in situ hybridisation was not performed, and the diagnosis of this subtype cannot be confirmed. The differential diagnosis for FDC sarcoma is wide, including, but not limited to, meningioma, thymoma, gastrointestinal stromal tumour and melanoma.⁸ Therefore, immunohistochemical markers such as CD21, CD23 and/or CD35 are crucial for narrowing the differential and arriving at a diagnosis.² Additionally, stains such as clusterin and podoplanin are highly specific for FDC sarcoma.² FDC sarcomas have a 40%–50% risk of local recurrence, and over a 20% risk of metastasis if the primary tumour originates in the abdomen.² Local recurrence and metastasis may be rare in IPT-like FDC sarcoma.⁹ Poor prognostic indicators for FDC sarcoma include abdominal location of tumour, size exceeding 6 cm, tumour necrosis, numerous mitoses (>5 per 10 high power fields) and cellular atypia.² The patient likely developed local recurrence and metastases given the presence of many of these poor prognostic factors, as well as the high risk of recurrence and metastasis that comes with a diagnosis of FDC sarcoma. There is no clear consensus on the management of FDC sarcoma but surgical resection of the tumour is preferred, with a questionable role of radiotherapy and chemotherapy.² Unfortunately, there is a scarcity of information regarding long-term outcomes of hepatic FDC sarcoma. Recent management recommendations include surgical resection followed by consolidative radiotherapy and frequent follow-up in patients found to have localised and resectable disease.¹⁰ For patients with non-localised and/or non-resectable disease, it is recommended that they undergo cytoreductive chemotherapy with a combination of gemcitabine and a taxane, followed by surgery with or without

radiotherapy if remnant disease after chemotherapy is found to be localised and resectable.⁸ Targeted monoclonal antibodies against tumours that express BRAF or EGFR can also be used.²

Learning points

- Follicular dendritic cell (FDC) sarcoma is a rare neoplasm of immune cell origin, comprising <0.1% of primary liver tumours.
- Diagnosis of FDC sarcoma is strongly dependent on immunohistochemical testing, especially CD21, CD23 and/or CD35.
- Treatment of FDC sarcoma is multimodal, with possible role for surgery, chemotherapy, radiotherapy and biologic pharmacotherapy.

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