Metastatic yolk sac tumor masquerading as multi-focal hepatocellular carcinoma in a young adult; a case report

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Abstract

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Written Informed Consent was taken from the father after the death of the patient in accordance with the journal's policy..

Abstract:

Primary yolk sac tumor of the liver is very rare and can present as multifocal liver lesions. Multifocal nature may mimic other diagnoses such as hepatocellular carcinoma. Early recognition and therapeutic intervention are important as the prognosis of metastatic yolk sac tumors is poor. We present a case of a young adolescent who presented with bleeding per rectum abdominal pain and multiple liver lesions.

Key Words: Yolk sac tumor, Germ cell tumor, Multifocal Hepatocellular carcinoma, Metastasis, liver lesion

Key Clinical Message: Multiple liver lesions in a young adults has a broad differential diagnosis. However, in patients with raised AFP and multiple liver lesions Yolk sac tumor should be suspected. The diagnosis should be confirmed by histology, as Yolk sac tumors can mimic a multifocal Hepatocellular carcinoma radiologically.

Introduction:

Extragonadal germ cell tumors occur much more commonly in males than in females and are usually seen in young adults(1). These are aggressive neoplasms and can arise virtually anywhere, but typically the site of origin is in the midline (mediastinum, retroperitoneum, or pineal gland). The diagnosis should be considered in any patient with a poorly defined epithelial malignancy, particularly young individuals. They are also associated with a high tumor burden on the diagnosis. (2,3) Yolk sac tumors of the liver are extremely rare and may not be considered until the biopsy is performed. In young patients with multiple liver lesions, one of the differential diagnoses to consider is the yolk sac tumor. We present one patient with multiple liver lesions which mimicked multifocal liver lesions.

Case presentation:

A 19-year-old boy with no chronic medical illness presented with abdominal pain, weight loss, and bleeding per rectum for the last two months. His abdominal pain was vague, colicky in nature, and associated with reduced appetite and food aversion.He also developed altered bowel habits mainly diarrhea and occasionally blood mixed in stools. No extraintestinal symptoms were reported. No family history of inflammatory bowel disease or any malignancy was present. No history of any prior surgery. He smoked cigarettes occasionally for less than 1 month. The clinical exam was remarkable for mild right upper quadrant tenderness. No palpable lymph nodes. The digital rectal exam was negative for fresh blood or melena. The scrotal exam was normal. Initial labs revealed mild anemia and slightly elevated transaminases (Table 1).

US abdomen revealed an enlarged liver measuring 19.7 cm in length. Multiple heterogeneous hyperechoic lesions were noted in the liver, the largest measuring 9.9 x 9.7 in the right lobe and 10 x 8.3 in the left lobe. The main portal vein measured 15 mm in diameter. There was a filling defect in the intrahepatic main portal vein extending into the main right and left branches, suggestive of thrombosis. A few periportal lymph nodes were noted, the largest measuring 17 x 14 mm. Mild ascites.

Based on the initial ultrasound malignancy was suspected and an MRI of the abdomen was performed which showed nlarged liver with multiple focal lesions 11 cm in maximal dimension, involving all segments with the largest two at the left lobe and the subdiaphragmatic part of the right lobe. Tumor thrombus

of the left and right portal branches as well as some of the segmental branches. The lesions had more radiological features of multi-centric primary malignant liver neoplasm particularly hepatocellular carcinoma than metastases. Dilated intrahepatic bile ducts particularly at the left lobe were seen. Enlarged lymph nodes at the retrocaval, porta hepatis, upper paraaortic, and mesenteric regions 23 mm in maximal short axis, impressive of metastatic lymph nodes (Figures 1a-1b). Alpha-fetoprotein (AFP) was requested and came very high (Table 1).

The patient was discussed in the tumor board although the radiologic impression was multifocal hepatocellular carcinoma plan was to biopsy the lesion and perform a colonoscopy and pan CT scan to rule out other primary lesions. Colonoscopy was performed as well to rule out primary colonic malignancy given a history of bleeding per rectum.

Contrast enhanced CT scan revealed multiple large necrotic liver masses in all segments, showing heterogenous enhancement, largest at segment VII, measuring 13.0 x 9.6 cm. large filling defect was seen at the distal part of the portal vein, likely representing tumor thrombus. A heterogenous soft tissue mass seen at the sigmoid mesentery infiltrating the sigmoid colon wall. Multiple enhancing peritoneal nodules were seen at the abdomen and pelvis, largest in the pelvic region measuring 3.8 x 2.8 cm suggesting peritoneal metastasis. Multiple enlarged lymph nodes at mesenteric, retrocaval, and paraaortic regions. Other structures were unremarkable. Moderate free fluid is seen in the abdomen and pelvis. No lung or bony lesions were seen. (See Figure 2).

Colonoscopic examination revealed a circumferential ulcerative and infiltrative mass lesion of around 6-7 cm, extending from 19-26 cm from the anal verge (Figure 3). The rest of the colonic mucosa appeared normal, and biopsies were taken, suspicion of the primary colonic tumor was raised. Gastroscopy was also performed to rule out the GI origin of the tumor and was normal. An ultrasound-guided liver biopsy was performed from one of the larger liver lesions.

The liver biopsy consisted of multiple fragments of tumor tissue, composed of predominantly clear cells arranged in reticular, solid, and focal hepatoid and microcystic growth patterns. In places, the tumor cells exhibited marked nuclear pleomorphism with a high nuclear-cytoplasmic ratio. Mitotic figures were easily identifiable. Frequent hyaline globules were noted, and foci of necrosis were also seen(Figure 4-5).

A wide panel of immunostains was performed, which revealed that the tumor was positive for Cytokeratin AE1/AE3, Glypican 3, CDX2 (strong patchy positivity), and SALL4(Figure 6-7). The hyaline globules stained weakly for AFP, but the tumor cells were AFP negative. Immunostains for arginase, Hep par 1, CD30, Oct3/4, and S100 were negative.

The tumor morphology, along with a combination of positive staining for cytokeratin, Glypican 3, SALL4, CDX2, and high serum AFP levels were highly suggestive of a yolk sac tumor. In addition, in this biopsy, no other germ cell tumor morphology was noted. The appearances in the separately sent sigmoid colon biopsy showed similar tumor morphology and were likely representing metastasis of the sigmoid colon.

After the diagnosis was confirmed and revealed to the family discussion was made regarding starting chemotherapy. Given the high tumor burden, there was a high risk of tumor lysis syndrome as well as the dose was adjusted for liver and renal parameters. The patient was started on Bleomycin, Etoposide 50 % dose reduction, Cisplatin 25 % dose reduction, and dexamethasone 5 mg IV. For tumor lysis syndrome Rasburicase IV pre-treatment, with allopurinol was started. After the first cycle patient became severely ill with respiratory distress and was admitted to ICU requiring non-invasive ventilation. After his condition stabilized, he received a second cycle of chemotherapy on day 5 of the first cycle. After the second cycle, his clinical condition deteriorated with episodes of vomiting resulting in aspiration pneumonia, and the patient was intubated and started on mechanical ventilation. The patient was neutropenic and was started on broad-spectrum antibiotics including Meropenem IV, and Vancomycin IV. On day 6 of the first cycle, the patient had a cardiac arrest and could not be revived.

Discussion:

Yolk sac tumors are germ cell tumors that most commonly arise from the gonads(4). Extragonadal germ cell tumors are rare and primary yolk sac tumors of the liver are extremely rare with only few case reports being described(5). Primary yolk sac tumors of the liver arise in young adults and the prognosis is variable with several case reports showing successful treatment with chemotherapy.

These tumors can pose a significant diagnostic challenge as multiple liver lesions in young adults have a broad differential diagnosis. Multifocal liver lesions in young adults and children can be of benign or malignant origin. Common benign causes include focal nodular hyperplasia, liver abscesses, and hepatic adenomas. While causes of malignant multifocal liver lesions in adults include Infantile hepatoblastoma, lymphoma, hepatocellular carcinoma, hepatic epithelioid hemangioendotheliomas, and metastases (6, 7). MRI abdomen with a histologic diagnosis is key to establishing a definite diagnosis. In our case, there was a high probability of primary liver tumor with a second likely differential of liver metastases from colon until the biopsy results revealed the histology of yolk sac tumor from liver lesion as well as from sigmoid colon. Correct diagnosis is essential for early recognition and early initiation of appropriate therapy.

Histologically, yolk sac tumors display marked heterogeneity, with numerous architectural patterns described. A combination of patterns is common, in varying proportions. The various histological patterns include microcystic/reticular, macrocystic, papillary, solid, sarcomatoid, glandular, hepatoid, myxomatous, perivascular, and polyvesicular vitelline patterns. Schillar-Duval bodies are another characteristic finding but are not required for diagnosis. Hyaline globules are usually noted in the hepatoid pattern, which are usually AFP positive.

Primary hepatic yolk sac tumors are rare and to date, several case reports have been reported(8–14). There are no specific radiologic diagnostic features of yolk sac tumors and hence their ability to masquerade other liver lesions(10). Several treatment modalities have been reported. The treatment depends on whether the tumor is resectable or not, the presence of metastasis, and the initial response to chemotherapy. Successful treatment with surgical resection has also been achieved (5). Treatment by embolization for liver yolk sac tumor has been reported. (14) While Liver transplant as a treatment option has also been reported successfully (11,12). Despite these options, the mainstay treatment modality in the extragonadal yolk sac tumors is chemotherapy as these tumors are highly sensitive to chemotherapy. The main chemotherapy is Bleomycin etoposide and cisplatin-based. Other regimens have also been used.

Yolk sac histology and the presence of metastasis are predictors of poor survival in germ cell tumors(3). Other established predictors of poor prognosis include mediastinal primary origin, non-pulmonary metastases and elevated markers (AFP $>$ 10,000 ng/ml, LDH $>$ 10x upper limit of normal, beta-HCG $>$ 50,000 IU/l(15). Our patient was classified as a poor prognosis group due to the presence of poor prognostic markers including Yolk sac histology and colonic metastasis.

Conclusion:

Yolk Sac tumors are rare germ cell tumors that are extragonadal and rarely present in the Liver. The yolk sac tumor of the liver can mimic other liver lesions such as hepatocellular carcinoma and metastatic lesions. Imaging and tumor markers are helpful but the ultimate diagnosis of yolk sac tumor is made by histology. Metastatic yolk sac tumor of the liver has a poor prognosis. Physicians evaluating multiple liver lesions with elevated AFP, especially in young adults should consider germ cell tumors such as yolk sac tumors as a differential diagnosis.

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Authorship Contribution:

KM, MUK and DS were involved in writing the case, reviewing the literature and clinical care of the patient. SMK and MP reviewed the histopathologic specimens and relevant literature. KA reviewed the literature and was involved in final review of the manuscript. All authors reviewed the final manuscript.

Conflict of interest:

All authors declare no relevant financial conflict of interest.

Ethical Approval:

The case report was approved by the Medical research center(MRC) of Hamad Medical Corporation (MRC-04-21-904), Doha, Qatar.

Informed Consent:

Written Informed Consent was taken from the father after the death of the patient.

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