Mesenchymal hamartoma mimicking hepatoblastoma: A cytological pitfall

ABSTRACT
The case of a 9-month-old infant who presented with an abdominal mass since birth is discussed here. Fine-needle aspiration (FNA) cytology of this mass was performed, from which it was thought to be a small round tumor, possibly a hepatoblastoma (HB). Histopathologically, however, it was found to be a mesenchymal hamartoma (MH). This case report thus highlights this cytological limitation.

Key words: Cytology; hepatoblastoma (HB); mesenchymal hamartoma (MH)

Introduction
Mesenchymal hamartomas (MH) are the second most common benign tumors of the liver in the pediatric age group and represent about 6% of all the primary hepatic tumors.[1] It occurs most commonly in the first 2 years of life.[2] A hepatoblastoma (HB) is the most common primary hepatic tumor in children, with 68% of cases manifesting in the first 2 years of life.[3] On fine-needle aspiration (FNA) cytology, MH can be confused with HB. This case report highlights this cytological limitation.

Case Report
A 9-month-old male infant presented to the pediatric outpatient department with complaints of progressively increasing abdominal distension since birth along with vomiting since 2 months. Contrast-enhanced computed tomography (CECT) abdomen revealed a large complex solid cystic lesion approximately 300 (craniocaudal) × 148 (anteroposterior) × 103 (transverse) mm³ abutting the undersurface of the right lobe of the liver. It was extending till the pubic symphysis inferiorly, crossing the midline and displacing intestinal loops laterally to the left. No calcification or hemorrhage was noted. The possibilities of MH, HB, and undifferentiated embryonal sarcoma (UES) were considered radiologically.

The serum alpha-fetoprotein (AFP) levels were elevated, being 334.22 ng/mL (normal: Less than 10 ng/mL). The ultrasound-guided FNA performed from the mass yielded 10 mL blood-mixed fluid and showed the presence of few loosely cohesive clusters of small round cells showing overlapping and vague acinar arrangement focally [Figure 1]. These cells had high nuclear/cytoplasmic ratios, indistinct cell boundaries, scant cytoplasm, and inconspicuous 0-1 nucleoli [Figure 2]. However, no spindle cells (mesenchymal component), extramedullary hematopoiesis, necrosis, giant cells, hyaline globules,
myxoid connective tissue, or mitosis was seen, thus ruling out the possibilities of MH and UES.

Based on the clinicoradiological findings, cytological findings, and raised serum AFP levels, a possibility of small round cell tumor, possibly HB, was given.

The patient was started on chemotherapy, but he did not respond. Thus after approximately 1 month, the liver mass was resected and sent for the histopathological evaluation. It was received in an already cut-open state, and was unencapsulated, gray-brown in color, measuring 14 cm × 12 cm × 8 cm in size. The cut surface was cystic-solid with a large cyst in the center measuring 7 cm in diameter, filled up with hemorrhagic fluid. The solid area surrounding it showed alternate dark brown (congested) and light areas, along with multiple cysts embedded in it varying in size from 0.2 cm to 0.5 cm and filled up with mucoid or hemorrhagic fluid. The microscopic sections showed unencapsulated tumor comprising multiple bile ducts, hepatocytic cords, and variably sized cysts embedded in a loose myxoid stroma with scattered infiltrate of lymphocytes and plasma cells [Figure 3]. Bile duct proliferation in the form of numerous bile ducts was seen, with many showing branching and distorted contours. The mesenchymal component comprising bland stellate cells was seen proliferating around bile ducts. The hepatocytes, arranged in cords and small nests, were seen at the periphery of mesenchymal lobules. The sinusoids between the hepatocytes were showing vascular congestion. The cysts were lined with flattened to cuboidal epithelium [Figure 3 inset]. The foci of extramedullary hematopoiesis were identified at places. Multiple sections taken did not show any features of HB. A final diagnosis of MH, liver was thus made.

After the histopathological diagnosis of MH, the cytological slides were reviewed again. However, no features supporting MH, such as spindle cells (mesenchymal component), extramedullary hematopoiesis, myxoid connective tissue, or bile duct cells were found.

Discussion

Our case showed few loosely cohesive clusters of small round cells showing overlapping and vague acinar arrangement focally on cytology. These cells had high nuclear/cytoplasmic ratio, indistinct cell boundaries, scant cytoplasm, and inconspicuous 0-1 nucleoli. Various possibilities were thought based on these cytological features and radioclinical findings. These were HB, UES and MH.

A HB is composed of epithelial and mesenchymal elements in varying stages of differentiation. The epithelial elements recapitulate the stages of hepatocyte development from primitive blastema through embryonal hepatocytes to fetal hepatocytes.[4] The distinctive cytologic features of FNA of HB include clusters of tumor cells showing acinar and trabecular patterns, smaller tumor cells with a high nuclear/cytoplasmic ratio and hyperchromatic nuclei having prominent nucleoli, and the presence of extramedullary hematopoiesis.[5]

Another important differential diagnosis, UES shows combination of polygonal and spindle cells with few intracytoplasmic and extracytoplasmic eosinophilic globules. The polygonal cells are large, with round or lobulated nuclei, and occasionally multinucleated, with one or several nucleoli and variable cytoplasm with poorly defined borders.[6] These features were absent in the present case, thus ruling out UES.
MH is a hamartomatous growth of mesenchymal tissue in the liver of uncertain etiology. It varies greatly in size, from a few centimeters to up to 30 cm. Seventy-five percent occur in the right side, with few occurring in the left and rarely involving both the lobes. It may bulge from the liver surface or can be pedunculated. Its pathogenesis is not clear. It has been postulated that the lesion arises from the mesenchyme of the portal vein and thus represents a duct plate malformation. An association with mesenchymal stem villous hyperplasia of placenta has been shown. MH is considered under the HB family of tumors, with features of mesenchymal–epithelial transition [under Revised Classification of Pediatric Liver Cell Tumors (Working Formulation)].

On cytology, MH is characterized by the presence of clusters of predominantly bland-looking bile duct or cuboidal epithelial cells presumably arising from the lining of cystic and distorted ducts. These epithelial cells are usually seen in conjunction with single or groups of spindle stromal cells. Loose fragments of myxoid connective tissue can also be seen in some cases. These findings were missing in our case.

Because our case showed only the round cell component with high nuclear/cytoplasmic ratio with the absence of any other element on fine-needle aspirate, along with high serum AFP levels, the embryonal or small-cell undifferentiated types of HB were considered as possibilities. However, of the different types of HB, mixed epithelial/mesenchymal HB is the most similar to MH, comprised of relatively bland-appearing hepatocytes (of fetal type) with spindle/stellate mesenchyme. However, the mesenchymal component was absolutely missing in the present case.

On pathological examination, hepatocytes in a MH can be seen at the periphery as plates or in the central part of the tumor as small clusters or single cells, smaller than normal, with vacuolated cytoplasm and pyknotic nuclei. When hepatocytes are abundant, the MH can mimic a malignant or benign hepatocellular tumor, either cytologically or histologically. Unal et al. and Boman et al. reported similar cases of MH in the past, which were misdiagnosed as HB on FNA smears. In the present case, the hepatocytes were found to be arranged as cords and small clusters at the periphery of the mesenchymal lobules on histopathological examination. Thus, there is a possibility of selective sampling of this component on FNA, which could have been the possible source of the round cell component on cytology slides. The selective sampling of this peripheral hepatocellular component along with raised serum AFP levels and clinicoradiological findings led to a misdiagnosis of HB in the present case. Unal et al. concluded that MH of the liver with increased serum AFP levels can mimic HB if the cytological examination samples only the peripheral hepatocellular component of MH, thereby emphasizing the importance of knowing this in order to avoid any misdiagnosis. Table 1 summarizes the comparison of cytological features between HB, MH, and UES.

### Table 1: Comparison of cytological features between HB, MH, and UES

| Variable/characteristic | HB | MH | UES |
|-------------------------|----|----|-----|
| Age                     | 90%: Less than 5 yrs | 85%: Less than 3 yrs | More than 50%: 6-10 yrs |
| M:F ratio               | 1.5-2: 1 | 2:3-1 | No gender predominance |
| Clinical presentation   | Abdominal distension | Abdominal distension | Abdominal distension and pain |
| Serum AFP               | 90% cases elevated | Normal but can be elevated in some cases | Not elevated |
| Cytological features    | Epithelial dominant smears showing epithelial cells forming cohesive crowded clusters, cords, ribbons and rosettes | Bland looking bile duct or cuboidal epithelial cells | Hypercellular smears |
|                         | Mesenchymal (spindle cell) component and/or heterologous elements especially extramedullary hematopoiesis and osteoid relatively scant | Loose myxoid mesenchymal stroma with benign appearing spindle cells | Large pleomorphic anaplastic cells with multinucleate giant cells and atypical spindle cells |
|                         | PAS positive, diastase resistant intracytoplasmic and extracytoplasmic globules | Necrosis | Necrosis |

HB- hepatoblastoma, MH- mesenchymal hamartoma, UES- undifferentiated embryonal sarcoma
Conclusion

We would like to conclude that MH should be considered in the differential diagnosis of hepatic cystic masses on cytology even if serum AFP level is elevated. It is important to note that MH is a benign tumor, while HB is a malignant tumor requiring chemotherapy. Thus, a definite diagnosis is essential, requiring histopathology to avoid the unnecessary risk of chemotherapy to the patient. This case highlights the limitation of FNA in diagnosing cystic lesions such as MH.

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Conflicts of interest
There are no conflicts of interest.

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