Nestor stromal-epithelial tumor (NSET) was first described by Ishak et al.\(^1\) in 2001, as a very rare mesenchymal liver tumor originating from non-hepatocyte cells in the liver. NSET has been defined as a non-hepatocytic and non-biliary tumor of the liver with epithelial and spindled cells with associated myofibroblastic stroma and variable intralobular calcification and ossification. It is often seen in young women and can be represented as large masses. This article is aimed to present the clinical and imaging findings of a 77-year-old male patient with a massive NSET including coarse calcification, with literature comparison. 

**Keywords:** Computed tomography, liver, nested stromal-epithelial tumor, non-hepatocyte, tumor

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**Case Report**

A 77-year-old man was admitted to our hospital with the complaint of abdominal pain and swelling for about 1 month. On the physical examination, a mass extending to the inguinal region was detected on the right side by palpation. There were no splenomegaly, ascites, or Cushingoid symptoms. Laboratory tests revealed leukocytosis and abnormal liver function tests. A heterogeneous mass with degenerative and cystic areas starting from the liver level extending to the pelvic region was seen in the US of the abdomen. Macroscopically, the tumor is mostly observed in the right lobe of the liver. Histopathologically, NSET is observed as well-defined multinodular mass lesions. The tumor is made up of groups of cells that vary in size and shape, ranging from large to small, round to spindle. Calcification can be observed as psammoma or ossification. Microscopically, ductal proliferation can be observed at tumor boundaries.
Computed tomography (CT) for characterization of the mass revealed a large mass lesion with coarse calcifications, central necrosis, and peripheral contrast enhancement, extending from the left lobe of the liver to the inferior pelvis (Fig. 1). A needle biopsy was performed to specify the tumor. The pathology report of the liver biopsy specimen was histologically evaluated as NSET (Fig. 2). The patient was finally referred to surgery for the removal of the mass.

Discussion

Although our case is an older male patient with a complaint of abdominal pain, this tumor is generally found incidentally in younger women. NSETs are more frequently located in the right lobe of the liver and are unencapsulated, well-circumscribed tumors range in size from 2.8 cm to 30 cm in greatest dimension, just like our case.

Despite limited information about clinical progress of this rare low malign tumor, there are publications in the literature which claim that the tumor may be aggressive and may have systematic spread and cause endocrinopathies such as Cushing’s syndrome. There were no evidence of endocrinopathy in our case. Radiologically, they appear as large masses with coarse calcifications in the solid central part of the lobulated contour just like our case. Calcification is a very important finding for the diagnosis and may progress to ossification over time.

Post-contrast examination reveals a slow and progressive enhancement pattern. Macroscopically, the tumor is mostly found in the right lobe of the liver. Procopia presented a case which revealed a well-circumscribed liver lesion involving the left hemiliver. The lesion appeared solid and heterogeneous with a rim-like enhancement at contrast phase with multiple intralesional calcifications and an extensive vascular invasion was evident on CT. On
magnetic resonance imaging (MRI), the tumor showed hypointensity on T1-weighted images and hyperintensity on both T2- and diffusion-weighted images, with small central necrotic collections. An inhomogeneous pattern with subcentimetric calcifications showing mostly hypointensity on both T1- and T2-weighted images was depicted. On gadolinium-enhanced images, the lesion showed a heterogeneous enhancement pattern on the arterial phase and washout in the portal and parenchymal phases. The hepatocyte-specific delayed phase showed a hypointense lesion on T1-weighted images, with well-defined margins and a hyperintense capsule.[8] We did not perform MRI on our patient because CT images were characteristic and the definite diagnosis was achieved by liver biopsy. Histopathologically, NSET is observed as well-defined multinodular mass lesions.[2, 5] Tumor cells include nested spindle cells and epithelioid cells. The nests are surrounded by dense fibrous tissue and myofibroblasts. Some bile ducts may surround the nests. Tumor cells are bounded clearly with round or oval nuclei. The cytoplasm is eosinophilic or pale. The epithelioid cells have marked membrane. No dysplastic bile duct plates can be found in the tumor.[9] Calcification can be observed in the form of a psammoma or ossification. Microscopically, ductal proliferation can be observed at the tumor boundary.[2, 5] Hepatoblastoma, Wilms tumor, desmoplastic small round cell tumor (DSRCT), and synovial sarcoma must be investigated in the differential diagnosis. Fibrolamellar hepatocellular carcinoma (HCC) is another pathology that should be considered in the differential diagnosis of ab-

Conclusion

In this article, it is aimed to the present clinical, histological, and radiologic features of NSET, a rare solid malignity of the liver and to raise awareness about this entity. This tumor should be considered in the differential diagnosis of abdominal masses that reach large sizes with heterogeneous internal structure, central scar, and coarse calcifications, especially in young ladies. However, it should be kept in mind that it may be seen in older patients. Our case is the oldest one we have met in literature.

Disclosures

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.


References


4. Systemic chemotherapy, often the same regimen of hepatoblastoma, is appropriate for unresectable tumors and recurrences. However, response to chemotherapy is controversial. Meletani reported an NSET case of a 31-year-old Caucasian man who underwent surgery for a 22 cm×13 cm×25 cm large, lobulated, multinodular mass of the right lobe of liver. After 6 months from surgery, a liver recurrence emerged and a chemoembolization was performed. After a further disease progression, a similar chemotherapy regimen of hepatoblastoma (with cisplatin and ifosfamide/mesna) was administered. However, no benefit was noted and a progression of disease was radiologically assessed after only four cycles. The worsening of the clinical status prevented further treatments, and the patient died a few months later.[7]

On the other hand, Procopio claimed that liver resection allowed the safe attainment of complete tumor clearance, even in advanced disease.[8] He did not recommend liver transplantation at least as a first choice, considering the low tendency of NSETs to relapse and previous unsuccessful experiences. Liver transplantation would be potentially useful for those patients with unresectable but not extrahepatic disease.[12]

NSETs, especially with large size and vascular invasion, tend to have more recurrences or metastasis due to that short-term radiological follow-up is recommended to detect liver recurrence and extrahepatic metastases.[8]

5. Immunohistochemically, the tumor cells are stained positive for cytokeratin AE1/AE3, keratin CK19 (focal), EMA, CD117 (c-kit), CD56, CD99, ACTH, chromogranin, synaptophysin, neuron-specific enolase, and S100 (focally weak in epithelioid cells). Vimentin stain is positive in the nested spindled cell and stroma. Muscle-specific actin and smooth muscle actin immunostains highlight stromal myofibroblastic cells. Alpha-fetoprotein and p53 are negative.[11]

The major therapeutic approach of NSET has been surgery. However, response to chemotherapy is controversial. Meletani reported an NSET case of a 31-year-old Caucasian man who underwent surgery for a 22 cm×13 cm×25 cm large, lobulated, multinodular mass of the right lobe of liver. After 6 months from surgery, a liver recurrence emerged and a chemoembolization was performed. After a further disease progression, a similar chemotherapy regimen of hepatoblastoma (with cisplatin and ifosfamide/mesna) was administered. However, no benefit was noted and a progression of disease was radiologically assessed after only four cycles. The worsening of the clinical status prevented further treatments, and the patient died a few months later.[7]

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