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CORRESPONDENCE

Malignant Peripheral Nerve Sheath Tumor of the Liver: A Case Report

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Abstract A large, rapidly growing malignant peripheral nerve sheath tumor (MPNST) of the liver in a young female patient, not associated with von Recklinghausen's disease, is presented. Diagnosis was based on detailed immunohistochemical and electromicroscopic examination beside the characteristic H&E picture. As far as we know, this is the first reported, unambiguously proven "de novo" MPNST in the liver. Differential diagnostic problems are discussed and a review of the literature is given.

Keywords Malignant peripheral nerve sheath tumor · Liver · S100 · Laminin

Introduction

MPNST can be defined as a malignant tumor arising from or differentiating toward cells intrinsic to peripheral nerve sheath. MPNST often occur in association with neurofibromatosis type 1 (NF1), or arise de novo in normal peripheral nerves. Visceral or organ MPNSTs are rare, often associated with multiple neurofibromas, from which they arise by malignant transformation. Regarding organ localization most reported examples either antedate immunohistochemistry or lack support of this method or ultrastructural evidence [1–3]. Though benign schwannomas may occur very rarely in liver or malignant transformation of schwannoma of liver has been reported, this is the first report of "de novo" MPNST of liver, diagnosis based on detailed immunohistochemical and electromicroscopic examination.

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Case

A 22-year-old woman, without any previous major disease, developed right upper quadrant pain and extreme edema. After, a relatively short investigation period primary liver tumor was detected in the right liver lobe and segment IV (Fig. 1) with rapid growth. The CT scan volumetry presented intact segment I–III with a calculated 540 ml normal liver-mass. Surgery was planned after the calculation of the liver/body mass ratio more than 1%, due to the compensatory hypertrophy of left lateral segments. The preoperative biopsy presented an atypical malignant tumor.

Anatomical, extended right hemihepatectomy was done after standard technique. After the total devascularization of the right liver lobe the resection was performed with CUSA (Valleylab), without vascular exclusion. No other tumor was detected by the preoperative examinations or during the surgery. No sign of café au lait spots or skin nodules were noted. The postoperative period was uneventful, only a pleural puncture was done, due to a consecutive pleural fluid on the right side. The patient was discharged 24 days

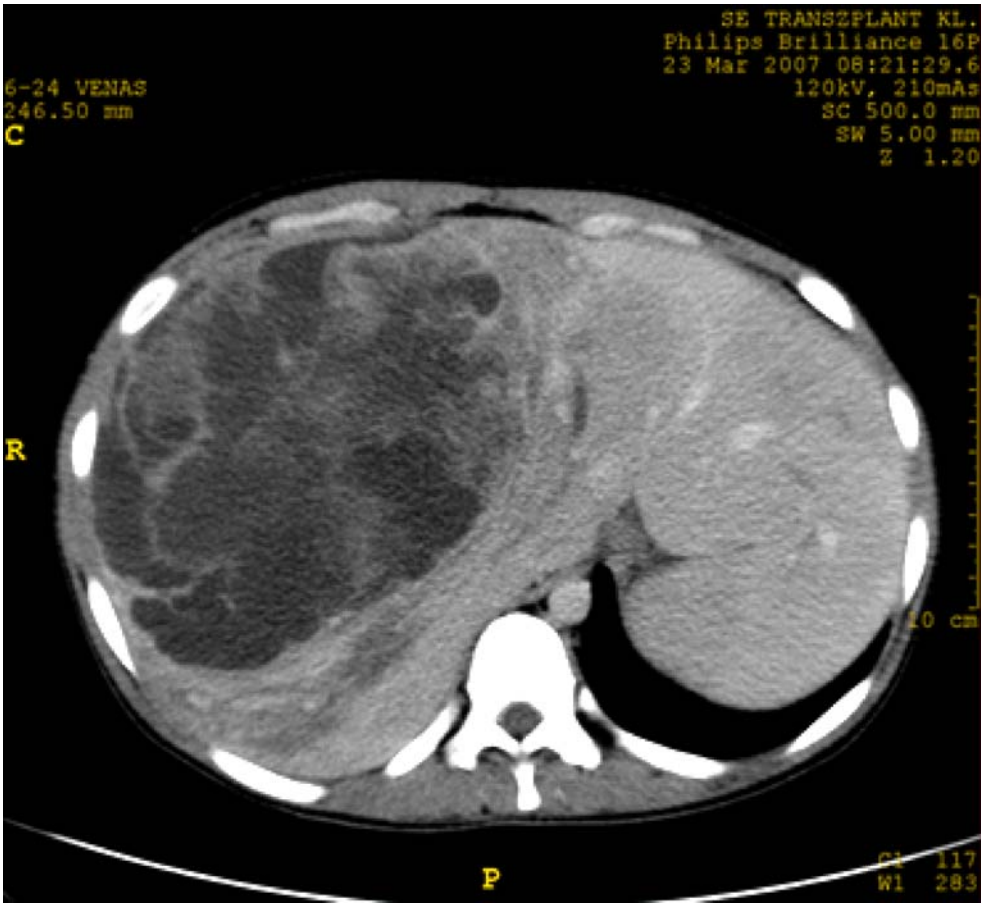

Fig. 1 Post contrast axial CT scan shows large inhomogeneous liver mass, and an enlarged and dislocated left liver lobe

after surgery without complications and with normal liver and kidney functions. She was offered for further oncological follow up after the histological findings.

Pathologic Findings

The largest diameter of the removed tumor was 26 cm. It contained several fluid filled cystic spaces. The solid areas had firm consistency, mostly grayish color with occasional yellow necrotic islands. The tumor was not encapsulated but relatively well separated from the surrounding non-cirrhotic liver tissue.

Histologically the lobular structure of the liver was retained. The structure of the tumor showed some degree of variation. The dominant component consisted of spindle cells sometimes arranged in fascicles. The cells were relatively monotonous but they showed signs of atypia (Fig. 2a). The nuclei were occasionally wavy, vesicular and contained large prominent nucleoli. The cytoplasm (usually slightly epithelioid in character) staining was pale and the cell borders were indistinct. Scattered giant cells could be observed in the tumor. The number of mitoses was 13–14 on 10 HPFs on the denser areas with atypical dividing figures. Densely cellular areas were alternating with fields occupied mostly by the tumor stroma, which was dense hyalinized but looser myxoid areas also were present. No areas resembling of benign schwannoma was observed in spite of extensive sampling. No pigment was noticed, the PAS reaction also did not decorate any part of the tumor. The tumor was mainly demarcated from the liver but occasionally invasive growth could be observed in the border zone.

The tumor cells were diffusely, strongly positive for vimentin (1:500 Dako, Carpinteria, USA) and S100 (1:1,000 Dako) (Fig. 2b) by immunohistochemistry. One of the major components of basement membrane, laminin (1:300 Dako) could be detected mostly in the tumor stroma but by double labeling (laminin and S100) it overlapped occasionally with S100 positive tumor cells (Fig. 2c). The following immunohistochemical reactions were completely negative in the tumor: panCK (1:50 Dako), CD 34 (1:20 Dako), CD 117 (1:20 Novocastra, Newcastle, UK), melan A (1:10 Dako), HMB 45 (1:50 Dako), SMA (1:150 Dako), desmin (1:100 Dako), H-caldesmon (1:100 Dako), CD1a (1:50 Dako) and CD68 (1:1,000 Dako).

Long, branching cytoplasmic processes could be observed by electron microscopy occasionally with desmosoma-like junctional complexes between them. Amorphous

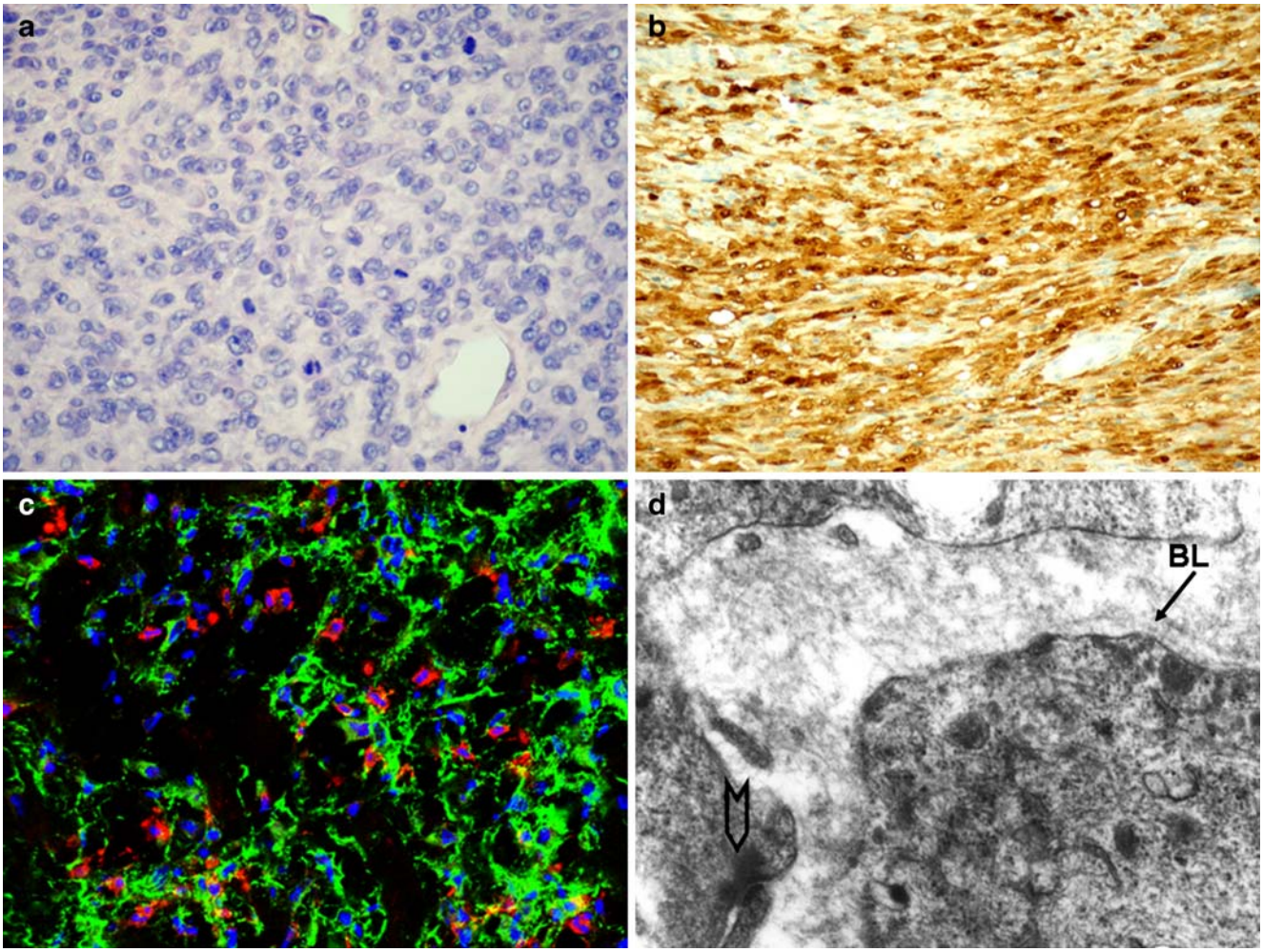

Fig. 2 **a** Relatively monotonous tumor cells with signs of atypia and a lot of mitotic forms (H&E, ×200). **b** Strong diffuse cytoplasmic S100 positivity of tumor cells (immunoperoxidase staining ×100). **c** Diffuse intense laminin (*green*) and more sporadic S100 (*red*) positivity in tumor cells. Note: in some cells there is overlapping positivity of laminin and S100 (*yellow*). (double labeled fluorescence staining of laminin and S100, ×200). **d** Amorphous basement-membrane like material (*arrow*) and desmosome-like junctional complexes (*arrowhead*) were constant findings on ultrastructural level

basement-membrane like material was present in the interstitium (Fig. 2d). No melanosomes or Birbeck granules were observed.

Discussion

MPNSTs are fairly rare tumors, they comprise about five percent of all malignant soft tissue tumors, and have a varied origin [4]. Most are derived from neurofibromas or develop de novo but very rarely they arise in schwannoma. Because MPNSTs often closely resemble nonneural soft tissue tumors, morphologic features alone may not permit the right diagnosis. Widely accepted criteria for a diagnosis of MPNST are: A, arises within a peripheral nerve; B, arises in transition from a benign or other malignant peripheral nerve tumor; C, develops in a patient of NF1 and has the same histologic features as do a MPNST arising from nerve; D, develops without NF1, but exhibits features of MPNSTs and shows unambiguous immunohistochemical and/or ultrastructural features of Schwann or perineural cell differentiation. Clearly, in cases of MPNSTs in the liver criteria's of B to D are acceptable. In our case we have observed a large, rapidly growing liver tumor in a young female patient not having von Recklinghausen's disease. The morphology and the immunophenotype of the tumor clearly excluded the hepatocytic or biliary origin. The strong vimentin and S-100 positivity might correspond, to malignant melanoma, but the lack of the immunohistochemical melanoma markers (melan A, HMB 45), melanosomes ultrastructurally and primary tumor contradicted to this possibility. Undifferentiated (embryonal) sarcoma is the most common malignant mesenchymal liver tumor in children and it occurs also in young adults [5]. The clinical presentation, vimentin expression and the dominant spindle cell component would be consistent with this diagnosis.

However, this tumor is reported to be S100 negative [6, 7] and diastase resistant globules, which are characteristic for the embryonal sarcoma were missing from the presently examined tumor. There are two more options: both dendritic reticular cell sarcoma and MPNST are vimentin, S100 positive and constituted mostly by spindle cells. The ultrastructure of the tumor: lack of Bierbeck granules, the presence of long cytoplasmic processes, junctional complexes and basement membrane material support the nerve sheath origin of the tumor. The negativity with CD1a and CD68 reaction also argues against the dendritic cell origin. The size, rapid growth rate of the tumor, the histological atypia and high mitotic rate proves the malignant nature of the tumor, so thus the described tumor is a malignant peripheral nerve sheath tumor (MPNST). Theoretically this tumor could be a metastasis but this is highly unlikely because no other tumor was revealed with the extensive preoperative examinations.

Five cases of malignant schwannoma have been reported in the liver [1–3, 8, 9] two of them in association with von Recklinghausen's disease, [2, 3], however the schwannian differentiation were not proved (lack of immunohistochemistry and ultrastructural features) [1, 8] or in cases associated with NF1, the malignant component raised from a benign neurofibroma component. The only case reported by Morikawa and al. [9] was analyzed with a fairly large panel of immunohistochemistry but the diagnosis of malignant schwannoma was "based" on "scattered S100 protein positivity of tumor cells", there was no ultrastructural examination and the patient had no sign of neurofibromatosis. Other nerve sheath tumors without von Recklinghausen's disease were benign [10–12]. The only well documented cases of primary hepatic MPNSTs were schwannomas that underwent malignant transformation [13, 14]. Thus, as far as we know, this is the first reported, unambiguously proven "de novo" MPNST in the liver.

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