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Case Report

The Clinical Investigator

Undifferentiated (embryonal) sarcoma of the liver in an adult patient with metastasis of the heart and brain

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Abstract. A 26-year-old woman with a tumor of the left liver lobe was admitted to the hospital. After incomplete resection of the tumor and histological diagnosis of an undifferentiated (embryonal) sarcoma of the liver a combination chemotherapy with ifosfamide and epidoxorubicine was started. 11 months later brain metastases were diagnosed. Routine ultrasound examination of the heart disclosed a pericardial tumor infiltrating the left atrium of the heart. After radiation therapy of the brain metastases the patient was treated with two cycles of high-dose ifosfamide and epidoxorubicin. Two years after diagnosis the patient developed signs of cardiac failure and died. Postmortem autopsy confirmed the local recurrence of the liver neoplasm and revealed its continuous spread to the pericardium via the diaphragm and infiltration of the left atrium.

Key words: Undifferentiated sarcoma – Embryonal sarcoma – Heart – Brain

The incidence of soft-tissue sarcomas has been reported to be 1 in 100 000 adults per year. Overall, 0.7 of all malignancies in adults are sarcomas. Up to the age of 15 years 6.5% of all malignancies have been found to be sarcomas. Of 813 primary malignant liver tumors collected by Edmondson and Peters 1.6% were sarcomas [2]. The hepatic angiosarcoma, which is often related to exposure to thorium dioxide, vinyl chloride, or arsenic, is the most common sarcoma of the liver. Fibrosarcomas, leiomyosarcomas, and malignant fibrous histiocytomas generally involve the liver after metastazation. Only very few soft-tissue tumors of these types are documented which are primarily tumors of the liver. The mesenchymal sarcoma, or undifferentiated (embryonal) sarcoma of the liver (UESL) is a rare primary malignant liver tumor composed of primitive spindle cells without further specific differentiation. Stocker et al. [17] described the first series of 31 cases from the Armed Forces Institute of Pathology in 1978. Up to now 122 cases of UESL have been documented [11], the majority (63%) of them in children (6–10 years). Only nine cases have thus far been described in adults ($\geq$ 18 years) [9, 14]. Two cases of UESL with cardiac involvement have been reported, in both of which the tumor invaded the vena cava inferior and grew directly into the right atrium [9]. To our knowledge, we present the first autopsy-confirmed case of an UESL in an adult patient with continuous spread through the diaphragm into the pericardium and left atrium and consecutive hematogenous metastasis into the brain.

Abbreviations: UESL = undifferentiated (embryonal) sarcoma of the liver; IFX = ifosfamide; Epi-DOX = epidoxorubicine

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Case report

A 26-year-old white woman was admitted with a tumor in the left liver lobe. On lobectomy the tumor (18 × 10 × 11 cm) was found to adhere to the diaphragm and the posterior wall of the stomach. Histological investigation revealed an undifferentiated mesenchymal tumor with large necrosis. The tumor was composed of fascicles with spindle cells and scattered pleomorphic giant cells with many mitotic figures. The tumor in part showed a storiform pattern resembling a malignant fibrous histiocytoma (Fig. 1, left). Immunohistochemically the tumor cells expressed only vimentin and did not react with antibodies against S-100 protein or desmin and α-smooth-muscle actin; thus malignant schwannoma and leiomyosarcoma were excluded. The tumor contained trapped preexisting bile ducts. Some tumor cells had periodic acid-Schiff positive, diastase-resistant droplets within the cyto-

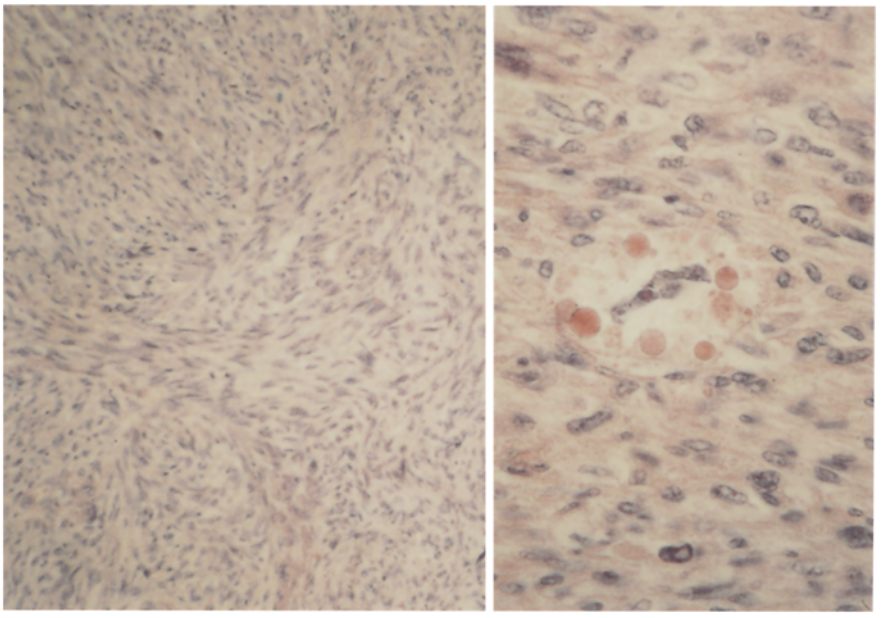


Fig. 1. *Left*, sarcomatous tumor tissue composed of interweaving bundles of spindle cells in a storiform pattern, H&E, × 80). *Right*, degenerated tumor cell with hydropic cytoplasm containing eosinophilic droplets, H&E, × 200

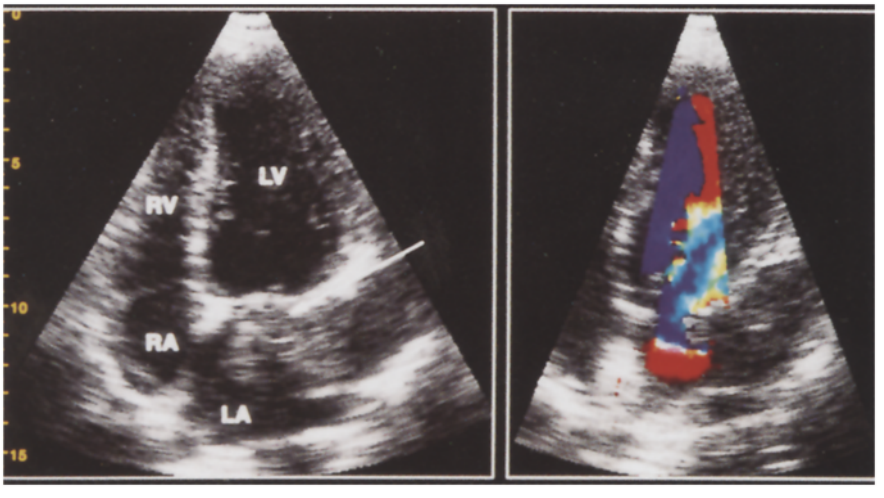
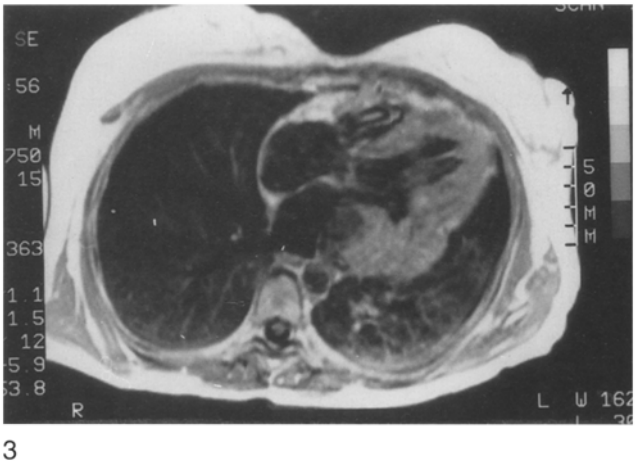


Fig. 2. *Left*, apical four-chamber view visualizing a large dorsolateral tumor protruding from the area of the dorsolateral wall into the left atrium. *Right*, moderate inflow obstruction demonstrated by the narrow high-velocity color flow image



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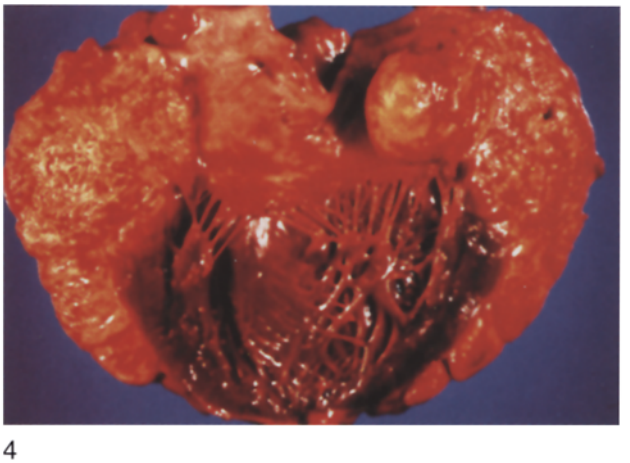

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plasm (Fig. 1, right). The morphological pattern in combination with the immunohistological findings led to the diagnosis of UESL.

Following surgery the patient received adjuvant chemotherapy of 520 mg epidoxorubicin (Epi-DOX) and 40 g ifosfamide (IFX) [6]. Eleven months after discharge the patient complained of left-sided paresthesia combined with nausea. Cerebral computed tomography showed two brain metastases in the right parietal lobe of the cerebrum. In addition, a middiastolic murmur at the left ventricular apex was heard on cardiac auscultation. Results of the electocardiogram and chest X-ray were normal. On color Doppler ultrasound (Fig. 2) and magnetic resonance imaging (Fig. 3) a heterogeneous tumor mass impended into the left atrium of the heart and partially obstructed the mitral valve. After radiotherapy of the brain metastases (40 Gy) two cycles of systemic chemotherapy (2.5 g/m^2 IFX on days 1–5, 150 mg/m^2 Epi-DOX as bolus on day 28) were administered. On follow-up the heart tumor was found to be progressive. Two years after diagnosis of the UESL the patient developed signs of cardiac failure and died. Autopsy findings confirmed recurrence of the UESL in the liver, involvement of the diaphragm, with continuous extension to the pericardium, infiltration of the left atrium (Fig. 4), and hematogenous metastasis to the brain.

Discussion

In this adult patient, with surgically and chemotherapeutically treated UESL involving the brain, a tumor impending into the left atrium of the heart was diagnosed by color Doppler ultrasound. Since hematogenous metastasis of the UESL to the endocardium or myocardium of the left atrium without concurrent lung metastases is very unlikely [3, 4, 7], the possibility of a primary undifferentiated sarcoma of the heart [1] was discussed. However, the incidence of primary cardiac tumors in postmortem studies is very low [13, 18], and only 25% of these tumors are believed to be primary sarcomas of the heart [15]. These considerations favored the local recurrence of the UESL with pericardial infiltration via the diaphragm with secondary involvement of the myo- and endocardium. The brain tumors diagnosed on cerebral computed tomography were explained as hematogenous metastases originating from the cardiac tumor. This proposed way of tumor spread was confirmed by postmortem autopsy. In addition to these diagnostic considerations the therapeutic aproach to patients with metastatic UESL played a part in our clinical decision making. There are no general recommendations for the treatment of metastatic UESL. Complete surgical removal of the primary tumor is correlated with prolonged survival [16]. Following complete surgical resection various combinations of adjuvant multiagent chemotherapy containing vincristine, cyclophosphamide, dactinomycin, doxorubicin have been instituted [8]. Some authors recommend additional radiotherapy [14]. In the case of cardiac metastasis cardiosurgery is not the treatment of choice. The radiotherapy of primary or metastatic cardiac tumors entails the risk of cardiac rupture [10, 11]. Data on the efficiency of chemotherapy in metastatic UESL are lacking. Despite these uncertainties, after treatment of brain metastases by radiotherapy, the patient was treated empirically with high-dose IFX and Epi-DOX [5]. The course of the cardiac tumor remained progressive. Whether systemic chemotherapy is of any benefit in metastatic UESL remains to be confirmed.

Fig. 3. T1-weighted magnetic resonance image with contrast (gadolinium). Within the left atrium a tumor is shown, impending into the atrium from the dorsolateral wall. Positive contrast enhancement of the tumor is shown. A lateral thrombus attached to the tumor could be discerned after injection of contrast material (gadolinium)

Fig. 4. Transsectional view of the left chamber of the heart. Tumorous pericardial spread and infiltration of the myocardium are shown. The tumor protrudes into the left atrium, forming a polypoid mass

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Book Review

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J.E.F. Reynolds (ed): Martindale: the extra Pharmacopolice. The Pharmaceutical Press, London, 1993. Approx. 2500 Pages. Hardcover, £160.00 (ISBN 0-85329-300-5)

In April 1993 the 30th edition of the *Martindale* was published. This reliable manual contains three parts:

1. 5132 monographs on drugs and *ancillary substances.*
2. Supplementary drugs and other substances, i.e., non-medicinal compounds (832), which can be of interest in therapy, such as glacial acetic acid that can be used for the removal of warts. Indications, however, are not given in this part of the book. Provided there is a commercially available product on the market that contains the substance, one can find the therapeutic indication in the third part.
3. The preparations, including the indications, are listed. This part contains 46000 preparations.

The *Martindale* is edited by the staff of the Royal Pharmaceutical Society of Great Britain and hence basically covers the interests of pharmacists and physicians in the UK. Since in Europe the medical sectors are also merging, it is worthwhile mentioning that foreign drugs are also listed, especially those from the US. This appears to me to be because of the traditional special relationship between Great Britain and the US.

Furthermore, the *Martindale* contains a Directory of Manufacturers and, last but not least, a broad index (450 pages!), which covers not only the commercial names of the products but also the INNs of the substances and, most importantly, their commonly used synonyms. Those who are engaged daily with drugs and therapy will be interested in the *Martindale,* which is a source one can safely rely on.

Prof. Dr. W. Forth (München)