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TITLE	**Primary Choriocarcinoma of the lung**
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KEYWORDS	Choriocarcinoma, lung, brain metastases
DIAGNOSIS	Choriocarcinoma of the lung
SUMMARY	A fatal case with a primary choriocarcinoma of the lung is presented. The 43 year old women developed pain of the left chest wall for two months. Chest radiographs displayed a small peripherally localized tumor in the left upper lobe measuring 1 cm * 2 cm involving the adjacent pleura. She has been a smoker with about 20 pack years. The histology revealed an undifferentiated carcinoma; the immunohistology tumor cells with strong staining against ß-HCG and (weakly) against alpha-fetoprotein. The diagnosis of a primary choriocarcinoma of the lung was stated. The patient died after twenty-one months due to generalized tumor spread including brain metastases.
CASE REPORT	A 43 year old women with non-suspicious history suffered from increasing pain of the left shoulder and chest wall. She was married and delivered a healthy son at the age of 26 years without complications. A history of 20 pack years was noted. No congenital abnormalities or severe diseases of the childhood were documented. After two months a chest X ray was taken, and a small peripherally localized tumor in the left upper lobe measuring 1 cm * 2 cm in diameters was diagnosed. A pre-operative CT displays a large tumor measuring 6cm in diameter (Fig. 1). An en-block resection of the left upper lobe including the chest wall and adjacent ribs (C2 – C4) was performed. A surgery, the resected tumor mass measured already 6 cm * 5 cm * 6 cm. The detailed exploration of the surgical specimen revealed only inflammatory infiltrates of the pleura and the chest wall. The post-surgical tumor stage pT2 N0 G3 R0 was stated. Serum levels for ßHCG and alpha fetoprotein were in the normal range. The post-surgical course was without complications; however, already one month later the patient developed loss of sensation in both hands, and a paresis of the left n. facialis. Brain CT was suspicious for brain metastases, and a radiation (40 Gy) of the brain was added.

	Examination of the female reproductive organs was without any abnormal findings. Two months later metastases in the colon and in both kidneys were diagnosed, and the right colon was resected. A chemotherapy (cisplatin, vinblastin, bleomycin) was performed, to which the metastases in the kidneys responded (partial remission). The patient died 21 months after diagnosis due to multiple organ failure. An autopsy was not performed. Quantitative asbestos fiber analysis measured 6 ferruginous bodies/g wet tissue (normal range).
PATHOLOGY	The surgical specimen measured 18 cm * 13 cm * 6 cm and weighted 465 g. The 6 cm * 5 cm * 6 cm sized tumor was localized in the lung periphery and adjacent to the pleura (Fig 2). Histology showed hemorhagic – necrotic tumor masses which grew in solid textures and were supplied by a moderate vascular network. (Fig. 3). Large tumor cells with abundant cytoplasm, remarkable nuclear variance, and sometime multinucleated tumor cells were noted. The nuclei presented with large nucleoli and numerous mitotic figures (Fig. 4). Only a weak inflammatory response of the host tissue and a patchy tumor boundary could be seen (Fig. 5). Immunohistochemistry and ligand histochemistry were as follows: Positive tumor cells to keratin (Fig. 6), vimentin , ß-HCG (Fig. 7), alpha-fetoprotein (Fig. 8), presence and binding capacities of galectin-1, galectin-3, and presence of galectin-8. High proliferation rate (MIB-1, Fig. 9) with 50%. The diagnosis of a primary choriocarcinoma of the lung was stated.
DISCUSSION	Primary choriocarcinoma of the lung are a rare entity [1,7,8,11]. Sekine et al. [11] reported two cases in a series of 32 rare lung cancer cases observed in a period of 20 years. They may arise at any age, and were reported already in a four month old boy [10]. Histologically, several cases display features of a large cell undifferentiated carcinoma of the lung [2-5,8,12]. As their distinction from large cell anaplastic carcinoma without immunohistochemistry is nearly impossible, some authors state that primary lung choriocarcinoma might be only a variant of a large cell anaplastic carcinoma [4,12]. A second theory favors a metastatic lung implantation of an extrapulmonary choriocarcinoma with spontaneously regression of the primary carcinoma [1,4,7,9]. Ikura et al. [7] proposed some minor differences between these tumor entities; however only based on a series of five patients (3 patients with extrapulmonary choriocarcinoma and two patients with so-called chorionic gonadotropin-producing giant cell carcinoma of the lung. The fate, morphology, and sex as well as age distribution between the two entities were nearly identical; only the serum levels of hCG and its presence in the tumor cells differed at a low degree. Our case differs

clearly from the far more common "usual" large cell anaplastic carcinoma of the lung in respect to vascularization, proliferation activity, inflammatory response of host tissue. However, if it is only a variant of a large cell anaplastic carcinoma with abnormal hCG production or a "real" choriocarcinoma of the lung cannot be answered with certainty. No elevated serum levels of ßHCG and alpha fetoprotein were found. In addition, some weak neuroendocrine properties could be observed in respect to positive staining of neuron-specific enolase (NSE) and synaptophysin. Despite these observations, to our opinion, it seems to be justified to classify these tumors into the entity of choriocarcinoma due to their specific immunohistochemical findings, vascularization, and poor prognosis.

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LEGENDS

Figure 1. Computed tomography of the upper lobes showing a solid, homogenous mass in the left upper lobe.

Figure 2: Macroscopic image of the surgical specimen showing an non-homogenous hemorrhagic – necrotic solid mass in the left upper lobe.

Figure 3: Microscopic image of the tumor showing large tumor cells with solid growth pattern and hemorrhagic necrosis (HE, *160).

Figure 4: Microscopic image with higher magnification showing large tumor cells with eosinophilic cytoplasm (HE, *240).

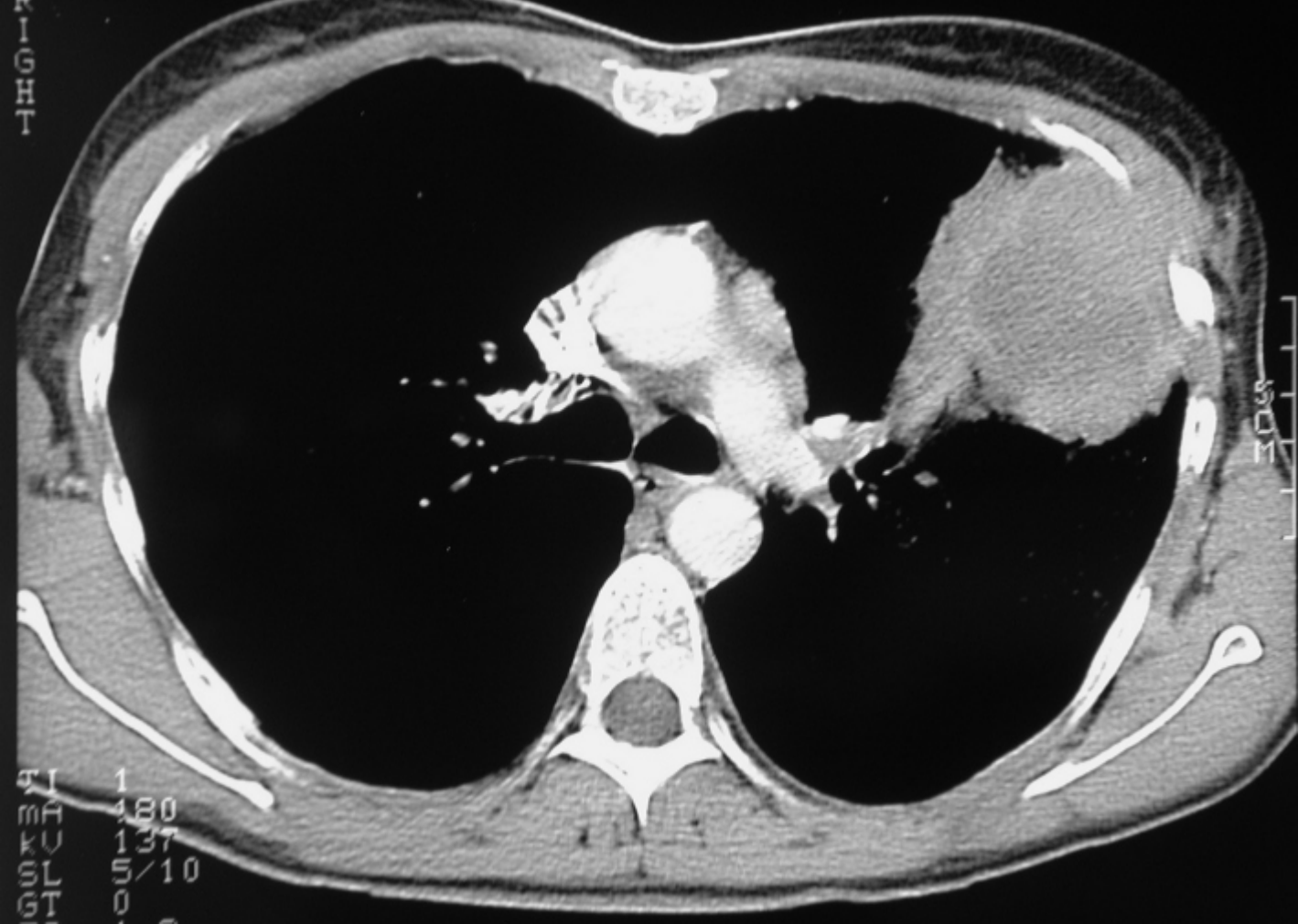
Figure 5: Microscopic image of the tumor showing a large cytoplasmic tumor cell with features mimicking immature syncytiotrophoblasts (HE, *400).

Figure 6: Microscopic image of tumor cells displaying the presence of keratin filaments (positive reaction to pan-cytokeratin, DAKO, Hamburg, Germany, ABC, *240).

Figure 7 : Microscopic image of the tumor cells displaying the presence of ß-HCG (positive reaction to ß-HCG-specific antibody, DAKO, Hamburg, Germany, ABC, *240).

Figure 8 : Microscopic image of the tumor cells displaying the presence of alpha fetoprotein (positive reaction to alpha Fetoprotein-specific antibody, DAKO, Hamburg, Germany, ABC, *240).

Figure 9 : Microscopic image of the tumor cells displaying a moderate to high proliferation rate according to the percentage of MIB-1 positive tumor cells (DAKO, Hamburg, Germany, ABC, *160).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