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Positive TTF-1 Expression in Malignant Mesothelioma: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Female, 70
Final Diagnosis: Malignant mesothelioma
Symptoms: —
Medication: —
Clinical Procedure: Radiation/Chemotherapy
Specialty: Oncology

Objective: Rare co-existance of disease or pathology

Background: The histopathological diagnosis of malignant mesothelioma is based mainly on the immunohistological profile of the neoplasia, using different immunohistochemical markers to distinguish between a malignant mesothelioma and a carcinoma.

Case Report: A female patient presented with a right paravertebral rapidly growing tumor and severe pain. Based on the immunohistochemical findings, we present the first case of a malignant mesothelioma with immunohistochemical expression of thyroid transcription factor-1.

Conclusions: The detection of a positive reaction for thyroid transcription factor-1 in the tumor cells may not exclude a malignant mesothelioma.

MeSH Keywords: Diagnosis, Differential • Mesothelioma • Pathology, Surgical • Pleural Diseases

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/895661

Background

Malignant mesothelioma is a rare malignant disease, but its incidence is increasing worldwide, strongly associated with amphibole asbestos exposure [1–3]. It is thought that the parietal pleura are the basis for malignant mesothelioma; however, there are rare cases of primary peritoneal mesothelioma [4–6]. The localized malignant mesothelioma is a very rare tumor that grossly appears as a distinctly localized nodular lesion without gross or microscopic evidence of diffuse pleural spread. There are many immunohistochemical markers known to distinguish between a malignant mesothelioma and a carcinoma, including pancytokeratin, cytokeratin 5/6, calretinin, WT-1, D2-40, BG8, MOC-31, EpCAM (BerEP4), Claudin, and TTF-1 [7–10]. The expression of thyroid transcription factor-1 (TTF-1) is positive in about 85% of lung adenocarcinoma and in thyroid carcinoma cases. Other tumors rarely show TTF-1 expression; for example, 10% of colorectal cancers show this expression, but so far none have been described in malignant mesothelioma [10].

Case Report

A 70-year-old white female presented with a right paravertebral rapidly (within 4 weeks) growing tumor and severe pain, for which morphine was administered. Since 2003, the patient had been under observation because of stable B-cell chronic lymphocytic leukemia (B-CLL), Rai staging 0, and slowly advancing Alzheimer disease. A cerebral metastasis had been excluded by computerized tomography (CT). The patient was employed as a commercial clerk without particular work-related exposure to noxa, such as asbestos or radiation. In the clinical examination, an approximately 4-cm lesion expansion, painful when pressed, was found in the area of the upper third paravertebral right of the thoracic spine. Further tumor manifestations were excluded clinically and by CT. The CT showed a 6×5 cm large lesion expansion with the beginning of shallow erosion of the 4th rib dorsal right. The lesion expansion extended continuously from the pleura (there was a pleura swelling approximately 1.5 cm large and 4.0 cm long) through the thorax wall in between the ribs to the margo lateralis scapulae (Figure 1). A vicinal triangular subpleural atelectasis and smaller pleural effusion were secondary findings.

Using a rechargeable pistol from Barth with insertable Tru-cut needles (14G), tissue cylinders from the lesion expansion were obtained for histological assessment. The sonography-guided puncture under sterile conditions is preferable, because with a one-person one-hand puncture necessary corrections can be performed quickly.

The specimens were routinely fixated in 4% buffered formalin, embedded in paraffin, and sectioned into 3–4 µm thick

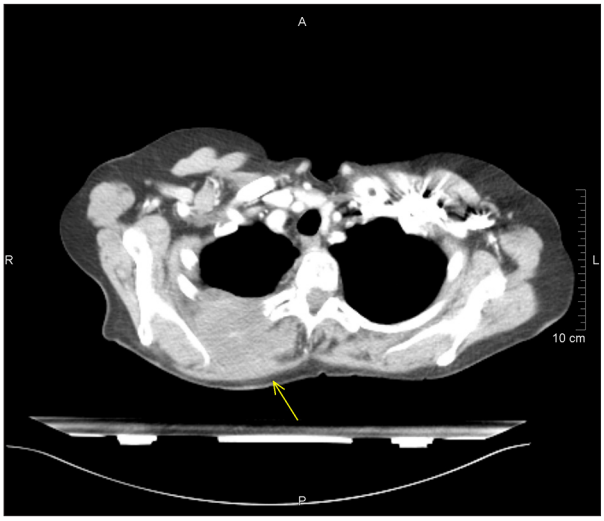

Figure 1. Axial CT scan showing an expansive lesion with the beginning of shallow erosion of the 4. rib dorsal right.

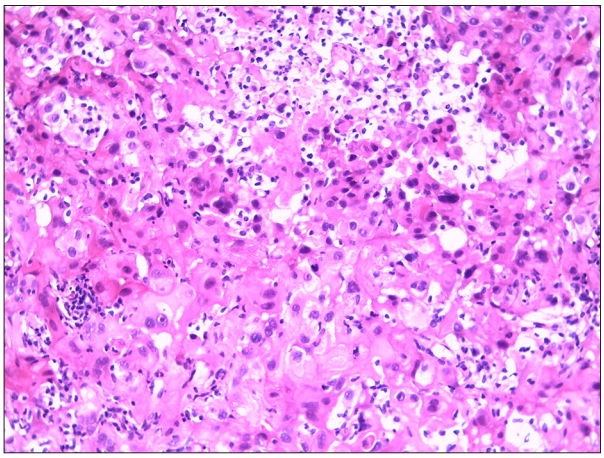

Figure 2. Micrograph hematoxylin and eosin staining (original magnification ×200).

sections. Then they were routinely stained with hematoxylin and eosin. They were also immunohistochemically stained with primary antibodies cytokeratin 5/6 (Cell Marque, Cell Marque Corporation, Rocklin, California, USA), cytokeratin 7 (Roche Diagnostics International AG, Rotkreuz, Switzerland), cytokeratin 20 (Roche Diagnostics International AG, Rotkreuz, Switzerland), calretinin (Roche Diagnostics International AG, Rotkreuz, Switzerland), and TTF-1 (Roche Diagnostics International AG, Rotkreuz, Switzerland) using the ultra-view™ universal alkaline phosphatase red detection kit (Roche Diagnostics International AG, Rotkreuz, Switzerland) on a Benchmark XT device (Ventana Medical Systems, Inc). In addition, on-slide positive controls were used.

Microscopical examination showed monotonous growth with uniform flat or cuboidal medium-size cells with round nuclei and eosinophilic cytoplasm [11]. Moreover, mitotic activity

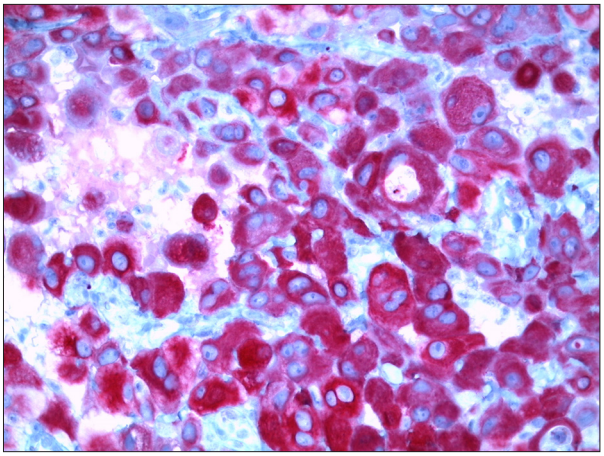

Figure 3. Micrograph immunohistochemical positive reaction for cytokeratin 5/6 (original magnification ×400).

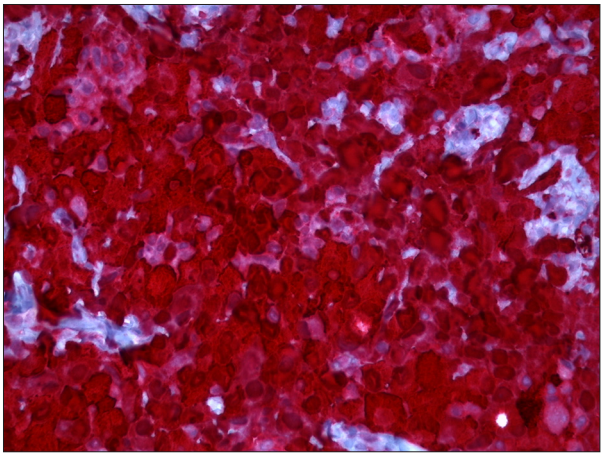

Figure 4. Micrograph immunohistochemical positive reaction for calretinin (original magnification ×400).

and giant cells could be detected. A lymphocytic inflammatory infiltrate was verifiable (Figure 2). There was a verifiable negative immunohistochemical reaction in the tumor cells for cytokeratin 7 and cytokeratin 20. A positive reaction was detected in the tumor cells for cytokeratin 5/6 (Figure 3), calretinin (Figure 4), and TTF-1 (Figure 5). In addition, the tumor cells showed an immunohistochemical positive reaction for D2-40 and WT-1 (not shown).

The treatment consisted of a combination of radiation/chemotherapy: Cisplatin weekly 20 mg/m^2, cumulative dose 240 mg. In addition, the patient was treated in a palliative setting [12,13] with a 6 MV photon beam [14,15] from a linear accelerator. The single dose was 2.5 Gray (Gy), 5 times a week, and the total dose 50.0 Gy. Target volume was the dorsolateral thoracic wall. At the end of this therapy, a sonographically measured 50% tumor reduction was achieved. Four months later, no growth gain was detected. The patient required no analgesic.

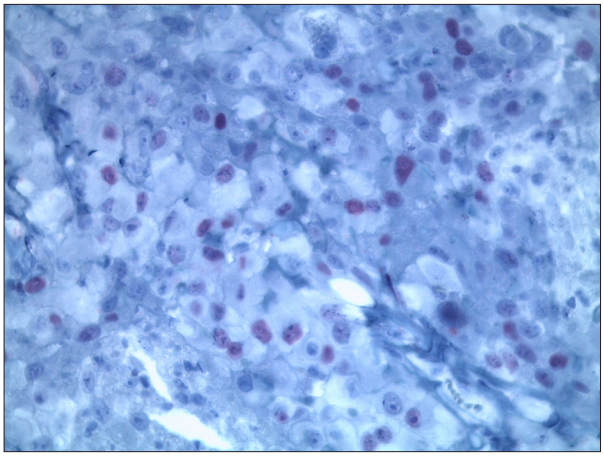

Figure 5. Micrograph immunohistochemical positive reaction for TTF-1 (original magnification ×400).

Discussion

We present the first report of a malignant mesothelioma with immunohistochemical positive expression of TTF-1. There are many immunohistochemical markers known to distinguish between a malignant mesothelioma and a carcinoma, including pancytokeratin, cytokeratin 5/6, calretinin, WT-1, D2-40, BerEP4, MOC-31, BG8, Claudin, and TTF-1. The expression of TTF-1 is positive in about 85% of lung adenocarcinoma cases and in thyroid carcinoma. Some other tumors rarely show an expression of TTF-1; for example, 10% of colorectal cancers show this expression, but so far none have been described in malignant mesothelioma. TTF-1 is a transcription factor essential for the morphogenesis and differentiation of several organs, including the lungs, ventral forebrain, and thyroid [16]. TTF-1 is necessary for the expression of some genes in the thyroid, lungs, and central nervous system. Human TTF-1 is located on chromosome 14 [17]. In the lungs, TTF-1 controls the expression of surfactant proteins that are essential for lung stability and, until now, TTF-1 was deemed to be negative in mesothelioma [18–20]. We detected a localized malignant mesothelioma with a positive reaction for TTF-1 (Figure 5) in the tumor cells. This was confirmed by the internationally renowned Professor A. Tannapfel, director of the German mesothelioma register of Ruhr University Bochum, who provided scientific consultations. This finding is important for prospective pathological diagnosis of mesothelioma because a positive reaction for TTF-1 may not exclude a malignant mesothelioma.

Conclusions

We present the first report of a malignant mesothelioma with immunohistochemical positive expression of TTF-1. Until now, the detection of TTF-1 seems to have ruled out the diagnosis

of a malignant mesothelioma, but now a positive reaction for TTF-1 may no longer exclude a malignant mesothelioma.

Acknowledgments

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Conflict of interests

The authors declare that there is no conflict of interests regarding the publishing of this paper.

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