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Malignant peripheral nerve sheath tumor in a patient without neurofibromatosis 1 (NF1) : a rare case of primary lung location

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Key words: malignant peripheral nerve sheath tumor, lung, primary location

Abstract

We present a rare case of a patient operated due to a lung tumor, which was ultimately diagnosed as malignant peripherial nerve sheath tumor (MPNST). MPNSTs are rare tumors of soft tissue with mesenchymal origin. The World Health Organization has distinguished this group in order to unify terms in mesenchymal heterogeneous malignant tumors, e.g. neurofibrosarcomas, malignant schwannomas and malignant neurilemmoma [1]. They can occur as a result of neoplastic expansion of peripheral nerves' branches, peripheral nerve fibers' sheaths or Schwann cells, although many researchers believe that these tumors can derive not only from one, but several cell lines. MPNSTs are very rare in thorax, where they show aggressive pattern of growth [2] and stem from pleural cells rather than lung tissue.

Case presentation

A 69 year old woman was admitted to the Clinic of Pulmonology, Oncology and Allergology in Lublin due to the following symptoms lasting for a few days: recurring intensive hemoptysis episodes, shortness of breath on exertion, cough, retrosternal pain and subfebrile temperature. The patient suffered from chronic obstructive pulmonary disease (COPD), chronic heart failure and hypertension. In the computed tomography (CT) of the chest, a nodule of 18 milimeters of diameter was found in the left parahiliar region in the 5th segment. In addition, an enlarged, 12 mm subcarinal lymph node was found, as well as pleural overlays and persistent post-tuberculosis cavities. In blood tests, C-reactive protein (CRP) level was slightly elevated and hemoglobin levels indicated anemia. No abnormalities were shown in the ultrasound examination of the abdomen. Bronchoscopy showed signs of chronic mucosal inflammation, no focal changes, unobstructed bronchi and a small focus of bleeding in the left bronchi 3,4,5 furcation. Endobronchial ultrasound revealed enlarged, 15 mm lymph nodes of group 7 (subcarinal) from which a biopsy was taken. The histopathological result of this biopsy was not diagnostic. Bacterial cultures and tuberculosis tests were negative (as well as tuberculosis cultures results received a few weeks later).

The patient was referred for surgery in the Department of Thoracic Surgery in Lublin, where she underwent upper left-sided lobectomy - intraoperative histopathological test revealed squamous cell carcinoma. The tumour was excised. A few weeks later, the patient was hospitalized for the second time in our clinic because of worsening of pain in the left half of the chest associated with breathing, shortness of breath and mucous cough. CT scan excluded pulmonary embolism, although it showed peribronchial mesenchymal consolidation with an air bronchogram in the lower left lobe which suggested inflammatory changes, as well as a region of whitening in the 10th segment of right lung. After supportive treatment and antibiotics administration, the patient's clinical status improved. In the next CT, a small regression of aforementioned lung changes was observed, but also new regions of whitening occurred in the 5th right segment. Soon, she was admitted again due to recurring hemoptysis, shortness of breath and clinical worsening.

Finally, the histopathological examination of the excised tumour showed a malignant tumor with a partially epithelioid, partially spindle cell structure, which which was consistent with malignant fibrous histiocytoma. Immunohistochemistry tests: S100 focal (+), NSE (+) in numerous cells, vimentine (intensive +)], MIB1=40% and negative tests for cytokeratin (CK 7, 5, 6), TTF-1, HM45, Melan A, CD 34 and muscle desmin and actin, allowed to exclude cancer, muscle derived tumor and synovial sarcoma. The final diagnosis was pleomorphic malignant peripheral nerve sheath tumor (MPNST) [Fig. 1,2,3]. The proliferation marker MIB1=40% suggested high malignancy.

The positron emission tomography (PET) performed two months after the operation revealed the recurrence of the neoplasm in the left lung hilum and metastatic changes in lymph nodes of the chest and the lower lobe of the left lung. There were no other pathological fluorodeoxyglucose (FDG) uptake regions found. The patient was referred to the Oncology Center for radiotherapy, where she died a few days later.

Discussion and Conclusions

Malignant peripheral nerve sheath tumors arise from major or minor peripheral nerve branches or sheaths of peripheral nerve fibers, and are derived from Schwann cells or pluripotent cells of neural crest origin. In the general population of the United States, malignant peripheral nerve sheath tumours occur with a frequency of 0.001%, which is about 5-10% of the 6,000 cases of soft tissue sarcomas diagnosed per year in this country. They

occur with similar frequency in both sexes, regardless of race [3]. In a study of 120 patients with MPNST, the mean age at the time of diagnosis was 34 [4]. Numerous reports have shown that this form of neoplasm is often associated with neurofibromatosis type 1 (NF1). According to Tucker, patients with NF1 have up to 10% risk of developing MPNST during their life [5]. MPNST occur in merely 2-5% of patients with NF1, on the other hand, over 40% cases of this type of neoplasm have an association with NF1 [1].

The only known radical therapy for MPNST is surgical resection with wide negative margins [6]. MPNSTs are considered chemotherapy and radiotherapy resistant neoplasms, however, postoperative radiotherapy is recommended in guidelines by international oncology consensus group [7].

The prognosis for these patients is poor: five-year survival of patients with advanced, unresectable or metastatic MPNST ranged from 20 to 50%, while the ten-year survival was only 7.5% [8]. Some research indicate significantly worse prognosis in patients with NF1 associated MPNST [9].

NF1 is considered an independent risk factor in MPNST cases, some researchers suggest there is a need for a separate evaluation systems for patients with and without neurofibromatosis; for example the size of tumor in NF1 patients determines survival time [10]. On the contrary, Kolberg's research did not confirm any statistically significant differences in survival time between MPNST patients with and without NF1 [9] The tumor has a high rate of local recurrence which is associated with a particular cell's ability to roam along the nerve trunk [4] Our patient presented no symptoms of NF1, there were no cutaneous changes typical for this syndrome and the medical history did not suggest any case of NF1 in relatives. Despite numerous imaging studies, the presence of the primary tumor was not confirmed in any other area and therefore the tumor in the lung was considered to be the primary focus of this neoplasm. The unlike secondary character of lung foci is also supported by the results of FDG PET performed after surgery to assess the radicality of surgical treatment, which, apart from the lungs, showed no pathological accumulation of FGD.

It should be noted that the primary location of MPNST in lungs is extremely rare [11]. We found only isolated cases of primary pulmonary location of MPNST. Attanoos et al. presented 14 cases of sarcomas of primary pulmonary tissue of which only 5 were the MPNSTs [12]. Etienne-Mastroianni et al. examined 12 cases of sarcomas with primary pulmonary manifestation and described only 1 case of MPNST [13].

In conclusion, it is worth noting that MPNST's can occur in patients without confirmed risk factors, in non-typical localisations and the diagnostics path might present a real medical challenge.

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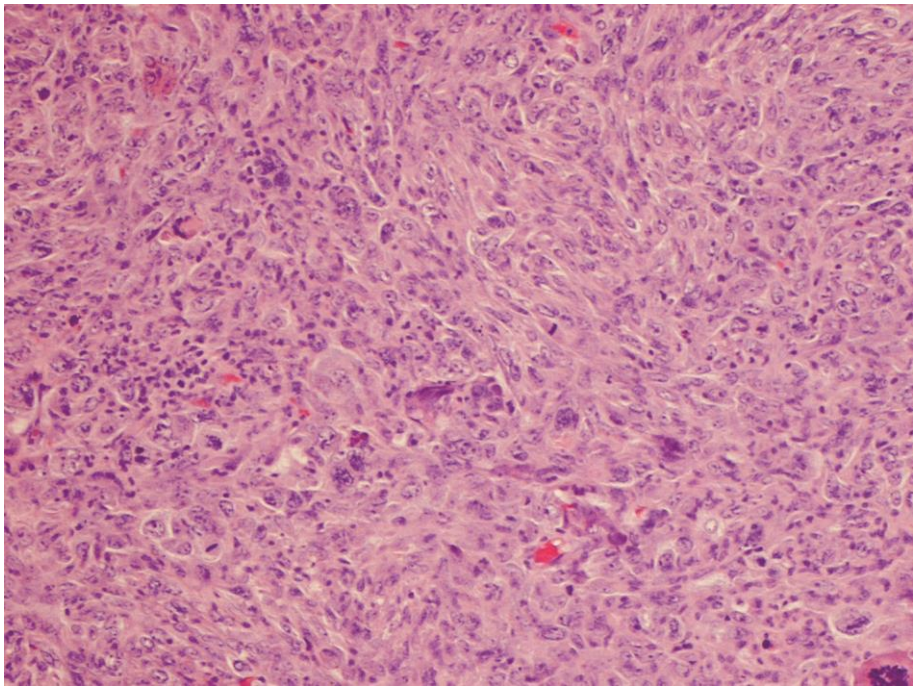

Fig. 1. Numerous multinuclear cells, abnormal mitotic figures and spindle-cell constellation in tumour.

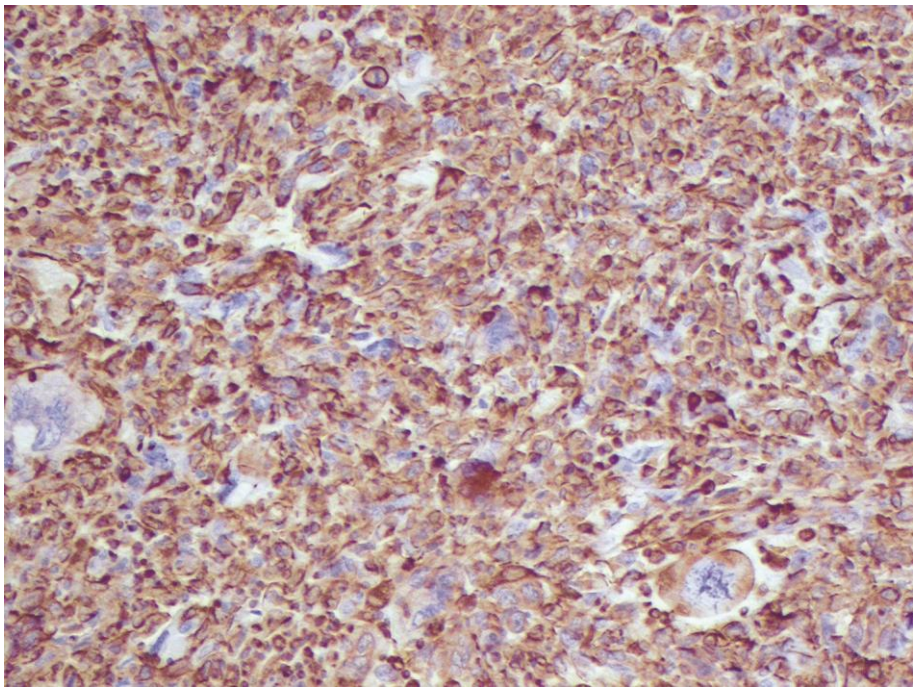

Fig. 2. Intensive immunochistochemical reaction to vimentin.

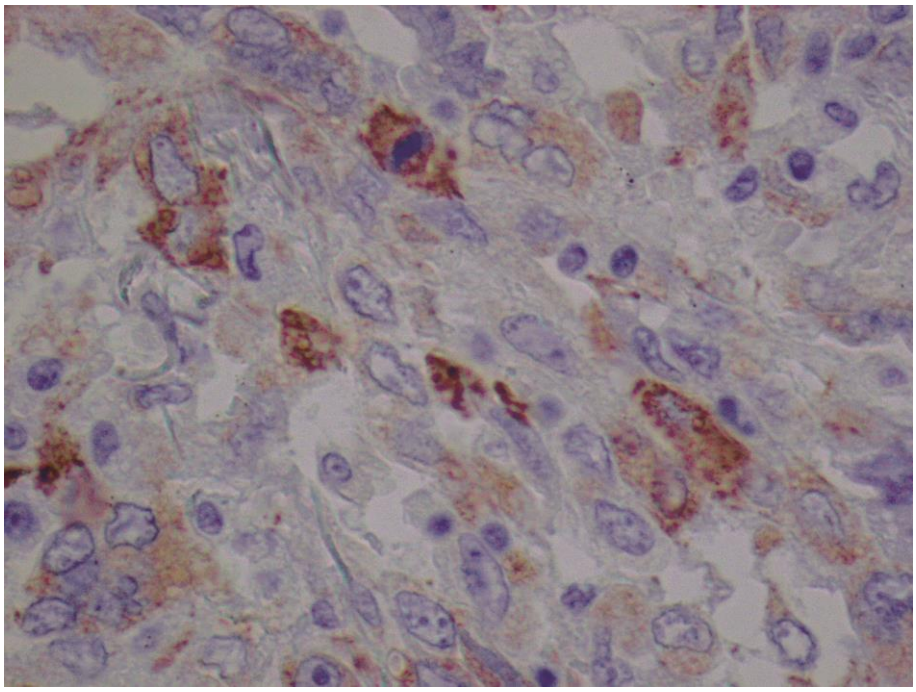

Fig. 3. Positive immunohistochemical reaction to neuron specific enolase.