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Malignant peripheral nerve sheath tumor associated with clear cell renal cell carcinoma — case report

Złośliwy nowotwór osłonek nerwów obwodowych współwystępujący z rakiem jasnokomórkowym nerki — opis przypadku

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Abstract

Malignant peripheral nerve sheath tumor (MPNST) is a rare malignant counterpart to benign neurogenes tumors such as schwannomas and neurofibromas and account for approximately 5–10% of all soft tissue sarcomas. This neoplasm is also referred to older designations as a malignant schwannoma, malignant neurilemmoma or neurogenic sarcoma. A patient was a woman of 59 years old with a diagnosed malignant neurilemmoma, treated since 1993. Operated several times and subjected to radiotherapy due to the local recurrence of the tumors located in the soft tissues of the back until 2002; Treated with chemotherapy (doxorubicin) and operated due to lung metastases. The therapy resulted in a total remission that lasted 12 months. In 2004 a new small tumor was diagnosed in the right lung, which had been followed up until 2006. The patient did not give permission to a second surgery, treated with ifosfamide. In 2006 she was operated for renal cell carcinoma of the left kidney. In 2009, due to a following progression of neurilemmoma and a worsening overall condition, she was subsequently treated with a combination of gemcitabine and docetaxel. The treatment resulted in a slight improvement, but was stopped due to complications (pancytopenia). In 2010 another progression of the disease occurred, which resulted in pleural metastases and osteolytic lesions in the vertebrae (Th6 and L2).

Key words: MPNST, neurilemmoma malignum, schwannoma malignum

Introduction

Malignant peripheral nerve sheath tumour (MPNST) is a rare neoplasm, a malignant counterpart of benign tumours of neurogenic origin such as schwannoma and neurofibroma [1, 2]. It accounts for 5–10% of all soft tissue sarcomas [1, 2]. In the past, other terms like malignant schwannoma, malignant neurilemmoma, or neurogenic sarcoma were also used for MPSNT. Neu-
rogenic tumours originate from primitive neuro-ectodermal cells [1, 2].

According to recent recommendations, a sarcoma is defined as MPNST when at least one of the following three criteria is met [1]:
1. a tumour develops in a peripheral nerve,
2. a tumour develops from a pre-existing benign nerve sheath neoplasm, most frequently from neurofibroma,
3. a tumour shows a set of histologic features consistent with Schwann cell differentiation [1–11].

A malignant peripheral nerve sheath tumour usually affects adult people aged 20–50 years, develops in deeper soft tissues, and typically shows connection with the main trunks of nerves. The majority of MPNST are highly malignant, with high rates of recurrence and remote metastases. The recurrence rate oscillates between 40 and 65%, and metastases rate between 40 and 68%. Both rates depend on the tumour’s degree of histological malignancy. The lungs are the most frequent site of MPNST metastases [1].

Around 40–50% of neurilemmoma malignum cases appear in patients with Recklinghausen’s disease [2, 4, 9, 12].

**Case report**

A 59-year-old female had been treated for MPNST and stayed under oncological and pneumological care since 1993. In Jan 1993 a 4 cm tumour of the subcutaneous tissue of the back was removed and the histopathological diagnosis was established — *neurilemmoma cum signis proliferationis et malignisationis focalis*. Subsequently, the patient underwent two surgical operations for local recurrence — in Jan 1995 and Oct 1996.

In 1996 postoperative radiotherapy (60 Gy) was applied. The treatment was finished in Jan 1997.

In Dec 2002 a control chest X-ray showed three nodules in the lungs — one in the right lung (1.5 cm in diameter) (fig. 1) and two in the left lung (2 × 1 cm and 1.5 cm in diameter, respectively). Those nodules were removed surgically and microscopic examination revealed *Neurilemmoma malignum metastaticum*. In immunohistochemical staining the presence of protein S-100 was detected, confirming the neurogenic origin of the tumour (fig. 2).

In Feb 2003 features of disease dissemination were found again. Nodules in lungs and in soft tissue of the lumbar area appeared. The patient was accepted for chemotherapy and radiotherapy for the lumbar area. She received nine courses of chemotherapy with doxorubicin and radiation of 50 Gy for the lumbar area. Remission of changes in lungs and lumbar area was achieved.

Another 14 mm nodule was found in the right lung during a CT scan in 2004. The patient did not agree for surgical treatment at that time.

In Feb 2006, during a follow-up examination, a left kidney tumour was detected. Left-sided nephrectomy was performed. The histologic examination showed clear cell carcinoma of the kidney (*Ca clarocellulare renis G1 diam 3 cm*).

In Oct 2006 a CT scan showed progression of the lesion in the right lung. Due to numerous co-existing conditions (second neoplasm, renal insufficiency, recent chemotherapy with doxorubicin) the decision to treat with ifosfamide in monotherapy was made. After the second course of chemotherapy complications of the treatment occurred: encephalopathy (that subsided after methylene blue administration) as well as thrombocytopenia and anaemia of the 3" and 4" degree. The chemotherapy was discontinued.

In Nov 2006 the patient was admitted to the Department of Pneumonology, Oncology, and Allergology of the Medical University in Lublin, Poland, in very severe condition, with intense breathlessness at rest, weakness, and pains in the lower legs. She was found to have respiratory failure, anaemia, and renal insufficiency. CT scan showed proximal pulmonary embolus and a tumour 3 cm in diameter located in segment 6 of the right lung (fig. 3). Thrombolytic treatment with Alteplase was administered, and subsequently antagonist of vitamin K was commenced.

By Nov 2007 the tumour in the right lung reached the size of 5 cm. In addition, associated ate-
selective changes appeared. Transthoracic biopsy of the lesion revealed histologic pattern of *neoplasma malignum fusocellulare verisimiliter neurogenes*. The patient, however, sustained her decision not to undertake surgical treatment.

Further progression of the right lung lesion (52 × 51 × 48 mm) was seen in Aug 2008. Therapy with photons × 20 MV in a single dose 10 Gy/metastatic tumour using EXAC-Track technique was commenced in Nov 2008 in Maria Skłodowska-Curie Memorial Cancer Centre and the Institute of Oncology in Gliwice. As a result the size of metastatic tumour decreased to 40 × 38 × 40 mm. The treatment was complicated by radiation-induced pneumonia (fig. 4).

In Jan 2010, the disease progressed again. CT showed a partly solid and partly cystic tumour
with weak contrast enhancement, 93 × 72 × 77 mm in size, in the right lung and a single enlarged lymph node 13.5 mm in size. The patient complained of: deterioration of general condition, shortness of breath, recurrent fever, chest pain, and haemoptysis.

Due to poor respiratory parameters the patient was rejected for surgery. Another attempt at cytostatic treatment was undertaken (gemcitabine on day 1 and 8 + docetaxel on day 8 of the course). Laboratory tests showed features of chronic renal impairment and respiratory failure.

The patient was hospitalised in the Department many times. Courses of chemotherapy had to be postponed several times due to leukopenia, anaemia, gemcitabine hepatotoxicity, and recurrent fever. She was given erythropoietin, granulocyte colony-stimulating factor (G-CSF), and iron supplementation.

Between May and Oct 2010 the patient received four courses of chemotherapy with gemcitabine and docetaxel. After the two first courses regression of the tumour was seen in CT study (down to 85 × 70 × 68 mm in size), while there was no improvement in pulmonary function tests.

After 4 courses of chemotherapy the disease stabilised in terms of imaging studies. Subsequently, the chemotherapy was continued as a mono-therapy with gemcitabine. During the first infusion of gemcitabine intense haemorrhagic rash and fever appeared, which led to cessation of the treatment.

In Dec 2010 the patient’s condition deteriorated further with intensification of chest pains. The progression was also seen in CT scan with metastases to the pleura and vertebral column (osteolytic lesions in Th6 and L2) (fig. 5). Palliative radiotherapy was applied for metastatic foci in the vertebrae, and the decision to continue only with symptomatic treatment was made.

Discussion

Malignant peripheral nerve sheath tumour originates from Schwann cells of the cranial and peripheral nerves [1, 3, 5–11].

MPNST are usually big, rubbery and of tan-white colour in their cross sectional surface, with areas of necrosis and sometimes with foci of haemorrhage.

Microscopically, in classical form, these tumours exhibit the presence of spindle cells arranged in dense cellular fascicles that closely resemble fibrosarcoma and they are included in the group of spindle-cell neoplasms. The tumour cells have features of normal Schwann cells. They contain slender nuclei of wavy contours and indistinct
Malignant peripheral nerve sheath tumors originate from pre-existing benign tumours from the beginning. However, they may also appear in association with large and small nerves, mainly within the extremities and neck [7, 10]. Tumours of the head and neck account for 25–45% of this neoplasm [3, 6, 9]. They may also appear in subcutaneous tissue, in the posterior mediastinum, or in retroperitoneal space. Neurinomas within parenchymal organs are very rare [5, 10].

Malignant peripheral nerve sheath tumours constitute around 10-20% of malignant neoplasms of soft tissues [1, 2, 4]. They are less common than their benign counterparts. Usually they arise in soft tissues [1, 2, 4].

Malignant peripheral nerve sheath tumours may appear at any age, most commonly at age of 20–50 years [1, 5, 6], with no sex predominance. Tumours may be solitary or multiple. In the reported case the disease occurred at the age of 43 years. Despite the recurrent character of the disease, Recklinghausen’s disease was not present.

Malignant peripheral nerve sheath tumours grow slowly, they are asymptomatic for a long time, and signs of the disease such as pain and motor or sensor disturbances appear late in the disease course, as a result of tumour pressure on the nerve [4, 5, 6, 11].

In the reported case the disease had also been asymptomatic for a long period of time, which was probably responsible for the patient's decision not to undertake surgical treatment. Pains, haemoptysis, and shortness of breath, occurred when the tumour size exceeded 50 mm — 4 years after the lesion in the lungs appeared. The treatment of choice is surgery, regardless of the tumour being a primary or recurrent one [2–4, 6, 11, 13]. The method of applied surgery depends on: size, affected area, risk of nerve injury, degree of malignancy, and distance from lungs and pelvis, but also on the tumour’s character (primary vs. recurrent) [4]. The operation should be radical with wide surgical margins (minimal recommended surgical margin in soft tissue sarcomas is 2 cm) [13]. The whole mass of the tumour should be excised, together with adjacent vessels, nerves, muscles (from one attachment to the other), and bones [2, 11, 13]. Post-operative radiotherapy is recommended [2, 9, 11, 13]. Radio- and chemotherapy can be considered only as a palliative treatment to reduce symptoms or to prevent micrometastases [2, 13].

In our patient, after several previous resections of soft tissue and lungs lesions, the disease recurred as metastatic tumours in the lungs and soft tissues of the lumbar area. Due to the disease extent and lack of the possibility for surgical treatment, chemo- (doxorubicin) and radiotherapy were applied, which resulted in complete remission. When the disease recurred in the lungs the patient declined surgical treatment and sustained that decision for many years. In addition, at that time she underwent surgery for another malignant neoplasm – clear cell carcinoma of the kidney. The procedure was complicated by pulmonary embolism. At the time of escalated symptoms (pains, haemoptysis, breathlessness) the tumour in the lung was so advanced and the patient’s respiratory parameters and general condition were so poor that surgery was not possible.

The prognosis is worse when MPNST appears in patients with Recklinghausen’s disease (five-year survival 16–23% in comparison to 47–53% in patients without Recklinghausen’s disease) [4].

Conflicts of interest
Authors have no conflict of interest to report.

References: