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Malignant peripheral sheath tumour of the neck mimicking a thyroid tumour. A case report and a literature review from a reference centre for endocrine surgery

Złośliwy nerwiak osłonkowy szyi imitujący guz tarczycy — opis przypadku i przegląd piśmiennictwa. Praca z ośrodka referencyjnego w chirurgii endokrynologicznej

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Abstract

Malignant peripheral sheath tumors (MPNST) are rare soft tissue sarcomas originating from peripheral sheath cells. The main risk factor is neurofibromatosis type 1 (NF-1). The localization in the head and neck region is uncommon (up to 15% of all cases of MPNST) making the diagnosis difficult due to anatomical and clinical reasons. We present a case of 45-years-old female with the NF-1- linked MPNST localized in the thyroid region with clinical manifestation as a left thyroid tumour. The patient underwent surgery and adjuvant radiation therapy, remaining disease-free for 14 months after the treatment.

Key words: malignant peripheral sheath tumour, head and neck tumours, thyroid tumours, neurofibromatosis type 1 (von Recklinghausen disease), soft tissue sarcoma

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Streszczenie

Złośliwe nerwiaki osłonkowe (MPNST) należą do rzadko spotykanych mięsaków tkanek miękkich, wywodzących się z komórek osłonek nerwów obwodowych. Najważniejszym czynnikiem ryzyka ich rozwoju jest nerwiakowłókniakowatość typu 1 — choroba Recklinghausena. Umiejscowienie tych nowotworów w regionie głowy i szyi zdarza się rzadko, a postawienie prawidłowego rozpoznania jest trudne z przyczyn anatomicznych i skrytego przebiegu klinicznego omawianych guzów. W pracy prezentujemy przypadek 45-letniej kobiety z nerwiakowłókniakowatością typu 1 i złośliwym nerwiakiem osłonkowym umiejscowionym w rzucie lewego płata tarczycy. Chora przebyła zabieg wycięcia guza z następczą radioterapią. W trakcie 14-miesięcznej obserwacji po leczeniu nie stwierdzono nawrotu choroby.

Słowa kluczowe: złośliwy nerwiak osłonkowy, guzy głowy i szyi, guzy tarczycy, nerwiakowłókniakowatość typu 1 (choroba von Recklinghausena), mięsaki tkanek miękkich

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Introduction

Malignant peripheral nerve sheath tumour (MPNST) is a rare malignancy originating from Schwann's sheath of peripheral nerves. It usually arises from Schwann cells, but other cells of nerve sheath may also be the point of its origin including perineural fibroblasts or fibroblasts [1–6]. It may develop de novo or upon the base of priorly existing neurofibroma. The main risk factor of this tumour is type 1 neurofibromatosis (von Recklinghausen disease) — a genetically backgrounded condition caused by the mutation in NF-1 suppressor gene. Other

risk factors include previous irradiation (5–10% of cases) [3, 7]. MPNSTs account for 5–10% of all soft tissue sarcomas in adult population with highest incidence in patients between 30 and 50 years of age, with no evident predominance of any gender[1, 8, 9]. About 30% of these tumours occur on the base of preexisting plexiform neurofibroma and in this group of patients MPNST occurs one to two decades earlier. In the absence of preceding neurofibroma it is possible to see the conjunction of MPNST and a large peripheral nerve as the sciatic nerve, the brachial plexus or the sacral plexus. In rare cases multiple MPNSTs can arise in the setting of NF1 [2]. The head and neck occurrence is rare (about 8 to 16% of all MPNSTs) but particularly difficult in the treatment due to small anatomical space and adjacency of the tumour to vital structures [10]. Most of these tumours are high-grade sarcomas with the potential to recur as well as to metastasize through the bloodstream. Nodal involvement is rare as in other soft tissue sarcomas. The main prognostic factors for local recurrence or metastatic disease are: histologic grade, tumour size, tumour depth and presence of metastases at the time of diagnosis. Five-years survival in most series remains at the level of 50%, being worse for patients with NF1 [1, 4, 6, 8]. Tumor size cutoff is 5 cm, with prognosis worsening precipitously in tumours over 5 cm in diameter. Wide local resection is still a mainstay in the treatment of MPNST [3, 6, 8]. Adjuvant radiation therapy showed its benefit in advanced cases (stage III and IV). Palliative radiation therapy is sometimes offered to the patients with inoperable or nonresectable tumours. There are very limited data concerning adjuvant chemotherapy in the treatment of MPNST, with no proven benefit in this disease.

Preoperative diagnostics consists of thorough collection of patient's history, physical examination, imaging (USG, CT/MRI), FNAB or tru-cut biopsy; open surgical biopsy is recommended in cases of doubtful or ambiguous diagnosis [3, 11, 12].

The rare occurrence of the head and neck MPNSTs is reflected in available literature where mostly small series of cases or casual case reports can be found with only very few large-group or population-based analyses. This may lead to the misdiagnosis in patients with tumours located in some regions of the body, e.g. in close adherence to thyroid gland. In such cases they can mimick primary thyroid malignancies thus resulting in suboptimal treatment and greater risk of non-radical resection. We publish our case report to add some information to our still poor knowledge of these uncommon malignancies.

Case report

45-years-old female was admitted to our centre for 1 year history of gradually enlarging left thyroid lobe mass, hoarse voice and moderate dysphagia (Fig. 1). The past history showed autoimmunological thyroiditis with hypothyreosis and numerous small neurofibromas of the skin. Preoperative imaging (USG, contrast-enhanced CT) showed the multinodular goitre with large (7.5 × 7.4 ×

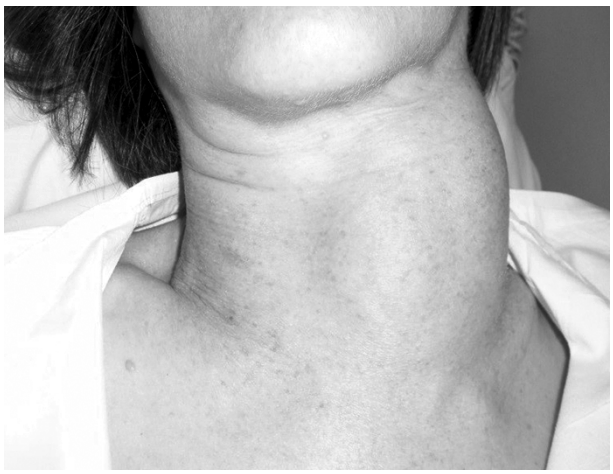

Figure 1. 45-years-old female with left cervical mass

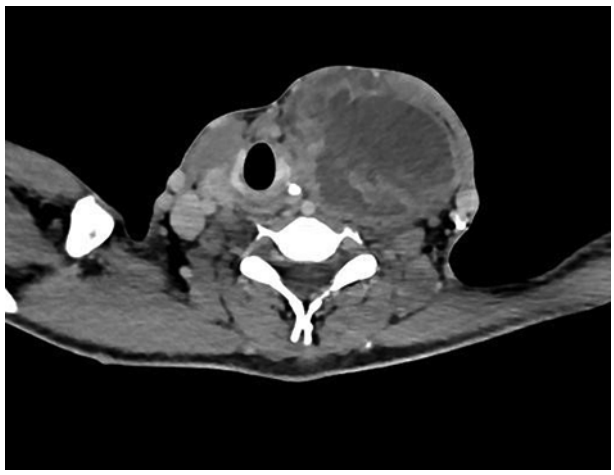

Figure 2. CT imaging showed the left thyroid mass without infiltration of blood vessels

14.7 cm) dominant tumour of the left thyroid lobe with central necrosis, without infiltration of the blood vessels (Fig. 2). The left cervical lymph nodes were slightly enlarged. No distant metastases were found. Fine needle biopsy showed malignant cells. The videostroboscopy showed the paresis of the left vocal chord with its intermediate position without glottal stenosis (Fig. 3).

The patient was included to the surgery with preoperative diagnosis of thyroid cancer. Intraoperative inspection of the neck showed the well separated encapsulated tumour adjacent closely to the left thyroid lobe but not infiltrating it. The tumour mass seemed to emanate from the left vagus nerve and encased the internal jugular vein (Fig. 4). The tumour was dissected and removed together with regional lymph nodes of groups III, IV and V. The left common carotid artery and its bifurcation as well as internal jugular vein were cleaned of the malignant tissue and the vagus nerve removed with the tumour. The thyroid gland was left intact (Fig. 5). The postoperative course was uncomplicated despite the permanent left vocal cord paresis. No signs of dysphagia or respiratory failure were found after the surgery. The drains were removed on the second and the skin suture on the fifth

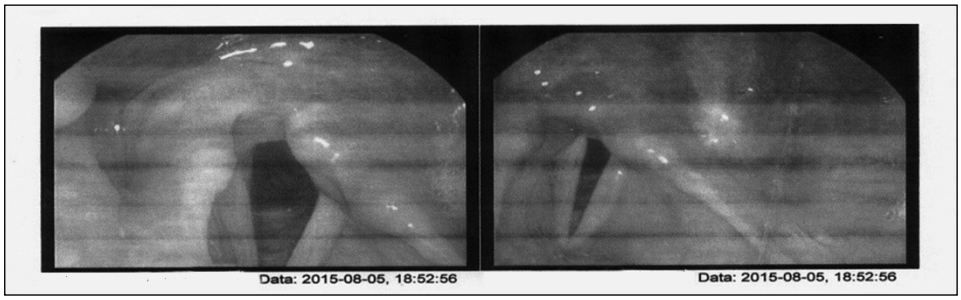

Figure 3. Left vocal chord paresis shown in videostroboscopy

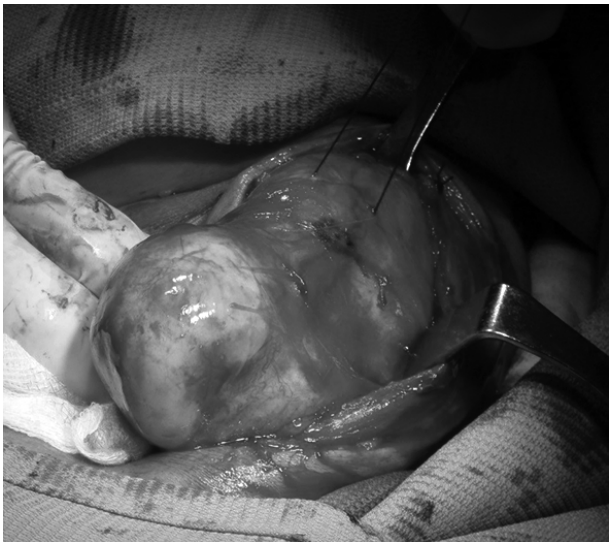

Figure 4. Well encapsulated tumour arising from parathyroid space

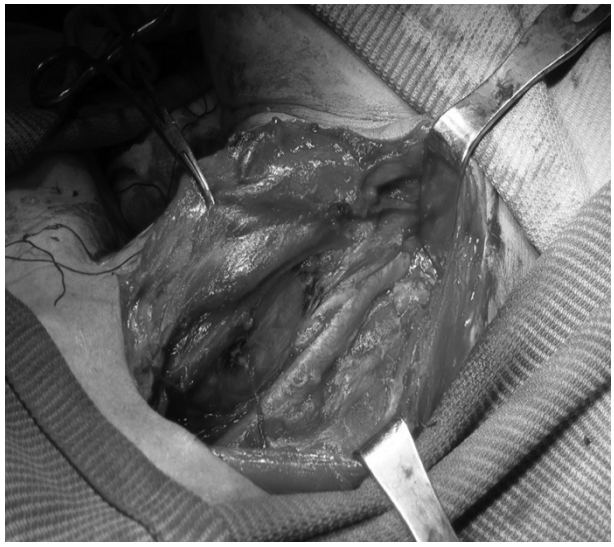

Figure 5. Postoperative view of the tumour bed

postoperative day and the patient was discharged home on sixth postoperative day.

The pathological report was as follows: Well delimitated tumour with histological and immunohistochemical features of malignant nerve sheath tumour; six lymph nodes with no metastases; no thyroid tissue found in the specimen; immunohistochemistry: NSE, S100, PGP9, CD34 (++); Ki-67 — 15%. Since one margin of resection was doubtful the patient was operated four weeks later with the excision of the retrosternal remnant tissue. The tumour bed was marked with titanium clips for radiation therapy planning. The pathological report showed no malignant tissue in the excised specimen.

The patient underwent the adjuvant radiation therapy up to the dose of 45 Gy which was well-tolerated. Despite the permanent left vocal cord paresis no other complications of the treatment were found.

The last follow-up within 14 months after the treatment showed no recurrent disease.

Discussion

MPNSTs are rare but highly aggressive soft tissue sarcomas, comprising 2–10% of all STSs [5, 6, 9, 11, 13–15]. About 30 to 50% of all MPNST are associated with neurofibromatosis type 1 (von Recklinghausen disease) which is an autosomal dominantly inherited disorder with the frequency 1 per 3500 newborns [3, 6]. NF-1 associated MPNST occur 1–2 decades earlier than sporadic cases [16]. MPNSTs occur mostly in proximal extremities or in the trunk, the head and neck location being extremely rare As it was previously mentioned MPNST are generally uncommon tumours and the head and neck location is very rare — 8–16% of all MPNST [2, 5, 13, 14]. In this region they may develop in the nasal cavity, on the skull base or in the sinuses; parathyroid or parapharyngeal locations seem to be very uncommon. Most MPNSTs present as the rapidly growing mass, with or without pain; sometimes rhinorrhea or nasal stuffiness occur [1, 2, 3, 13]. The tumours mimicking thyroid neoplasms were described only in several case reports. Their incidental occurrence may lead to the misdiagnosis and suboptimal treatment if they were considered to be typical thyroid cancers [2, 3].

The diagnosis is based upon contrast-enhanced — CT or MRI, followed by the fine-needle biopsy. In some cases FNAB may be non-diagnostic given that proper diagnosis of sarcomas need core-needle or incisional biopsy. Ultra-

sonography is a safe, easy and cost-effective modality but useful only in superficially located tumours [10]. PET-CT is a very sensitive in scanning the whole body for metastases but it lacks specificity. Contrast-enhanced computed tomography remains a very useful imaging modality, especially for planning the surgery or irradiation. MRI is mostly recommended for diagnostics of MPNST, being a multi-parameter modality, providing information about different components of the tumour [4, 10].

Surgery remains the principle modality in the treatment of MPNST. Since the effective treatment of MPNSTs as well as other soft tissue sarcomas requiring wide surgical excision with free margins is difficult to be achieved in the head and neck region without significant morbidity. The anatomy of this part of the body often limitates the extent of surgery. The positive margins of resections are quite common in head and neck MPNST increasing the risk for local recurrence or spread of the disease [3, 13, 17].

The recommendation for adjuvant radiation therapy has been clearly established. Most authors advocate the postoperative radiation therapy in all cases of MPNST of the head and neck region, only few of them recommend this modality in cases with positive margins of resection [1, 2, 12, 13, 16]. The benefit of adjuvant radiation therapy on overall survival and local recurrence has been confirmed, especially in patients with positive margins [1, 3, 11–13]. The dose of irradiation has also its impact on local control of the disease, eg. Wong et al. reported the 5-years local control as 73% for cumulative dose over 60 Gy (e.g. external beam, IORT and brachytherapy) versus 50% for lesser doses, but without the impact on survival [12].

Chemotherapy is mostly recommended in locally advanced, recurrent and metastatic cases [14]. Protocols are based upon doxorubicin and ifosfamide (Moretti) as a first-line treatment. Second-line chemotherapy remains poorly defined. The regimens consisted of gemcitabine/ /docetaxel or carboplatine/etoposide or ifosfamide/etoposide. Etoposide was introduced to the therapy upon the preclinical data of elevated topoisomerase II in MPNST. A phase II study with tyrosine kinase inhibitor — erlotinib — showed the lack of activity of this agent in MPNST [3, 4]. The results are inconsistent and the benefit of chemotherapy has not been statistically proven [1, 3, 11, 13, 14].

Overall survival in MPNST is still unsatisfactory. It still remains at the level of about 50%, with poorer prognosis for NF-1 patients. The negative prognostic factors are also: tumour size > 5 cm in diameter, male gender, positive surgical resection and need for radiation therapy [4, 7, 11, 12, 14].

In our case the preoperative imaging pointed to the diagnosis of rapidly growing thyroid tumour. Even though the patient presented the clinical features of neurofibromatosis, she had not been previously diagnosed for this condition neither had she had any clinical surveillance. We ourselves also did not initially consider the link between her skin lesions and a tumour in the neck region. It was the first case of MPNST in our centre during last 10 years and most of our thyroid surgeons did not even know about such a rare malignancy as MPNST. Considering the biopsy result the patient was operated with the preliminary diagnosis of thyroid cancer. Given that the surgery is the first-line treatment in thyroid cancer and that there is no neoadjuvant therapy in this kind of malignancy, the decision of surgical resection seemed to be quite obvious. Despite the fact that the tumour turned out to be a soft tissue sarcoma arising from the nerve sheath we do not find our decision as a wrong one. Neoadjuvant therapy in MPNST is not a standard option, mostly due to uncertain diagnosis in the biopsy. We resected the tumour as radically as possible with the addition of radiation therapy in the postoperative course. Given that the patient shows no recurrent disease after 14 months after first operation we may hope that the treatment was successful.

Generally, patients with neurofibromatosis type 1 are at particular risk of developing MPNST in comparison with general population, with a lifetime risk of MPNST of any location at about 6–10% [2, 3, 6, 13, 15]. Thus they should remain under clinical surveillance, especially if they present with plexiform neurofibromas. The estimation of the risk of malignant transformation of plexiform neurofibroma to MPNST is difficult. There are some issues concerning the diagnostics of loss of neurofibromin in NF-1 associated and sporadic MPNST. It was found that the loss of neurofibromin detected with the use of specific monoclonal antibodies occurs in almost 88% of NF-1 linked MPNST versus 43% in sporadic MPNST [7]. Neurofibromin specific antibody may also be used to differentiate MPNST from other spindle cell neoplasms [7]. The diagnostics and treatment of MPNST in different body sites are still unsatisfactory, with 5-years survival at about 50%. The schedule of postoperative follow-up has not been established due to rarity of the disease. No specific prevention is known. Since there are no specific imaging modalities allowing early diagnosis of MPNST in NF-1 patients the careful surveillance for any enlarging tumour of any location may prevent those patients from the death from this aggressive and life-threatening malignancy. As far as the head and neck MPNSTs are concerned it should be remembered that they can mimick different malignancies of this body part. Any rapidly enlarging mass of thyroid region should always undergo a differential diagnosis between an aggressive thyroid cancer and other malignancies like MPNSTs or lymphomas in order to avoid misdiagnosis and suboptimal treatment.

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