

A rare case of high-grade sarcoma as a true mixed tumor of the parotid gland – case report

Rzadki przypadek mięsakoraka o wysokim stopniu złośliwości jako prawdziwego guza mieszanego ślinianki przyusznej – opis przypadku

Authors' Contribution:

A – Study Design
B – Data Collection
C – Statistical Analysis
D – Manuscript Preparation
E – Literature Search
F – Funds Collection

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Article history: Received: 11.06.2020 Accepted: 25.06.2020 Published: 26.06.2020

SUMMARY:

Introduction: According to the National Cancer Registry, head and neck cancers account for 5.5 to 6.2% of all malignancies, which translates into about 5,500 to 6,000 new cases per year. Salivary gland tumors are a heterogeneous group of cancers, which results from the complex embryogenesis of salivary glands; they are divided into benign and malignant tumors. Common benign tumors include mixed tumors and Warthin tumors. Carcinosarcoma is called a true malignant mixed tumor because the tumor process involves both epithelial and mesenchymal elements. We reported the case of true malignant mixed tumor comprising three components: adenocarcinoma, synovial sarcoma (80%) and osteosarcoma (20%). This tumor develops rapidly and has an adverse course with a tendency to form metastases.

Case report: The work presents a case report of a 65-year-old patient who reported to the Department of Otolaryngology, ENT Oncology, Audiology and Phoniatics at the WAM Hospital due to a tumor of the right parotid gland. The patient was concerned with the rapid growth of the tumor that occurred within 2 months prior to hospitalization, causing deformation of facial features. ENT examination revealed a polycyclic tumor with limited mobility and asymmetry of the corners of the mouth (lowering on the right side). FNA diagnosed typical cancer cells suggesting malignant growth. The patient was qualified for surgical treatment. Under general anesthesia, the right parotid gland tumor with superficial lobe of the salivary gland and region II cervical lymphadenectomy on this side were removed. The postoperative course was normal. Postoperative histopathological examination described high-grade malignant parotid carcinoma, pT3Nx. The patient was referred to an oncology center to undergo radiotherapy.

KEYWORDS:

adenocarcinoma, carcinosarcoma, osteosarcoma, parotid gland cancer, synovial sarcoma

STRESZCZENIE:

Wprowadzenie: Zgodnie z Krajowym Rejestrem Nowotworów, nowotwory głowy i szyi stanowią od 5,5 do 6,2% wszystkich nowotworów złośliwych, co przekłada się na ok. 5,500 do 6,000 nowych zachorowań w ciągu roku. Guzy gruczołów ślinowych stanowią heterogenną grupę nowotworów, co wynika z faktu złożonej embriogenezy gruczołów ślinowych. Dzielą się na guzy łagodne i złośliwe. Do często spotykanych nowotworów łagodnych należą guzy mieszane i guzy Warthina. Mięsakorak nazywany jest prawdziwym złośliwym guzem mieszanym, gdyż proces nowotworzenia obejmuje zarówno elementy gruczołowe, jak i struktury zrębowe. Prezentujemy przypadek prawdziwego złośliwego guza mieszanego przyuszniczy zbudowanego z trzech komponentów: raka gruczołowego, mięsaka maziówkowego (80%) oraz kostniakomięsaka (20%). Nowotwór ten rozwija się szybko i ma niepomyślny przebieg z tendencją do tworzenia przerzutów.

Opis przypadku: Opisano przypadek 65-letniej pacjentki, która zgłosiła się do Kliniki Otolaryngologii, Onkologii Laryngologicznej, Audiologii i Foniatrii Szpitala im. Wojskowej Akademii Medycznej z powodu guza prawej ślinianki przyusznej. Pacjentka zaniepokoiła się szybkim wzrostem guza, który nastąpił w ciągu 2 miesięcy przed hospitalizacją, powodując zniekształcenie rysów twarzy. W badaniu laryngologicznym stwierdzono policykliczny guz o ograniczonej ruchomości oraz asymetrię (obniżenie po stronie prawej) kąćców ust. W BACC rozpoznano atypowe komórki nowotworowe sugerujące rozrost złośliwy. Chora została zakwalifikowana do leczenia operacyjnego. W znieczuleniu ogólnym usunięto guz ślinianki przyusznej prawej wraz z płatem powierzchownym ślinianki oraz lymfadenektomią szyjną regionu II po tej stronie. Przebieg pooperacyjny był prawidłowy. W badaniu histopatologicznym pooperacyjnym opisano mięsakoraka o wysokim stopniu złośliwości ślinianki przyusznej, pT3Nx. Pacjentka została skierowana do ośrodka onkologicznego celem podjęcia radioterapii.

SŁOWA KLUCZOWE: kostniakomięsak, mięsakorak, mięsak maziówkowy, rak gruczołowy, rak ślinianki przyusznej

ABBREVIATIONS

Ca ex PA – carcinoma ex pleomorphic adenoma

CRP – C-reactive protein

CT – computed tomography

ECG – electrocardiography

FNAB – fine needle aspiration biopsy

MRI – magnetic resonance imaging

WHO – World Health Organization

INTRODUCTION

Malignant neoplasms of the salivary glands are estimated to account for 3% to 5% of all head and neck cancers worldwide. They appear with a frequency of 2.5–3 per 100,000 cases per year [1]. According to the National Cancer Registry, in Poland head and neck cancers represent from 5.5 to 6.2% of all malignant neoplasms, which translates into approx. 5,500 to 6,000 new cases per year. In 2016 there have been reports of a total of 347 new cases of malignant neoplasms affecting the major salivary glands, whereby 181 men and 52 women died of salivary gland cancer.

The crude incidence rate of malignant neoplasms of major salivary gland in Poland was 0.3/100,000 (0.9 for the parotid gland) for men and 0.2/100,000 for women (0.6 for the parotid gland), 51 new cases were detected in men for malignant neoplasms of other and unspecified major salivary glands (and 165 cases of neoplasms of the parotid gland), and 46 in women (126 cases of malignant neoplasms of the parotid gland).

In the Lodzkie Voivodship there were 14 cases of malignant neoplasms of the parotid gland and 6 cases of malignant neoplasms of other and unspecified major salivary glands in women, while in men, 13 new cases of malignant neoplasms of the parotid gland and 9 cases of malignant neoplasms of other and unspecified major salivary glands were detected [2].

Salivary gland tumors constitute a heterogeneous group of neoplasms due to the complex embryogenesis of the salivary glands. They are divided into benign and malignant tumors. Benign neoplasms stand for around 80% of salivary gland tumors. The most numerous groups are benign tumors, i.e. Warthin's tumor, mixed tumor. Malignant neoplasms represent approximately 25–30% of salivary gland tumors, those are mainly: mucoepidermoid carcinoma, acinocellular carcinoma, adenoid cystic carcinoma; pleomorphic carcinoma, adenocarcinoma, squamous cell carcinoma [3].

In the 4th edition of 2017, the WHO histopathological classification distinguishes 19 types of malignant neoplasms of the salivary glands [4]. Malignant pleomorphic adenoma stands for 20–25% of malignant neoplasms of the salivary glands. The condition is classified as a form of carcinoma ex pleomorphic adenoma

(Ca ex PA), carcinosarcoma or metastasizing pleomorphic adenoma. The disease occurs usually in the 6th and 7th decade of life, with a similar frequency in both sexes [5].

Carcinoma ex pleomorphic adenoma may arise de novo (5–10% of tumors) or simultaneously in benign form and is characterized by the presence of benign adenomas and malignant carcinomas (undifferentiated carcinoma, ductal carcinoma, myoepithelial carcinoma, unspecified adenocarcinoma). The appearance of the malignant component promotes tumor growth and triggers the formation of distant metastases to the lymph nodes, lungs, liver and bones. The prognosis is poor. It is estimated that 30% survive the period of 5 years; distant metastases (more frequent than local) to the lungs, bones affect 25–40% of patients [6].

Metastasizing pleomorphic carcinoma has the characteristics of a benign tumor but is accompanied by metastasis to lymph nodes and distant organs, such as bones, lungs, skin, kidneys, pelvis, pharynx, and central nervous system. Metastases can occur several decades after the diagnosis of primary tumor and are often preceded by tumor recurrence. Although histopathological examination does not reveal any elements of malignant neoplasm in the primary tumor and the metastatic focus, almost 50% of patients die from neoplastic disease within 3 years [7, 8].

In 1967, Ordie H. King was the first to use the name carcinoma [9]. The neoplastic process in carcinosarcoma involves two components – epithelial and mesenchymal, therefore it is called a true malignant mixed tumor; in such case, the most commonly observed are cells of ductal carcinoma, mucoepidermoid, chondrosarcoma, sporadically osteosarcoma, undifferentiated sarcoma [10]. Most often it appears on the grounds of pleomorphic adenoma, although the occurrence of a de novo tumor is also possible [11].

We present a case of a true malignant mixed tumor made of three components: adenocarcinoma, synovial sarcoma (80%) and osteosarcoma (20%).

CASE REPORT

Patient E.D. 65 years old, medical history no. 20-5064 admitted to the Department of Otolaryngology, Laryngological Oncology, Audiology and Phoniatrics of the WAM University Clinical Hospital for elective surgery. The patient reported changes in the right parotid gland 30 years ago. The tumor gradually enlarged in size, but there has been an acceleration in growth in the last two months. The patient experienced discomfort within the lesion – the tumor distorted her facial features, and she also reported periodic aching pain (Fig. 1.). For 3 weeks, the patient had observed a change in facial expressions – the present asymmetry (lowering on the right side) of the corners of the mouth and biting of the lower lip on the right side during meals. She denied other head

and neck disturbances and injuries; she also suffers from chronic diseases – type 2 diabetes, hypertension, ischemic heart disease, hypercholesterolemia.

The patient provided the result of fine needle aspiration biopsy (FNAB) on 27/02/2020: atypical cells/most likely cancerous. Contrast-enhanced computed tomography of the neck revealed: on the right side of the neck, a polycyclic nodular lesion of approx. 83 x 54 x 71 mm, with solid and cystic component, with the presence of calcifications within the outer wall and numerous internal partitions. The tumor is likely to arise from the right parotid gland. The tumor adjoins the lateral outline of the branch and the angle of the mandible on this side, in the area of the mandibular angle, it causes a segmental loss of the cortical layer approx. 13 mm in length – erosion/local infiltration. The tumor pushes the upper section of the sternocleidomastoid backwards, it is not adjacent to the vascular bundle. A single enlarged oval level II lymph node on the right, 11 mm on the short axis, with a normal fatty hilum – it does not meet the meta criteria. In addition, the cervical lymph nodes are not enlarged (Fig. 2).

Laryngological examination: the right parotid gland projection shows a visible tumor of approx. 15 cm x 10 cm in diameter, hard, immovable relative to the substrate; skin covering the tumor unchanged, no ulceration, normal temperature of skin. Disturbed facial expression – asymmetrical corners of the mouth. In laboratory tests: morphology, creatinine, CRP, ionogram, no significant deviations were observed. Additional ECG and chest X-ray (pulmonary fields without focal changes) also did not describe pathological changes.

The patient was qualified for surgery to remove the right parotid gland tumor together with the superficial lobe of salivary gland and cervical lymphadenectomy of region II on that side under general endotracheal anesthesia. The incision in the right preauricular region extended to right submandibular region allowed to produce a skin flap, revealing the tumor of the right parotid gland, dimensions approx. 90 x 60 x 70 mm, which progressed to the superficial lobe of the right parotid gland and adhered to the mandibular branch and shifted posteriorly to the upper insertion of the sternocleidomastoid without infiltrating the neurovascular bundle. After presenting the facial nerve trunk between the superficial and deep lobe of the parotid gland, the tumor was completely dissected together with the superficial lobe of the parotid gland. The lymph node of region II on the right side, 11 mm in the short axis with a normal fatty hilum, was also removed. Hemostasis was achieved by electrocoagulation. This was followed by the placement of a drain and sutures. Facial expressions were preserved (a visible slight drop of the right corner of the mouth was also present before the surgery). The material (right parotid gland tumor with a superficial lobe of the salivary gland and a region II node on this side) was sent for histopathological examination (Fig. 3.). Histopathological examination of the postoperative material revealed that the tumor consists of two weakly intertwined components. The first is G3 adenocarcinoma embedded with hyaline stroma, and the second is a high-grade mesenchymal component. The mesenchymal component has changes that support synovial sarcoma (80%) and osteosarcoma (20%). Immunohistochemical



Fig. 1. Visible tumor of the parotid gland on the right side.



Fig. 2. CT of the neck with a visible tumor of the right parotid gland.

profile of cancer cells: Vimentin (+), CD 99 (+), CK AE 1/AE 3 (+), EMA (+), SMA (-), S-100 (-), Desmin (+/-), CK 7 (+), CK 20 (-). Ki67 proliferation index of about 90%. Histochemical reactions: Masson's Trichrome and PAS. The tumor adheres to the salivary gland, although there are no clear signs suggesting the presence of a mixed tumor. The focal tumor is visible in the line of surgical tissue dissection. Final diagnosis: high-grade sarcoma of the parotid gland, pT3Nx. The patient was referred to an oncology center for radiotherapy.

DISCUSSION

In English literature, sarcomatoma also referred to as pseudosarcoma, pseudosarcomatous squamous cell carcinoma, pleomorphic



Fig. 3. Isolated tumor after resection.

carcinoma, spindle cell carcinoma [12] is an extremely rare cancer of the salivary glands. It stands for from 0.04% to 0.4% [13, 14] of all salivary gland tumors, 0.4–1.0% [15] of malignant tumors of the salivary glands.

The tumor consists of two elements: epithelial, which is most often adenocarcinoma or squamous cell carcinoma, and mesenchymoma, mainly osteosarcoma, chondrosarcoma [11].

The primary site of occurrence are the major salivary glands – parotid (about 65%), submandibular (19%), sublingual (14%) glands [16], sporadically in the minor salivary glands [17], the maxillary sinuses [18], the larynx [19], and individual cases are described on the tongue [20]. It can appear where there is squamous epithelium – the mammary glands, upper and lower respiratory tract, gastrointestinal tract, urogenital tract, skin. The neoplasm is aggressive with a tendency to recur locally and form distant metastases, which are most common in the lungs, and are also found in the bones, liver and central nervous system [21]. There is a report of a patient with the first manifestation of the disease caused by metastases to the brain [15] as well as a case of a patient with metastases of sarcoma to the abdominal cavity [22].

Depending on the literature, the age of patients with this rare neoplasm is estimated at the 6th and 7th decade of life, between 60 and 65 years [13], 14 and 87 years (average age 58 years) [16], 35–83 years (average age 64) [22].

The symptoms reported by patients include: dysphagia, pain when swallowing, ear pain, hoarseness, apnea, weight loss [23], facial paralysis [24]. They can also be asymptomatic [11].

Symptoms that may suggest a malignant nature of the tumor are rapid growth (exception – highly differentiated mucoepidermoid carcinoma); hard, motionless, painful tumor covered with

ulceration, lymph node metastases, swollen, hard lymph nodes, and facial paralysis or recurrent inflammation in parotid gland tumors [25].

Sarcomas are rapidly growing [22], hard, immovable tumors, often distorting facial features [26].

They appear in two periods, within a few months (3–6 months) [11] or a few or several years (15–30 years) [27], when there is a sudden, rapid growth of an existing tumor [26].

Sarcomas are malignant neoplasms of soft tissues, they stand for approx. 1% of malignant tumors of the head and neck [28]; in this region synovial sarcoma appears more often in the lower pharynx and parapharyngeal space than in the area of the salivary glands [29]. In the parotid glands it may resemble a mixed tumor [30]. Primary treatment options are radical surgery and post-operative radiotherapy [31].

Osteosarcoma is a malignant bone tumor that rarely occurs outside of the bone tissue [32].

Fine-needle aspiration biopsy of the salivary glands is highly specific (97%) but not very sensitive (80%). The identification of atypical spindle cells, pleomorphic epithelial cells in the vicinity of necrosis constituted an indication to consider the diagnosis of sarcoma. The detection of sarcoma by fine-needle aspiration biopsy (FNAB) is a challenge [33], but due to its complex structure, it often does not reveal the type of tumor [11].

Imaging tests to detect tumors in the salivary glands include: ultrasound, CT with contrast, MRI [23, 24]. MRI imaging gives a more precise picture of neoplastic infiltration, while CT allows to assess bony destruction and metastasis to lymph nodes. Differentiation of benign lesions from malignant on the basis of CT and MRI was estimated at 83% and 85% for computed tomography and 81% and 89% for MRI [34, 35].

The primary option of treating sarcoma is surgery, which consists in removing the lesion with the margin of healthy tissues and the use of postoperative radiotherapy or chemotherapy [36]. If the tumor is present in the parotid gland, total parotidectomy is performed using facial nerve monitoring [23].

Cancer diagnosis is made on the basis of a histopathological examination with an immunohistochemical assessment. The expression of Ki67 [37], the presence of cytokeratin, PAS and epithelial antigens in the cancer component, and vimentin [11, 33], S-100, SMA, desmin [14] have been demonstrated in sarcoma cells.

In malignant neoplasms of the salivary glands, survival is impacted by the level of Ki67, age and tumor advancement level [34].

The prognosis for sarcoma of the salivary glands may depend on their structure. Marcotullio et al. [11] described a patient with sarcoma (squamous cell carcinoma, osteosarcoma) of the submandibular salivary gland who was followed for 6 months without recurrence. Taki et al. [23] presented a patient with sarcoma (squamous

cell carcinoma, chondrosarcoma) of the parotid salivary gland, in whom the disease had not recurred within 14 months. Carson et al. [27] described a patient with parotid carcinoma (adenocarcinoma, osteosarcoma) who died within 9 months of diagnosis, and showed that patients with this tumor die within the first year. Stafieri et al. [24] estimated that 31.6% of patients die within an average of 10.1 months from diagnosis. Gnepp et al. [38] estimated life expectancy at 29.3 months on the basis of 18 patients. Stephen et al. [21] believe that the average life expectancy after surgery was 3.6 years.

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Word count: 3671 Tables: – Figures: 3 References: 38

Access the article online: DOI: 10.5604/01.3001.0014.2502

Table of content: <https://otorhinolaryngologypl.com/issue/13389>

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Competing interests: The authors declare that they have no competing interests



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Cite this article as: Kolary-Siekierska K., Jalocho-Kaczka A., Olszewski J.: A rare case of high-grade sarcoma as a true mixed tumor of the parotid gland – case report; Pol Otorhino Rev 2020; 9 (3): 59-64
