Myogenic sarcoma of larynx – a case report and review of the literature

Myogenic sarcoma krtani – opis przypadku i przegląd piśmiennictwa

Maria Molga-Magusiak1DEF, Małgorzata Czesak1ADE, Anna Furman2F, Ewa Osuch-Wójcikiewicz2DE

1Chair and Clinic of Otorhinolaryngology, Head and Neck Surgery, Medical University of Warsaw, Poland; Head: prof. Kazimierz Niemczyk MD PhD
2Students' Scientific Circle at the Chair and Clinic of Otorhinolaryngology of Head and Neck Surgery at the Medical University of Warsaw, Poland

ABSTRACT:

Introduction: Myogenic sarcomas (MS) are malignant tumors of mesenchymal origin that include sarcomas of smooth muscle differentiation (leiomyosarcoma, LM) and skeletal muscle differentiation (rhabdomyosarcoma, RM). These neoplasms are extremely rare entities in larynx and often cause diagnostic difficulties.

Case: We present a case of laryngeal myogenic sarcoma partially differentiated into LM, treated with a surgical resection and an adjuvant radiotherapy. This study presents management and treatment according to the current literature.

KEYWORDS: head and neck surgery, laryngeal sarcoma, leiomyosarcoma, myogenic sarcoma

STRESZCZENIE:

Wprowadzenie: Mięśniakomięsaki (ang. myogenic sarcomas; MS) to mezenchymalne nowotwory złośliwe, wśród których wyróżniamy mięśniakomięsaki gładkokomórkowe (ang. leiomyosarcoma; LM) i prążkowanokomórkowe (ang. rhabdomyosarcoma; RM). Nowotwory te niezwykle rzadko występują w krtani, a ich diagnostyka sprawia wiele trudności.

Opis przypadku: Przedstawiamy przypadek pacjenta, u którego stwierdzono mięśniakomięsak krtani z dominującą komponentą komór gładkokomiesięcznych. Leczenie polegało na chirurgicznej resekcji i uzupełniającej radioterapii. Przentujemy postępowanie i leczenie mięśniakomięsaków zgodnie z aktualnymi wytycznymi.

SŁOWA KLUCZOWE: chirurgia głowy i szyi, mięsak krtani, mięśniakomięsak gładkokomórkowy, mięśniakomięsak

ABBREVIATIONS

ADIC – adriamycin and dacarbazine
AJCC – American Joint Commission on Cancer
COVID-19 – coronavirus disease 2019
CT – computed tomography
EBV – Epstein-Barr virus
EMA – epithelial membrane antige
G3 – myogenic sarcoma
LM – leiomyosarcoma
MRI – magnetic resonance imaging
MS – myogenic sarcoma
RM – rhabdomyosarcoma
RT – radiotherapy
SMA – muscle-specific actin
TNM – tumour, node, metastasis classification

INTRODUCTION

The most common malignancy of the larynx is a squamous cell carcinoma. It accounts for 95–98% of all malignant tumors at this site, with the remaining part consisting of adenocarcinomas and sarcomas. Tumors of mesenchymal origin are rare (less than 1% of laryngeal malignancies), with chondrosarcoma being the most common [1]. Myogenic sarcomas (MS) include sarcomas of smooth muscle differentiation (leiomyosarcoma; LM) and skeletal muscle differentiation (rhabdomyosarcoma; RM). These neoplasms are uncommon in the larynx, with only a sparse number of cases reported in international literature [2–6]. Clinical presentation is similar to laryngeal cancer, usually with hoarseness as the first sign. Depending on the tumor localization and size, symptoms include sore throat, dysphagia, and respiratory distress in case of advanced progression. Diagnostic evaluation is based on fiberoptic laryngoscopy and radiological
imaging, starting with computed tomography (CT), followed by magnetic resonance imaging (MRI). The final diagnosis is confirmed in histopathological examination of deep biopsy specimen taken in direct laryngoscopy. Immunohistochemical staining is a necessary complementation of conventional microscopic examination. Surgery with or without radiotherapy is a standard treatment [7].

**CASE REPORT**

A 63-year-old male with a 2-year history of hoarseness and dysphonia was referred to the clinic. The patient was a heavy smoker for over 40 years and had no comorbidities. During the year prior to the admission, he had five direct laryngoscopies with a biopsy performed at a regional hospital. Histopathological examinations were indicative of an inflammatory process, but no dysplasia was found. On admission, indirect laryngoscopy revealed a lesion of the anterior aspect of the left vocal fold without restriction of vocal fold mobility. The tumor was removed with a 1–2 mm margin during type III laser cordectomy. Histopathological findings were described as connective tissue cells with proliferating fibroblasts.

Four months later, another transoral laser microsurgery was performed due to tumor relapse (Fig. 1.).

The whole lesion was resected. The result of histopathological examination was identical with all prior findings – tissue fibrosis, inflammatory fibroblasts. Three months later, the patient suffered from respiratory distress and required emergency tracheostomy, performed at a regional hospital. On admission to the clinic, indirect laryngoscopy revealed yellowish masses entirely obliterating the patient’s vocal folds. The patient had a contrast MRI of the neck on account of contraindications for contrast CT. The finding was a 21 x 3 x 35 mm mass, most probably originating from the left vocal fold. The tumor infiltrated the anterior commissure, paraglottic space on the left side, and adhered to the thyroid cartilage, without evident infiltration. The cervical lymph nodes were not enlarged (Fig. 2.).

Based on clinical presence and radiological findings, the patient was qualified for a surgery with intraoperative biopsy. Specimens were taken in direct laryngoscopy. After the Pathology Department informed about the presence of spindle cell malignant neoplasm, the second part of surgery proceeded – total laryngectomy with construction of a tracheoesophageal fistula and insertion of a laryngeal prosthesis, with elective lymphadenectomy on the left side. The surgical specimens were sent for microscopic examination (Fig. 3.).

Postoperative course was uncomplicated and the patient was discharged on the fourteenth day following the surgery.

Gross pathological examination described a 4 x 2.8 x 2 cm exophytic tumor comprising all levels of the larynx, localized on the left side, infiltrating the right vocal fold. Microscopy and immunohistochemistry [SMA (+), Caldesmon (-), Desmine (-), EA (-), CKAE1/AE3 (-), CK5/6 (-), EMA (-), p40 (-), CD34(-)] determined the presence of a high-grade sarcoma with non-full differentiation into leiomyosarcoma (myogenic sarcoma; G3). Surgical margins varied from 0.5 to 1.6 cm. No metastatic cells were found in the resected lymph nodes of levels II and III on the left side. Final staging classified the tumor as T2N0M0, R0. The Pathology Department reevaluated all of the previous samples and compared them with the current findings, but previous conclusions remained unchanged.

The patient was referred to an Oncology Center for 66 Gy adjuvant radiotherapy. Fourteen months following the surgery, he was diagnosed with pulmonary metastases. He was qualified for palliative chemotherapy; three cycles of adriamycin and dacarbazine (ADIC). Due to progression, he was treated with second line chemotherapy – gemcitabine and docetaxel. The patient died 22 months after total laryngectomy, the cause of death being defined as complications from a COVID-19 infection.

**DISCUSSION**

MS are malignant neoplasms of mesenchymal origin are divided into RS and LS, depending on differentiation. Both sarcomas account for a fractional number of head and neck cancers and their presence in the larynx is extremely rare. International literature describes less than 20 cases of laryngeal RS [4–6] and about 50 cases of laryngeal LS [1–4]. In our case, myogenic sarcoma presented a partial differentiation into smooth muscle cells.

No more than 3% of MS cases are located in the head and neck region. Smooth muscles of this area are located in pili, esophagus and tunica media of vessels and ducts. Therefore, such tumors could arise in the scalp, paranasal sinuses, orbit, oral cavity, and cervical esophagus [8]. LS account for about 5–6% of all soft tissue sarcomas [1]. This neoplasm occurs in the gastrointestinal tract, uterus, and retroperitoneal cavity. The first LS of the larynx was reported in 1939 by Jackson [9]. The etiology of laryngeal LS remains uncertain; a possible theory is primary carcinogenesis in smooth muscles of the laryngeal vessels or transformation of aberrant mesenchymal tissue [2].

The pathogenesis of MS is not associated with common larynx cancer risk factors, such as smoking or alcohol abuse. The factors correlating with higher MS incidence are: Von Recklinghausen’s disease, EBV infection combined with immunosuppression, and a past history of

---

**Fig. 1.** Tumor relapse on the left vocal fold.
Because of such casuistic occurrence of laryngeal LS, there are no guidelines for treatment. It should be resected surgically with a safety margin. The extent of surgery depends on the tumor size and localization, and the safety margins for soft tissue neoplasms are 0.5 cm [7]. Elective resection of cervical lymph nodes is considered controversial. Some authors claim it is unnecessary since metastasis in regional lymph nodes is rarely found. On the other hand, Cocks et al. suggest an elective resection in every case [13]. Radiotherapy (RT) is not recommended [10]. There is no evidence of malignant transformation of leiomyoma, thus LM is considered a neoplasm arising de novo [11].

The peak incidence of head and neck region LS is in the fifth decade of life; males are affected four times more often than females [8]. Mariotti et al. analyzed the localization of this tumor based on the available literature – approximately 40 cases. The results showed it involved the following regions of the larynx: 48.4% glottis, 32.3%, supraglottis, 6.5% subglottis, 6.5% supraglottis-glottis, 3.2% glottis-subglottis, and 3.2% all levels [10]. There is no TNM classification of laryngeal MS, the applicable TNM covers sarcomas of the whole head and neck region (Tab. I.) [7, 12].

A standard diagnostic tool is endoscopic examination with fiberoptic or stiff laryngoscopy. In radiological evaluation, the first step is contrast CT, complemented by contrast MRI. The final diagnosis is made after histopathological examination of deep biopsy specimen.

Myogenic sarcomas are a diagnostic challenge for pathologists. Microscopic evaluation shows spindle cells with signs of malignancy – cellular pleomorphism and high nuclear mitotic activity. MS are hard to differentiate from other mesenchymal neoplasms such as fibromas, fibrosarcomas or spindle cell squamous cell carcinoma. In recent years, diagnosis has become more accurate due to specific immunohistochemical staining, most importantly for desmin. MS does not have a specific immunohistochemical profile, but in most cases, it shows a positive reaction to SMA (muscle-specific actin), desmin and vimentin, and negative to CD34, S100 and cytokeratin [13].

LS rarely gives metastasis, typically hematogenously to the lungs and less often to the liver, bones, central nervous system, and skin [2]. Metastasis in regional lymph nodes is found infrequently, only in advanced progression of the disease in about 10–15% of cases [3].
of response is necessary – in case of no reaction, the patient should be treated surgically. Wider indications for chemotherapy exist for different types of sarcomas [7].

The assessment of prognosis and life expectancy for patients with LS of the larynx is uncertain due to lacking data. Based on the available literature, Goda et al. predict recurrence rates of approximately 30% and 5-year survival rates of 50%. Cases of organ-preserving surgery tend to have higher recurrence rates. The tumor size (>5 cm) and surgical margin are the most important prognostic factors [3].

In the metastatic stage, the treatment should follow recommendations for sarcomas located outside of the head and neck region [7]. In most cases, the location of metastatic disease for soft tissue sarcomas are the lungs. Surgical treatment of a single metastatic tumor is possible, although typically not recommended. Therapy should begin with chemotherapy, particularly in high grade neoplasms [15, 16]. Adequate chemotherapy can stabilize progression or even decrease the tumor mass, allowing further metastasectomy. Unfortunately, LS is characterized by low chemosensitivity, so metastasis certainly should be considered a poor prognosis.

As reported in this case, diagnostic evaluation of MS is hard and deceitful; clinical presentation is ambiguous and histopathological findings can be misleading. Despite its low incidence rate, MS must be considered in differential diagnosis since its progression can be rapid and life-threatening.

**CONCLUSIONS**

1. MS are extremely rare tumors of the larynx that are difficult to diagnose;
2. Immunohistochemical staining is a very important part of the diagnostic process;
3. Standard treatment is surgical resection with at least 0.5 cm margin and adjuvant radiotherapy.

**REFERENCES**
