DOI: https://doi.org/10.2298/SARH211104008U
UDC: 616.22-006.3

CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Primary sarcomas of the larynx – a report of three cases and literature review

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SUMMARY

Introduction Primary sarcomas are uncommonly seen in the larynx and comprise around 1% of all laryngeal malignant tumors. We present three cases of patients with different types of laryngeal sarcomas and discuss about diagnostic and treatment difficulties.

Case outline Each patient presented with hoarseness and shortness of breath. Computed tomography scans showed large transglottic tumors of the larynx with no signs of cervical lymphadenopathy and definitive diagnoses of sarcomas were made by pathologists. Each patient underwent total laryngectomy with clear resection margins. Patient with laryngeal leiomyosarcoma developed large locoregional relapse of malignant disease and pulmonary metastasis four months after surgery and patient with laryngeal osteosarcoma was diagnosed with inoperative locoregional relapse of malignant disease three months after surgery. Both patients died within six months after surgery. On the other hand, patient with laryngeal chondrosarcoma was disease-free during the three-year follow-up.

Conclusion Primary laryngeal sarcomas have low incidence and they differ from squamous cell carcinoma by their biological characteristics and behavior. Radical surgical resection remains the mainstay of treatment with uncertain outcome due to their high potential for recurrence or metastatic spread.

Keywords: sarcoma; leiomyosarcoma; osteosarcoma; chondrosarcoma; laryngeal neoplasms; laryngectomy

INTRODUCTION

Squamous cell carcinoma (SCC) accounts for 95–98 % of laryngeal carcinoma. On the other hand, primary sarcomas are uncommonly seen in larynx and comprise around 1 % of all laryngeal malignant tumors [1]. Considering the low incidence of laryngeal sarcomas, most of the literature data are obtained from single case reports and scanty [2, 3, 4]. The fact that they differ a lot in their biological behavior from SCC is what makes the accurate diagnosis essential in their management.

We present three cases of patients with different types of laryngeal sarcomas and discuss about diagnostic and treatment difficulties.

CASE OF LARYNGEAL LEIOMYOSARCOMA

A 58-year-old male presented to our clinic with complaints of shortness of breath and hoarseness which had been ongoing for several months. The patient had a medical history of previous endoscopic laryngeal surgery due to vocal fold polyp. Also, the patient had been exposed to toxic substances for years while working in a paint and varnish production facility. Indirect laryngoscopy and microlaryngoscopy revealed large infiltrative laryngeal tumor of the right ventricular fold and both vocal folds with subglottic extension for 10 mm, which was seen also on computed tomography (CT) scan (Figure 1). The tumor paralyzed the right vocal fold and partially obstructed the airway. CT scan and neck ultrasonography showed no signs of cervical lymphadenopathy, and chest radiograph was normal. The diagnosis of low-grade laryngeal leiomyosarcoma (LLMS) was made after immunohistochemical analysis (Figure 2). The patient underwent total laryngectomy with clear resection margins (T3 tumor stage). He had a quick recovery and a successful voice rehabilitation. Unfortunately, the patient developed a large locoregional relapse of malignant disease and pulmonary metastasis four months following the surgery. Chemotherapy was not used due to pronounced bleeding from the tumor recurrence which caused the patient's death six months after laryngectomy.

CASE OF LARYNGEAL OSTEOSARCOMA

A 59-year-old male was admitted to hospital treatment due to severe dyspnea. Initial management was conducted as urgent tracheostomy and followed by CT scan and microlaryngoscopy, which point to a large, locally destructive

Received • Примљено: November 4, 2021
Revised • Ревизија: December 24, 2021
Accepted • Прихваћено: December 30, 2021
Online first: January 17, 2022

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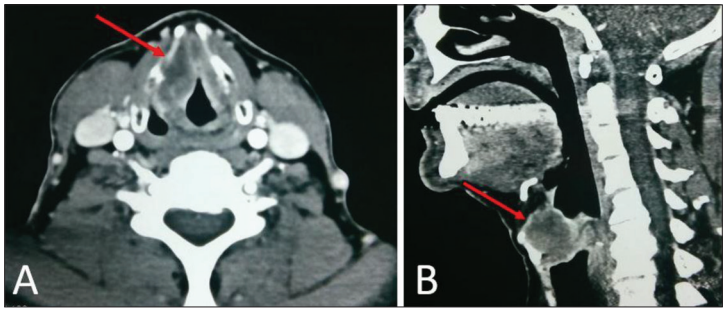

Figure 1. Computed tomography scan of the neck: axial (A) and sagittal view (B); arrows point to laryngeal leiomyosarcoma

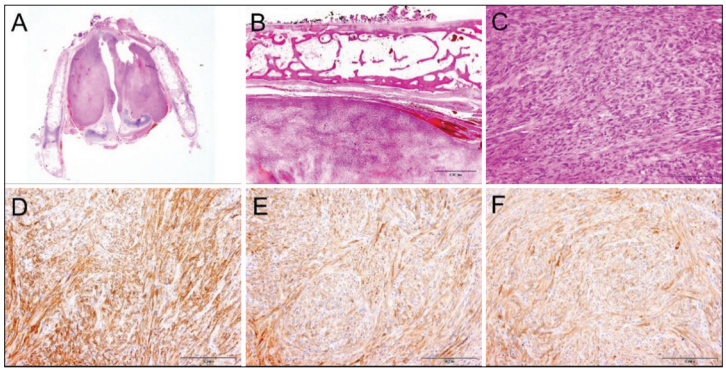

Figure 2. Histopathological finding of laryngeal leiomyosarcoma; hematoxilin-eosin; A – tumor fills paraventricular space (whole organ section); B – but not infiltrates thyroid cartilage; C – tumor is cellular and is composed of fascicles of atypical smooth muscle cells; mitoses are numerous and atypical; Ki67 proliferative index is 40% (not shown); D – tumor is positive for ASMA; E – calponin; F – h-caldesmon

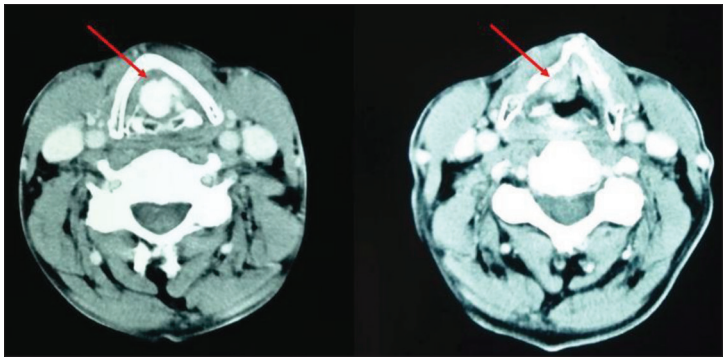

Figure 3. Computed tomography scan of the neck: axial views; arrows point to laryngeal osteosarcoma

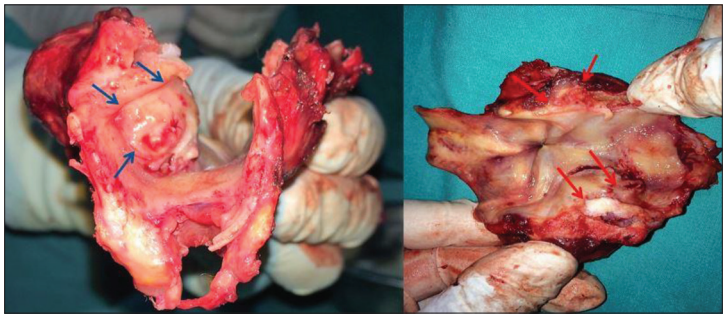

Figure 4. Surgical removal of the larynx with osteosarcoma

laryngeal tumor with bone tissue density (Figure 3). Patient did not have enlarged lymphatic nodes of the neck and total laryngectomy was performed with clear surgical margins (Figure 4). Definitive diagnosis of high-grade laryngeal osteosarcoma (LOS) was made after surgery by a pathologist (Figure 5). The patient was diagnosed with inoperative locoregional relapse of malignant disease three months after surgery and had no distant metastases. Unfortunately, lethal outcome occurred five months after laryngectomy.

CASE OF LARYNGEAL CHONDROSARCOMA

An 87-year-old male visited an ear, nose, throat specialist because of hoarseness that began several months ago. Patient had no history of tobacco or alcohol consumption. Indirect laryngoscopy showed submucosal lesion of the left ventricular and vocal fold with subglottic extension and substantial airway reduction. An expansive lesion of both laminas of thyroid cartilage, as well as cricoid cartilage (size 30 × 37 × 29 mm) with no cervical metastatic lymph nodes was seen on CT scan (Figure 6). Microlaryngoscopy revealed that the lesion is quite hard after submucosal resection and histopathology finding was inconclusive, whether the tumor is chondroma or chondrosarcoma. The patient underwent total laryngectomy and postoperative histopathological analysis confirmed low-grade chondrosarcoma on multiple sites of larynx (Figure 7). Despite his age and tumor extensiveness, the patient had an excellent recovery and mastered the esophageal speech technique with success. Patient was closely controlled and was disease-free during the three-year follow-up.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written consent to publish all shown material was obtained from all patients.

DISCUSSION

Very low incidence of LLMS has been attributed to the scarcity of smooth muscle tissue. Although it is widely accepted that LLMS originates from vascular smooth muscle in the tunica media of the vessels, some authors reported the aberrant differentiation of mesenchymal tissue as an alternative mechanism in the pathogenesis [5]. Abnormal differentiation after posttraumatic healing process may lead to LLMS formation, although the exact pathway has not been defined yet. Metachronous LLMSs after resection of SCC have been reported and laryngeal

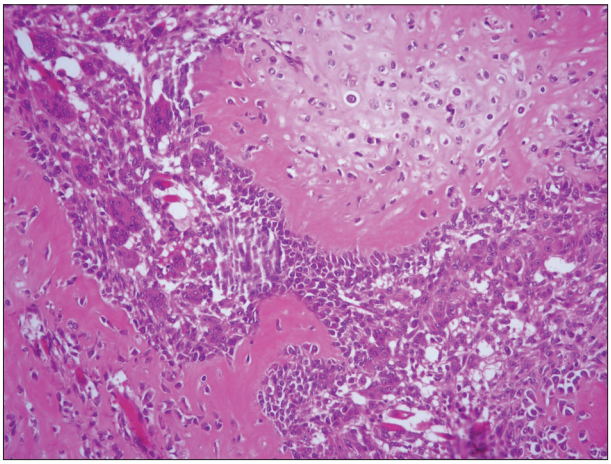

Figure 5. Conventional osteosarcoma, high-grade; Haematoxillin & Eosin, original magnification × 200

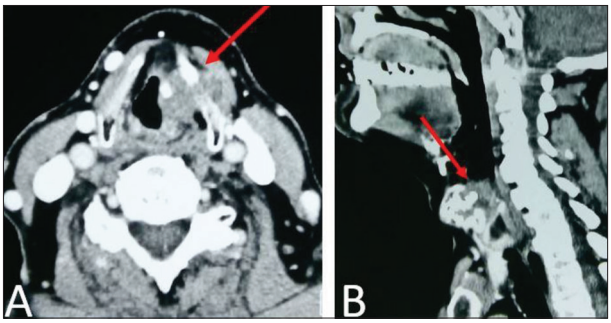

Figure 6. Computed tomography scan of the neck; A – axial; B – sagittal view; arrows point to laryngeal chondrosarcoma

surgery has been identified as a predisposing factor [5]. On the other hand, cases of concurrent LLMS and SCC suggest the involvement of more than one neoplastic process [6].

LOS is considered to originate from immature bone forming cells or after differentiation of chondroblasts and fibroblast into osteoblasts. Skeletal Paget's disease, fibrous dysplasia and previous exposure to the radiation are thought to be a risk factor for LOS development [7]. Further predisposing factors include laryngeal ossification and dedifferentiated chondrosarcomas. Direct correlation between tobacco smoking or alcohol and LOS is no established and the etiology still remains unclear [8].

Laryngeal chondrosarcoma (LCS) arises from cricoid cartilage in 80% of cases [2]. LCSs present with hoarseness in most of the cases. Involvement of the glottis is seen in about 60% of the patients with LLMS and in about 40% of patients with LOS [7], often in combination with supraglottic involvement. It is highly likely that localization of endolaryngeal tumor does not make a significant difference in the clinical outcome. On the other hand, there is a strong correlation between symptoms and tumor sites, so it is expected that any tumor of the glottis might be diagnosed and treated in early stages of the disease, due to its presentation with hoarseness. About one-third of patients with LLMS have dyspnea or stridor at the moment of diagnosis [9]. Other symptoms such as dysphagia, hemoptysis or metastatic lymph nodes are indicators of advanced stage of malignant disease.

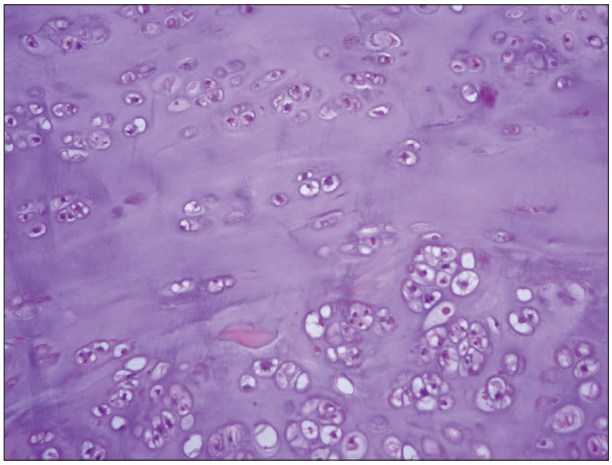

Figure 7. Low-grade malignant mesenchymal proliferation consistent with the diagnosis of chondrosarcoma, Grade 2; Haematoxillin & Eosin, original magnification × 200

Clinical presentation of laryngeal sarcomas should be considered with respect to their biological behavior that differs from SCC. In leiomyosarcomas and osteosarcomas, hematogenous spread of tumor cells is seen far more frequently than lymphatic spread. Furthermore, jugular vein invasion or metastatic deposits in lung and liver may be present without any sign of cervical lymph node involvement. Therefore, it is very important to perform a detailed preoperative evaluation of possible distant metastases and neck dissection is not mandatory in number of cases. On the other hand, LCSs usually present as local disease and distant metastases are quite uncommon, especially in non-aggressive low-grade forms of chondrosarcoma.

Laryngeal sarcomas are macroscopically similar to SCC and definitive diagnosis is made by histopathology. CT and magnetic resonance imaging provide additional information regarding tumor extension and lymph cervical lymph node status. Differential diagnosis of LLMS may be challenging with small biopsies and should include spindle cell tumors, such as rhabdomyosarcoma, melanoma, malignant fibrous histiocytoma or sarcomatous carcinoma [10]. Histologically, leiomyosarcoma is characterized by fascicles of spindle cells with cigar-shaped, blunt-ended nuclei, but light microscopy is insufficient to make an accurate diagnosis [5, 11]. Therefore, immunohistochemistry is mandatory and provides a reliable diagnosis in most cases. Leiomyocytes are positively stained with smooth muscle actin, desmin, and vimentin, whereas stained negatively with cytokeratin and S-100. In most of the LOS cases, multiple biopsies are necessary to achieve a proper diagnosis [8]. Spindle cell sarcoma, metastases from the primary sarcoma, carcinosarcoma and other malignancy with osseous metaplasia should be considered in diagnostic work-up [12]. It is essential to differentiate LCS from chondroblastic osteosarcoma that is characterized by the presence of osteoid material with signs of high-grade malignancy surrounded by hypercellular spindle cells [13]. Also, it is not unusual for chondrosarcoma to be misdiagnosed as laryngeal chondroma.

The primary choice of treatment for laryngeal sarcomas is surgical resection with wide surgical margins. Stage and

localization of malignant disease affect the type and range of surgical procedure. Total laryngectomy showed lower recurrence rate and better prognosis, compared to organ preservation surgery. All of our patients underwent total laryngectomy due to advanced stage of sarcomas, although they had different outcome.

Neck dissection is not recommended, unless there is radiological evidence for regional metastasis. Sarcomas are considered to be radioresistant tumors and no efficacy of postoperative radiation therapy (RT) has been demonstrated in patients with osteosarcoma [7]. There are some evidences regarding the adjuvant use of RT which slightly reduce the risk of local recurrences in patients with LLMS [14]. Conventional RT is proved to be ineffective as treatment of laryngeal chondrosarcoma due to slow-growing nature of the tumor, although it has a role as adjuvant treatment or palliative measure. Furthermore, local control has been achieved by adjuvant RT in 94% of patients with residual tumor after chondrosarcoma resection [15]. The role of chemotherapy as a treatment of laryngeal sarcoma is controversial. Sarcomas are not chemosensitive tumors and chemotherapy is usually reserved for the treatment of distant metastasis and may also provide some benefit where surgery is not an option.

Although the most chondrosarcomas are low grade and are not characterized by aggressive behavior, recurrence rate is reported to be 18–40%. On the other hand, high-grade chondrosarcomas have 70% higher metastatic potential, compared to low-grade chondrosarcomas and are associated with poorer prognosis and 10-year survival rate of 29% [2]. LLMSs showed recurrence rate of 30% with five-year survival rate of 50% [15], whereas mean time to locoregional LOS recurrence and LOS distant metastasis is five months and 12 months, respectively [7]. About half of the patients with laryngeal osteosarcoma die within 20 months after surgery [8].

In conclusion, primary laryngeal sarcomas are rare malignant tumors that differ from SCC by their biological characteristics and behavior. Radical surgical resection remains the mainstay of treatment with uncertain outcome due to their high potential for recurrence or metastatic spread.

Conflict of interest: None declared.

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Примарни саркоми ларинкса – приказ три болесника и преглед литературе

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САЖЕТАК

Увод Примарни саркоми ларинкса су веома ретки и чине око 1% свих ларингеалних малигних тумора. Представљамо три болесника са различитим типовима саркома ларинкса и расправљамо о дијагностичким и терапијским потешкоћама.

Приказ болесника Сва три болесника имала су промуклост и осећај тежег дисања на прегледу. Компјутеризована томографија је код сваког показала велике трансглотисне туморе ларинкса без знакова лимфаденопатије врата, а дефинитивна дијагноза саркома постављена је од стране патолога. Сваки болесник је подвргнут тоталној ларингектомији са слободним линијама ресекције. Болесник са лејомиосаркомом ларинкса развио је велики локорегионални релапс малигне болести и плућне метастазе четири месеца после операције, а болеснику са остеосаркомом ларинкса дијагностикован је иноперабилни локорегионални релапс малигне болести три месеца после операције. Оба болесника су умрла у року од шест месеци након операције. С друге стране, болесник са хондросаркомом ларинкса био је без болести током трогодишњег праћења.

Закључак Примарни саркоми ларинкса имају ниску учесталост и разликују се од сквамоцелуларног карцинома по биолошким карактеристикама и понашању. Радикална хируршка ресекција остаје главни терапијски избор са неизвесним исходом због високог потенцијала за настанак рецидива или метастатског ширења.

Кључне речи: сарком; лејомиосарком; стеосарком; хондросарком; ларингеална неоплазма; ларингектомија