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Rare non-squamous cell neoplasms of the larynx

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Wojciech Smółka[1], Agnieszka Piotrowska-Seweryn[1], Jarosław Markowski[1], Piotr Paleń[2], Wirginia Likus[3], Włodzimierz Dziubdziela[4]

[1] Clinical Department of Laryngology, Medical University of Silesia, School of Medicine in Katowice
[2] Department of Pathology, Medical University of Silesia, School of Medicine in Katowice
[3] Division of Human Anatomy, Medical University of Silesia, School of Medicine in Katowice
[4] Outpatient Clinic of Chronic Pain Treatment, Sosnowiec

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ABSTRACT: Squamous cell carcinoma is the most common malignant neoplasm of the larynx. However, there are other rare malignancies that are reported by worldwide literature, such as neuroendocrine tumors, mesenchymal sarcomas, malignant salivary tumors, adenocarcinomas, lymphoepitheliomas, plasmocytomas and non-Hodgkin lymphomas.

The authors present several cases of rare laryngeal neoplasms with a particular consideration of their origin, histopathological characteristics and methods of treatment. They emphasize the necessity of careful diagnosis in case of laryngeal tumors with respect to patomorphological examination.

KEYWORDS: laryngeal neoplasms, mucoepidermoid carcinoma, chondrosarcoma, squamous cell neoplasms, synovial sarcoma

STRESZCZENIE: Rak płaskonabłonkowy jest najczęstszym złośliwym nowotworem krtani. Literatura światowa donosi jednak o istnieniu innych nowotworów tego narządu, takich jak: guzy neuroendokrynne, mięsaki mezenchymalne, złośliwe guzy ślinianek, gruczolakoraki, nowotwory limfoepitelialne, plazmocytomy oraz chłoniaki nieziarnicze.

Autorzy prezentują kilka przypadków takich rzadkich nowotworów krtani ze szczególnym uwzględnieniem ich prawdopodobnej etiologii, cech histopatologicznych oraz metod leczenia. Podkreślają także konieczność ostrożnego diagnozowania guzów wywodzących się z krtani pod kątem ich oceny histopatologicznej.

SŁOWA KLUCZOWE: nowotwory krtani, rak śluzowo-naskórkowy, mięsak, chrzęstniakomięsak, nowotwory płaskonabłonkowe, mięsak maziówkowy

INTRODUCTION

Squamous cell carcinoma (SCC) is the most common malignant neoplasm of the larynx and it comprises ca. 95% of all malignancies. Among non-SCC malignant cancers that occur in this location there are: 1) neuroendocrine tumors (NET), such as typical and atypical carcinoid, small cell neuroendocrine carcinoma and combined small cell carcinoma neuroendocrine type, 2) mesenchymal sarcomas, i.e. those arising from bone (osteosarcoma) or cartilaginous tissues (chondrosarcoma) or of soft tissue origin, like fibrosarcoma, liposarcoma, malignant fibrous histiocytoma, leiomyosarcoma, rhabdomyosarcoma, angiosarcoma, Kaposi sarcoma, synovial sarcoma, 3) malignant salivary tumors, i.e., mucoepidermoid carcinoma (MEC), adenoid cystic carcinoma and spindle cell carcinoma, 4) malignant melanoma, 5) adenocarcinomas, 6) lymphoepithelioma, 7) plasmocytoma, 8) non-Hodgkin lymphomas and other rare entities [1].

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The authors present several cases of the following malignant tumors: sarcomatoid carcinoma, MEC and chondrosarcoma, as well as two cases of benign neoplasm, i.e. granular cell tumor.

Chondrosarcoma is the second most common malignant neoplasm of the larynx, next to squamous cell carcinoma. It comprises about 75% of all laryngeal sarcomas and about 0.07-0.2% of all tumors in this region. It concerns mainly males, in the seventh decade of life. It usually derives from cricoid cartilage (78%) and it is characterized by slow growth. Chondrosarcoma is resistant to chemotherapy and radiotherapy, therefore surgical procedure remains the only effective treatment [1].

Sarcomatoid carcinoma is a rare neoplasm of the larynx with a reported incidence of 2% to 3% of all laryngeal cancers. Sarcomatoid carcinoma or spindle cell carcinoma or metaplastic carcinoma is a highly malignant variant of squamous cell carcinoma [2-4]. The treatment of spindle cell carcinoma is the most influenced by the tumor location and the stage of the tumor. The majority of spindle cell carcinomas are detected early in stages T1 or T2. These tumors are correlated with a better prognosis. Most spindle cell carcinomas are polypoid and a wide local incision can completely eliminate the entire tumor mass. Resection of the tumor via partial or total laryngectomy is the first-line treatment in tumors that are in stage 3-4. Spindle cell carcinoma of the larynx has a very good 5-year prognosis of 65-95%. Tumors with the presence of metastasis to local lymph nodes are followed by a combination of radiotherapy and chemotherapy [5-6].

Mucoepidermoid carcinoma (MEC) is a malignant neoplasm most commonly observed in the salivary glands, mostly the parotid gland and minor salivary glands. It was first described by Arcidiacomo and Lomeo in 1963 and it concerned a 39-year-old male, in whom total laryngectomy and adiuvant radiotherapy was performed [7]. MEC is characteristic for its histological composition - combined of epithelial tissue and mucous cells in between [8].

Granular cell tumors (GCT, Abrikossoff tumor) are uncommon benign neoplasms of the head and neck and they are rare in the larynx, as the anterior part of the tongue seems to be the most common setting. The origin of these neoplasms remains unknown. However, most authors believe in their neuroectodermal derivation. Its malignant transformations are observed in about 1-2% of cases.

The authors discuss the characteristics, probable etiology and treatment of above tumors based on available worldwide publications and own observations.

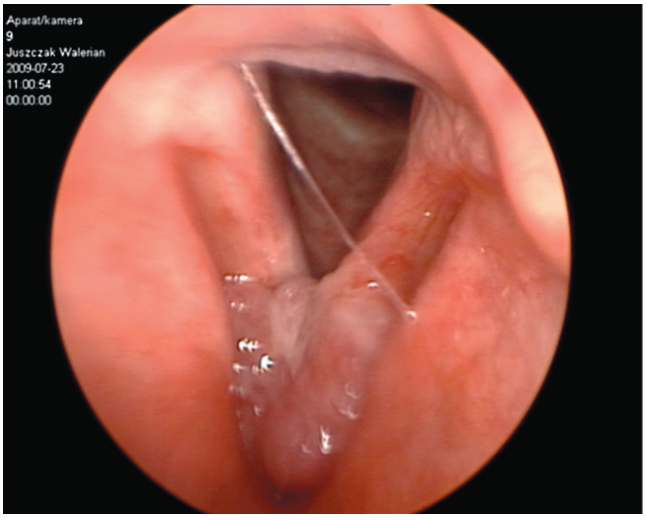

Fig.1. Videolaryngoscopy – laryngeal tumor of the anterior commissure and 1/3 part of both vocal folds, covered with unchanged mucosa.

CASE REPORTS

Sarcomatoid carcinoma - 1 case

A 68-year-old male patient with a history of 6-month hoarseness was admitted to our hospital in July 2009. An operation with excision of a tumor of the left vocal fold was undertaken in March 2009 in a municipal hospital. Histopathological examination (No. 231125/H) revealed chronic inflammation of the larynx. On admission to our Clinical Department a tumor of the anterior commissure and 1/3 part of both vocal folds, covered with unchanged mucosa was found in videostroboscopy [Fig.1]. Therefore, Kleinsasser's directoscopy with biopsy was performed. Patomorphological findings of the material (No. 1292221/H) showed the presence of sarcomatoid carcinoma. Immunohistochemical profile revealed positive reactions with vimentin, CK7, CD99, CD138, p63, Ki-67 – 90%. Negative reactions were found when analyzing with CK AE1/AE3, CK 5/6, desmin, actin, SMA, Myo-D1, EMA, LCA, CD56, NSE, chromogranin, synaptophysin, WT-1, S-100, HMB-45, E-cadherin. [Fig.3-5].

Due to patient's lack of agreement for radical treatment, he was referred to Radiotherapy Unit. However, no further actions were undertaken, as the patient gave no permission to it again.

Chondrosarcoma - 2 cases

Case 1

A male patient, aged 63, was admitted to our Clinic in March 2007 due to dyspnea and neck tumor. An assumption of re-

current chondroma was made. Tracheotomy and left hemilaryngectomy due to a 5x4x2-cm tumor deriving from thyroid cartilage had been performed in 1998. The follow-up visits in our outpatient department revealed no local recurrence between 2003 and 2015.

On admission the patient presented with plain tumor located in the right laryngeal ventricle and a hard, partially moveable tumor of 5 centimeters in diameter situated on the right side of the neck on the level of the thyroid cartilage. High-resolution computerized tomography showed an expansive tumor of 58 x 37 centimeters in size, of smooth outline with several calcifications that infiltrated the right thyroid cartilage and the upper part of the trachea [Fig.6].

The patient underwent total laryngectomy with resection of the upper three rings of the trachea. The postoperative pathomorphological examination revealed chondrosarcoma G1.

Case 2

A 84-year-old patient with a 2-year history of hoarseness and dyspnea was admitted to hospital in order to undergo urgent tracheotomy. The physical examination showed a hard tumor at the level of the cricoid cartilage on the left side. Videolaryngoscopy revealed tumor of the left side of the larynx covered with unaltered mucosa, constricting the glottis. The findings of biopsy showed myxoma. The patient gave no permission to radical operations, therefore laryngofissure with tumor resection were undertaken. Chondrosarcoma G2 was found in the histopathological examination. No recurrences have been observed so far.

Granular cell tumor (Abrikosoff tumor) – 2 cases

Case 1

A 44-year-old male patient was admitted to the Department in March 2001 due to hoarseness of 1.5- year duration. No weight loss was reported on. Videostroboscopy revealed the presence of an oval, plain tumor located in the anterior 2/3 of the left vocal fold. No infiltration of the contralateral vocal fold was seen. There were no metastatic lymph nodes, nor distant metastases. All laboratory test were normal.

Laryngofissure procedure with excision of an 8-mm-long tumor within free margins was performed. Postoperative histopathological findings (No. 1129654-5/H) showed the following results: mucosal polyp with granular cell tumor (Abrikosoff tumor) [Fig.7].

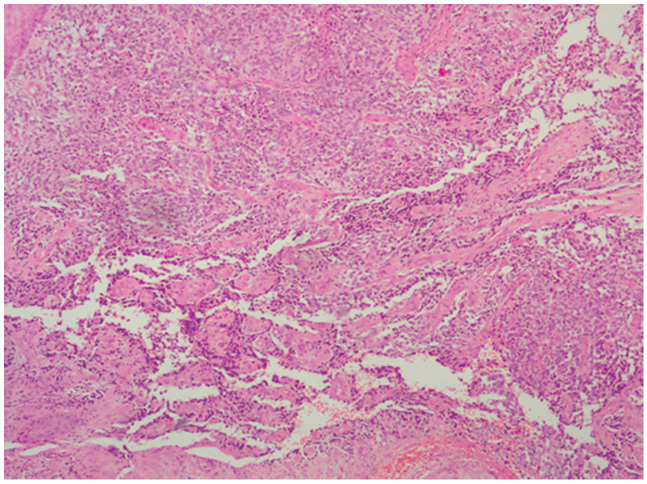

Fig. 2. Sarcoma synoviale monophasicum G II. HE staining. Magnification 10x.

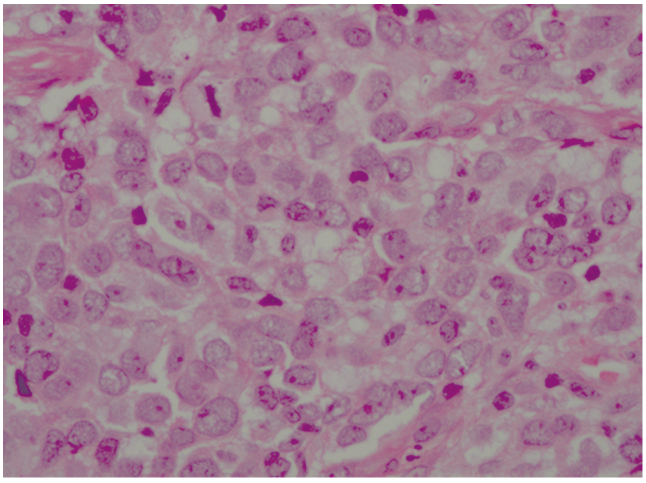

Fig.3. Sarcoma synoviale monophasicum G II. HE staining. Magnification 200x.

Case 2

A 56-year-old female was hospitalized in our Clinical Department in September 2001 due to hoarseness. Additional diseases included diabetes mellitus type 2 and hyperthyroidism.

On admission, a white tumor of 4 mm in diameter located on the lateral surface of the right arytenoid cartilage was discovered. Both vocal folds remained moveable, without pathologies. There were no enlarged lymph nodes of the neck palpable. The tumor was dissected totally during Kleinsasser's directoscopy. Pathomorphological examination (No. 1138528/H) revealed the presence of granular cell tumor [Fig.8].

Up to date, no recurrences have been reported. The patients remain under laryngological control in the outpatient department.

Mucoepidermoid carcinoma – 3 cases

Case 1

A 57-year-old male was admitted to our Clinic due to hoarseness of several months' duration. His previous history covered nasal polipectomy and septoplasty. On the physical examination, a tumor of 3 mm in length in the anterior 1/3 of the right vocal fold was revealed. Additionally, nasal polyps obstructing both nostrils were present. No enlarged cervical lymph nodes were palpable. Laboratory tests were insignificant. Kleinsasser's directoscopy with tumor excision and nasal polipectomy under general anaesthesia were performed. No postoperative complications were observed. The histopathological findings showed the presence of epithelial and mucosal tissues [Fig. 9]. The results were proved by Ab paS and mucicarmin staining for mucous and cytokeratin for the epithelial component of the tumor. There were three types of epithelial cells found: responsible for the production of mucous, intermediate and squamous cells. No neoplastic cells were observed in the lumen of blood vessels. The diagnosis was: 'Mucoepidermoid carcinoma of low-grade malignancy'.

The pathomorphological examination of the polyps proved the initial diagnosis.

No recurrences were observed in a 5-year follow-up. The vocal fold mobility remained normal.

Case 2

A 62-year-old male patient suffered from intermittent hoarseness for 5 years, with its intensification and continuity for 2 months prior to admission. Biopsy (No.103196) of the right false fold of the larynx performed in one of the municipal hospitals revealed chronic laryngitis with suspicion of carcinoma. On admission a tumor of uneven surface, covered with white coating located in both vocal folds, anterior commissure, right false vocal fold and right arytenoid cartilage with partial fixation of the right vocal fold was visualized endoscopically. Biopsy (No. 658384/P) of the right arytenoid cartilage proved the presence of squamous cell carcinoma and of the left vocal fold - chronic inflammation with proliferation and leukoplakia. There were no cervical lymph nodes palpable. Laboratory tests were normal, except for elevated ESR (25/48).

Total laryngectomy was performed in the patient. Macroscopically tumor's image was relevant to endoscopic findings. The results of histopathological examination (No.27701-13/K) showed mucoepidermoid carcinoma of high grade. Mucous cells and cyst-like forms containing mucus comprised majority of the tumor and they were surrounded by epithelial cells [Fig.9].

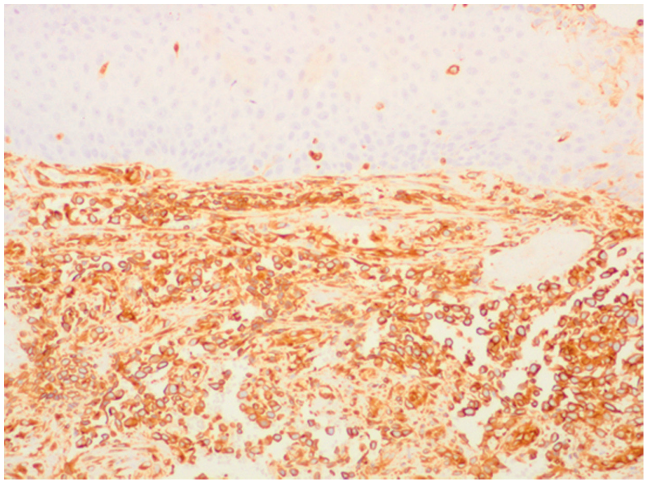

Fig.4. Sarcoma synoviale. Cytokeratin-7 antibody staining.

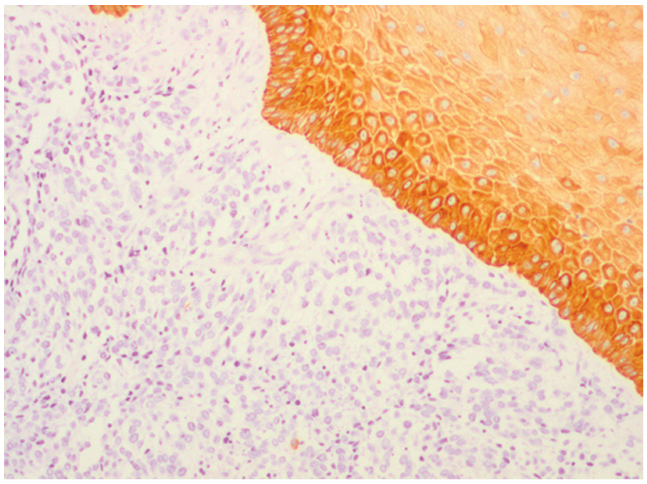

Fig.5. Sarcoma synoviale. Ki-67- proliferation index – 90%.

The patient underwent adjuvant radiotherapy with a total dose of 60 Gy. Until now no recurrences have been observed.

Case 3

A 56-year-old male patient complained of hoarseness present for 7 months and increasing dyspnea. Due to life-threatening dyspnea, tracheotomy was performed in a municipal hospital in September 2000. Additional biopsy (No.154097) revealed the presence of laryngeal squamous cell carcinoma. The patient was referred to our Clinical Department.

On admission a tumor infiltrating the left part of the larynx was visualized endoscopically. No enlarged cervical lymph nodes were found on physical examination. Concomitant diseases in-

cluded hypertension and diabetes mellitus type 2. There were no abnormal results of laboratory tests except for ESR (42/67) and glucose (7.3 mmol/l).

The patient underwent total laryngectomy. Postoperative pathomorphological examination (No.11244659/H) revealed the presence of MEC of high grade. The tumor infiltrated all layers of the mucosa and thyroid cartilage.

Adjuvant radiotherapy was performed. Up to date no recurrences nor metastases have been observed at follow-up visits.

DISCUSSION

Soft tissue sarcomas of the head and neck region account for 4-15% of all soft tissue sarcomas and less than 1% of all neoplasms in this region [9].

As far as chondrosarcoma is concerned, it has been proved that it is the second most common malignant neoplasm of the larynx, after squamous cell carcinoma. Laryngeal chondrosarcoma was first described by Volkmann in 1855. Among Polish authors who have presented cases of this kind of malignant tumor Zakrzewski, Stankiewicz, Walewska and Gierek should be mentioned [10, 11, 12, 13]. In the worldwide literature above 350 cases of laryngeal chondrosarcoma can be found. Its etiology still remains unknown, yet several studies speculate disordered ossification of the laryngeal cartilage to be one of the reasons for the development of chondrosarcoma. It is also presumed that chondrosarcoma might originate from metaplasia on the basis of chondroma, Paget's disease, chondromatosis or osteochondroma [14]. Depending on the degree of differentiation, image of nuclei, cellular polymorphism and mitotic index, three types of chondrosarcoma (low, medium and high grade tumors) can be specified [15]. Chondrosarcoma may spread endo- or extralaryngeally. On CT examination punctuate calcifications are the most characteristic within the tumor masses [16]. If the neoplasm derives from the cricoid cartilage, hoarse voice and gradually increasing dyspnea can be observed. In case of infiltration of the thyroid bone, a partially moveable tumor is the first symptom of the disease.

In the presented cases above characteristics are equal to observations of other authors. Windfuhr et al. described cases in which the first surgical procedure was performed due to chondroma and the recurrent tumor was qualified as a malignant one [17]. A similar situation was observed in the first case mentioned above. Also, slow growth and all symptoms provided strong evidence for the presence of chondrosarcoma and showed the similarity of our cases to other publications. The authors indicate surgical treatment as the recommended option in case of chondrosarcoma.

Sarcomatoid carcinoma is a rare tumor with a reported incidence of 2% to 3% of all laryngeal cancers. Sarcomatoid carcinoma can demonstrate varied histopathological appearance, depending on the case or within different areas of the same tumor tissue. Immunohistochemical studies of epithelial and mesenchymal markers are used to diagnose the tumor. Differential diagnosis includes such tumors as fibromatosis, nodular fasciitis, reactive epithelial proliferations, squamous cell carcinoma, fibrosarcoma, malignant fibrous histocytoma, leiomyosarcoma, rhabdomyosarcoma, malignant peripheral nerve sheath tumour, synovial sarcoma [3]. According to other authors, immunohistochemistry remains determinant in the differential diagnosis between sarcomatoid carcinoma and other neoplasms [18,19].

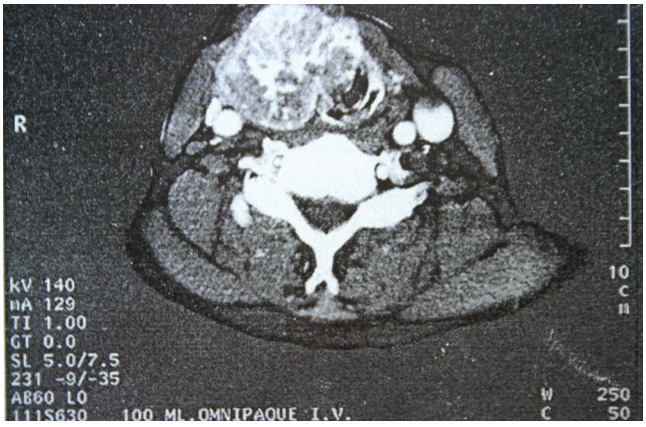

Fig.6. CT scan of laryngeal chondrosarcoma.

Mucoepidermoid carcinoma of the larynx remains a rare entity. More than 100 cases have been described in worldwide literature [20].Cady presented a study of 2 patients with MEC out of 2500 operated on due to laryngeal cancer in the Memorial Hospital of New York [21].Similarily, a low number of patients with MEC, i.e. 6, were noted in the analysis of 3100 cases of laryngeal malignancies in the Mayo Clinic [22].

MEC usually occurs in males (male to female ratio = 6:1) in the 7th decade of life. Only one case of a pediatric MEC in a 13-year-old patient has been reported by Mitchel [23].

Laryngeal location mostly concerns the supraglottic part of the larynx and rarely vocal folds and subglottis [24]. The reason for that situation lies in the fact that no muco-serous glands can be found in the glottic part of the larynx. The only possible explanation for the occurrence of MEC on vocal folds is the

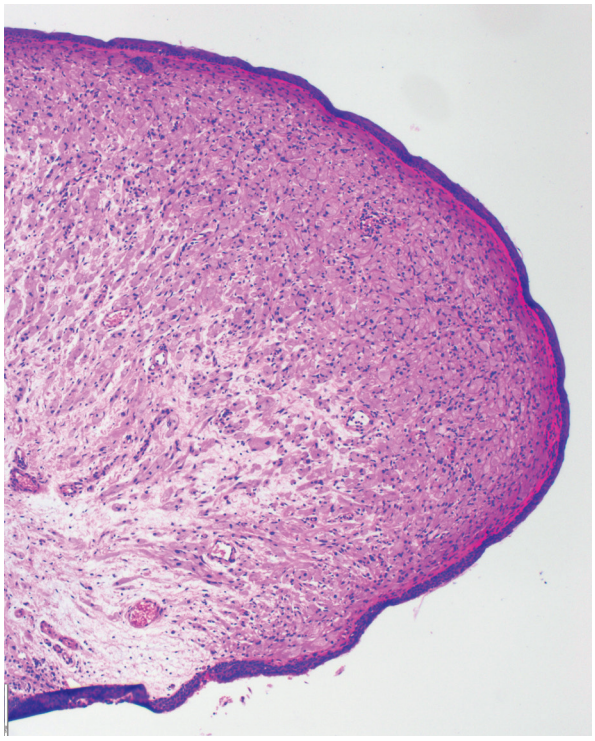

Fig.7. Polypoid granular cell tumor. Magnification 4 x.

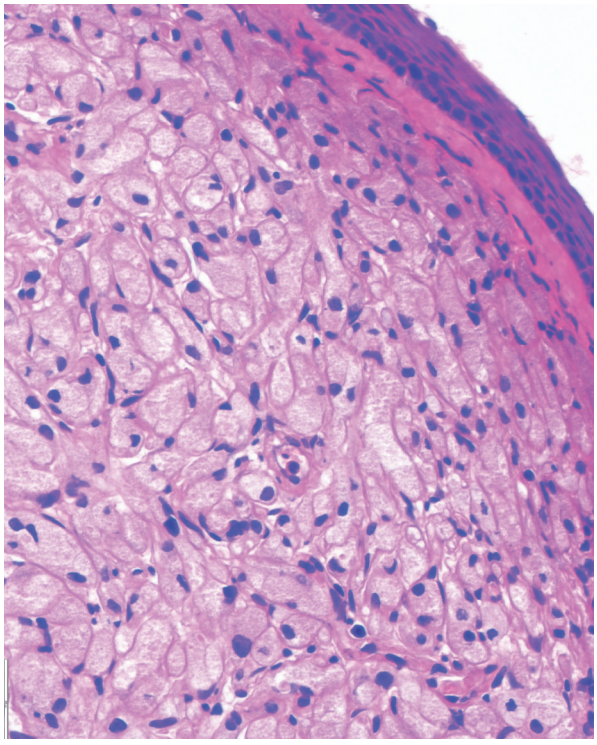

Fig.8. Granular cell tumor. Magnification 20 x.

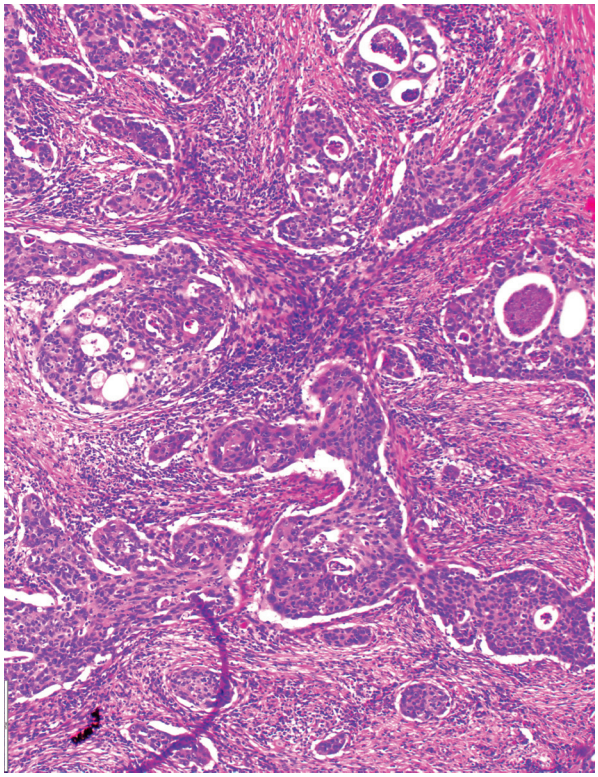

Fig.9. High-grade mucoepidermoid carcinoma with mucous-secreting cells. Magnification 4x.

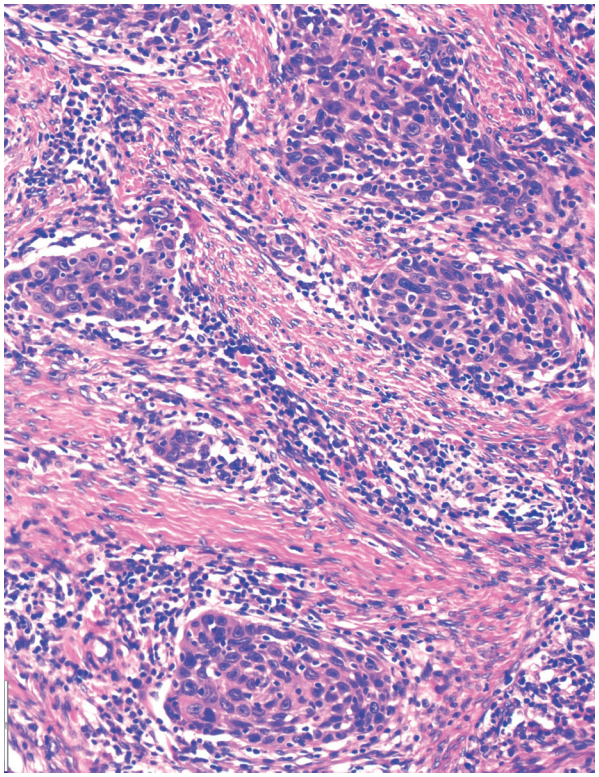

Fig.10. High-grade mucoepidermoid carcinoma with squamous and intermediate cells. Magnification 4x.

presence of glandular ectopy or irregular differentiation of the reserve cells on the surface of the epithelium [25].

The treatment of laryngeal MEC is based on radical surgical excision, although some authors are in favor of radiotherapy. According to us, surgical procedure combined with adjuvant radiotherapy is an optimal solution.

The etiology of granular cell tumor arises many controversies. The initial suggestion on its origin was made by Abrikosoff who stated that it derived from damaged myoblasts [26]. Other scientists proved that it was created on the basis of Schwann cells, fibroblasts and endothelial cells [27]. However, the recent studies promote the theory of neurogenic origin of granular cell tumor.

It occurs in both genders with the same incidence, with a slightly higher predominance of males (according to some authors). Tongue remains the most common location of the tumor. Laryngeal infiltration occurs in 10% of cases and it usually concerns the posterior parts of the vocal folds and arytenoid cartilages, rarely subglottically. Although Abrikosoff tumor is a benign one, several cases of its malignant transformation have been reported on [28].

Pathomorphological examination reveals the presence of big, oval or spindle cells with eosinophylic granulomas, which are characteristic for the tumor. They are assumed to be the fragments of lyzosomes. Positive staining is present for S-100 peptide, NSE and CD-68. Proliferation of squamous cells with acantosis and keratosis is often observed.

The symptoms depend on the location and growth of tumor, yet the disease is often asymptomatic and is accidentally found on ENT examination. The tumors grow slowly. The main treatment is based on a surgical procedure.

CONCLUSIONS

The authors emphasize the necessity of careful diagnosis in case of laryngeal tumors, which are not always squamous cell ones. They indicate that the final decision on the treatment method should be based on histopathological findings.

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Corresponding author: Wojciech Smółka MD PhD, Clinical Department of Laryngology, Medical University of Silesia Francuska St. 20-24 40-027 Katowice, Poland, Tel. +48 32 3591460, E-mail: wojciech.smolka@op.pl

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