Localized laryngeal amyloidosis – a case report

MIHÁLY SZÖCS1), GHEORGHE MÜHLFAY1,2), SIMONA LILIANA MOCAN3), ANDOR BALÁZS1), RADU MIRCEA NEAGOE4)

1)Department of Otorhinolaryngology, Emergency County Hospital, Târgu Mureș, Romania
2)Department of Otorhinolaryngology, University of Medicine and Pharmacy of Târgu Mureș, Romania
3)Department of Pathological Anatomy, Emergency County Hospital, Târgu Mureș, Romania
4)Department of Surgery, University of Medicine and Pharmacy of Târgu Mureș, Romania

Abstract
Amyloidosis encompasses a variety of conditions, caused by extracellular, insoluble protein fibrils that disturb the normal functioning of cells and organs. The disease may be localized or systemic, hereditary or acquired (associated with chronic inflammatory or hematological diseases).

We present the case of a 49-year-old woman, with symptoms including dysphagia, dysphonia and dyspnea. After taking the case history and performing clinical examination, we suspected a laryngeal tumor to be the cause of the symptoms. Microlaryngoscopy and biopsy were performed. The histopathological examination result of the biopsy specimen was amyloidosis. Surgical excision of the tumor was performed.

Our case presentation describes this rare pathological finding, its clinical manifestations, the histopathological and surgical diagnostic problems, treatment, patient evolution and the difficulties we encountered along the way, through the scope of our personal experience.

Keywords: localized laryngeal amyloidosis, benign laryngeal tumor, Congo red staining, airway obstruction, dyspnea, dysphonia.

Introduction
Amyloidosis is a very rare disease, with an incidence of approximately 5–10/million/year, and with up to 20% of the cases involving the head and the neck [1, 2]. The disease may be systemic, affecting several organs or localized at one, such as the larynx [3]. Furthermore, it could be subclassified as primary, associated with a monoclonal plasma cell proliferation or secondary, associated with a chronic inflammation [4]; hereditary or familial type is another form of systemic amyloidosis [5]. Localized laryngeal amyloidosis was first described by Borrow & Neuman in 1873, and represents only 0.5–1% of all benign laryngeal tumors [6]. Depending on the size of the tumor, the symptomatology may include dysphonia, stridor, difficulties on swallowing or even local pain [7]; large tumors may cause breathing insufficiency where tracheostomy may be necessary [8]. The diagnosis is established after laryngoscopy and tissue biopsy; the pathological test reveals the deposition of amyloid fibrils by using Congo red staining and examination under polarized light microscopy [9]. Depending on the clinical symptoms, the treatment of localized laryngeal amyloidosis consists of microsurgical excision of the affected tissue or laser vaporization through direct laryngoscopy, and depending of the size of the tumor partial, total or extended laryngectomy [10].

We herein present a rare case of localized laryngeal amyloidosis, which has some interesting particularities: (i) the technical difficulty of the biopsy, due to the subepithelial position of the tumor, which required a second external procedure with further histopathological examination to confirm the diagnosis; (ii) the dimension of the tumor, which exceeded the cartilaginous limits of the larynx, raising questions in the differential diagnosis.

Case report
We report the case of a 49-year-old woman with a four-month history of progressive dysphonia, dysphagia and moderate dyspnea admitted in our clinic for a left paralaryngeal tumor. Her past medical history also included major depressive disorder, right eye pterygium, macular degeneration both eyes, arterial hypertension, type II diabetes, tonsillectomy. Clinical examination reveals a slightly asymmetric left hemilarynx with a palpable painful tumor in the proximity of the thyroid cartilage. A laryngeal tumor was suspected. We further examined the patient by computed tomography, which confirms the presence of a 28 mm endolaryngeal tumor, situated in the left laryngeal ventricle and false vocal cord with a 12 mm extralaryngeal fragment (Figure 1). Microlaryngoscopy reveals a left sided false vocal cord hypertrophy and tumor which bulges from the ventricle towards the laryngeal aditus, entirely covered by normal epithelium; the incision of the mucosa reveals the granular appearance of the tumor and its possible origin from the laryngeal ventricle (Figures 2 and 3). Histopathological examination, using Congo red staining, reveals an amorphous, eosinophilic material, possibly amyloidosis, but was unable to rule out malignancy. Thus, we performed a second biopsy from the extralaryngeal segment of the tumor, through a laterocervical external approach. Histopathological examination revealed fragments of laryngeal mucosa, covered by respiratory epithelium, with significant deposits of an amorphous, eosinophilic material consistent with amyloid. The deposits were predominantly located around small vessels and seromucinous glands with atrophic appearance, sparing the epithelium; a minimal inflammatory infiltrate, represented by lymphocytes and plasma cells was present at the periphery. The deposits...
were positive at Congo red staining, with an apple green birefringence with polarized light (Figures 4–6). To exclude a systemic form of amyloidosis, biopsy from the abdominal adipose tissue was performed, but the histopathological analysis showed no abnormal deposits in the specimen. Due to its obstructive nature, we considered the surgical treatment of the tumor and performed a vertical partial laryngectomy. A horizontal cervical incision and a median thyrotomy were performed. The tumor has a vegetative, brittle appearance and invades the laryngeal ventricle, ventricular fold, the anterior third of the left vocal cord; it extends towards the superior margin of the thyroid cartilage, protruding through the prelaryngeal muscles and invading the paraglottic space and the pyriform sinus. Surgical resection is performed, the integrity of the hypopharynx is restored, while the right and the remainder of the left vocal cord are sown to the anterior commissure. The integrity of the thyroid cartilage is restored by suturing together the two sides through small holes previously drilled into the cartilage. The histopathological examination of the entire specimen also confirms the diagnosis of amyloidosis.

The postoperative period was uneventful, with residing obstructive symptoms, but persistent dysphonia; 45 days after the operation, the surgical closure of the tracheostoma was performed. Phonatory function was relatively good, but dyspnea started to progressively worsen. The patient was readmitted approximately eight months after the vertical hemilaryngectomy with an anterior glottic stenosis due to a synechia; we performed the excision of the scar tissue and inserted a laryngeal stent (Figures 7 and 8) which is subsequently removed a month later. At the two years follow-up, the patient has no clinical complaints or imagistic signs of tumor recurrence; however, a slight dysphonia persists, due to the fixation of the left vocal cord in abduction (Figures 9 and 10).

Discussion

The term “amyloid” was firstly used by Rudolf Virchow in 1854 to describe a “starchy” material, with positive iodine staining reaction deposited in tissues. Amyloidosis describes a variety of conditions, determined by extracellular deposition of abnormal, insoluble protein fibrils that eventually alter the physiologic functioning of organs [11]. Up to 20% of confirmed amyloidosis cases exhibit head and neck involvement [12]. Localized laryngeal amyloidosis represents only 0.5–1% of all benign laryngeal tumors, being rarely a manifestation of systemic amyloidosis; nonetheless, systemic amyloidosis still has to be excluded [13] through histopathological examination of abdominal subcutaneous fat or rectal biopsy [14].
Localized laryngeal amyloidosis – a case report

Figure 6 – Examination of Congo red stained slides with polarized light show apple green birefringence of the amyloid deposits (×40 magnification under Nikon Eclipse E600 microscope).

Figure 7 – Anterior synechia after vertical partial laryngectomy.

Figure 8 – Incision of anterior laryngeal synechia.

Figure 9 – Endoscopic view of the larynx two years after the operation (larynx in inspiratory position, fixed left vocal cord in abduction, normal breathing function).

Figure 10 – Endoscopic view of the larynx two years after the operation (larynx in phonatory position).

The disease usually affects adults, especially males, but few pediatric cases have also been reported [15]. Pathogenesis of the localized disease is still unclear, although the immunoglobulin nature of the laryngeal amyloid is generally accepted [16]. Ultimately, it is considered a localized monoclonal immunoproliferative disorder rather than an inflammatory infiltrate reacting to the amyloid, in which the plasma cells, associated with the amyloid deposits, produce the light chain immunoglobulin deposited as amyloid [17, 18].

Due to its clinical and imagistic characteristics localized laryngeal amyloidosis may mimic other types of benign or malignant laryngeal tumors, i.e., laryngocele, granular cell tumor, neurofibroma, schwannoma, hemangioma, lipoma, sarcoidosis, pempigus, pachydermy, papilloma, carcinoma, angioleiomyoma, rhabdomyosarcoma, leiomyosarcoma, non-chromaffin paraganglioma, the differential diagnosis being essential [19]. As noted by others upon laryngoscopic examination, the disease may sometimes be confused with laryngeal cancer as well [20]. In our patient, the tumor was covered by normal laryngeal epithelium and was very firm upon instrumental palpation, therefore performing a biopsy from the lesion was difficult. Depending on the clinical symptoms, surgical treatment may be deemed necessary; taking into consideration the benign nature of the lesion, the surgical intervention has to be as conservative as possible in order to protect upper airway, breathing and phonatory function [21]. In our case, we gave priority to ensuring normal breathing, through the upper respiratory tract, without tracheostomy, to the detriment of the phonatory function of the larynx. Presently, the patient does not have a tracheostomy, upper airway function is excellent, but unfortunately, there is a slight dysphonia with whispered voice, due to the fixation of the left vocal cord in abduction, these complications being encountered by other authors as well [22–24]. The final diagnosis is established after histopathological examination. The term of amyloid encompasses a family of different types of extracellular protein fibrils each with specific immunohistochemical methods for positive diagnosis. The gold standard however remains the tissue biopsy demonstrating the typical microscopic appearance and Congo red birefringence [25, 26]. Histopathological results were fairly difficult to obtain as well and the special staining and examination with polarized light were needed to confirm the diagnosis. In our case, the inflammatory infiltrate was represented predominantly of plasma cells, identified at the periphery of the deposits. In the postoperative period, after localized excision, amyloidosis can reappear, either as
localized or generalized form; therefore, regular patient follow-up is crucial [22]. Two years after the surgical intervention, our patient is tumor free, and does not show any clinical or imagistic signs of tumor recurrence.

Conclusions

Laryngeal localized amyloidosis is a rare disease that mostly affects male patients that can cause airway obstruction, dysphonia and surgical therapy may be necessary, situations in which the therapeutic decision must be based upon a precise histopathological diagnosis. In certain cases, a series of surgical interventions have to be performed in order to successfully treat the patient: endoscopic laryngeal biopsy, tracheostomy, vertical partial laryngectomy, incision of postoperative laryngeal synechiae, closure of tracheostomy. When choosing the type of surgical intervention, we must take into consideration the preservation of the life quality of the patient. In our case, we gave priority to ensuring the patient with normal breathing function, to the detriment of the phonatory function. We conclude that even if laryngeal amyloidosis is a benign tumor, it can manifest itself through various clinical forms, a biopsy result may be difficult to obtain, the surgical treatment of the disease and the possible complications are complex and may seriously affect the life quality of the patient.

Conflict of interests

The authors declare that they have no conflict of interests.

References


Corresponding author

Gheorghe Mühlfay, Associate Professor, MD, PhD, Department of Otolaryngology, University of Medicine and Pharmacy of Tîrgu Mureș, 38 Gheorghe Marinescu Street, 540139 Tîrgu Mureș, Romania; Phone +40722–363 411, Fax +40265–211 925, e-mail: ghe.muhlfay@gmail.com

Received: October 2, 2014    Accepted: June 30, 2015