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Subglottic Masses Revealing Rosai-Dorfman Disease

Mouna Snoussi[1], Abir Derbel[1], Yosr Hentati[2], Zeineb Mnif[2], Sameh Marzouk[1], Zouheir Bahloul[1]

[1] Department of Internal Medicine, Hedi Chaker Hospital, Sfax, Tunisia

[2] Department of Medical Imaging, Hedi Chaker Hospital, Sfax, Tunisia

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ABSTRACT

Rosai-Dorfman disease (RDD) is an uncommon lymphoproliferative disorder; RDD with oropharyngeal involvement is extremely rare, especially in adults. A 65-year-old woman with a complaint of progressive dyspnoea since 2016 presented with laryngeal involvement of RDD. A laryngoscopy examination revealed two solid, polypoid masses in the subglottic region, and a laryngeal biopsy concluded chronic inflammation without signs of malignancy. A second biopsy of axillary lymph nodes was performed, supporting the diagnosis of histiocytosis. The patient was treated with corticosteroids and then lost to follow-up. In 2019, she suffered from dyspnoea and a hoarse voice. Laryngoscopy examination showed a polypoid lesion causing airway obstruction at 70% and thickening of the lateral wall of the cavum. Physical examination found left axillary and submandibular adenopathy, and computed tomography revealed thickening of the supraglottic larynx narrowing the laryngeal pathway. Lymphadenectomy with immunohistochemical analysis revealed typical protein positive S-100 histiocytes and emperipolesis. The patient was treated with high doses of corticosteroids for six weeks then these were progressively decreased. The outcome was favourable; the laryngeal lesion disappeared after two weeks of treatment.

LEARNING POINTS

- Rosai-Dorfman disease is a rare cause of lymphadenopathy in adults. Extranodal presentation of the disease is possible mainly in the head and the neck region.
- The diagnosis is based on histological examination with the presence of histiocytes, which are S-100 positive, CD68 positive, and CD1a negative immunohistochemistry.
- The outcome is usually good in asymptomatic forms of the disease with no critical organ involved. The surgical resection is appropriate to the localised symptomatic form of the disease while corticosteroids are indicated in disseminated RDD as a first-line therapy.
- Inspired by our case, rare localisation of Rosai-Dorfman disease (RDD), led to clinical and therapeutic issues. That is why a review of the literature must be undertaken, to share experiences.

KEYWORDS

Rosai Dofmann disease, laryngeal involvement, steroids

INTRODUCTION

Rosai-Dorfman disease (RDD) is an uncommon lymphoproliferative disorder characterised by painless cervical lymphadenopathy. It was described by Rosai and Dorfman as “sinus histiocytosis with massive lymphadenopathy”. Extra nodal involvement is seen in 40% to

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50% of the cases and is more common in the head and neck region [1,2]. In the head and neck region, there are the nasal cavity, paranasal sinuses, meninges, orbit, skin, salivary glands, and tracheobronchial tree. They are the most affected sites in 75% of cases of head and neck involvement[3–6]. RDD with laryngeal involvement is extremely rare especially in adults, and there are only isolated cases in the literature and one cohort of five cases. Laryngeal masses are even rarer [7,8]. Here is an unusual case of RDD that involved the subglottic region of the larynx in 65-year-old female. Through this case we will focus on the clinical and therapeutic features of this rare localisation.

CASE DESCRIPTION

A 65-year-old woman with medical history of hypertension was admitted to our Department of Internal Medicine in December 2019 for progressive dyspnoea.

Her medical history started in 2016 when she was complaining of dyspnoea. She was treated by inhaled corticosteroids for bronchitis. Nevertheless, she maintained an expiratory dyspnoea with a hoarse voice. A laryngoscopy examination was made in April 2018, which revealed two solid, polypoid masses in the subglottic region. These nodular lesions had smooth surfaces and were located at 1cm under the right vocal cord and at 1.5cm under the left vocal cord. A laryngeal biopsy concluded chronic inflammation without signs of malignancy. Then, the area was explored by computed tomography of the thorax revealing left axillary adenopathy measuring 4-3 cm in diameter. The biopsy of this adenopathy was performed in September 2018 and supported the diagnosis of histiocytosis. Microscopic examination revealed a preserved architecture of the lymph node with predominant histiocytes, which had an abundant acidophilic cytoplasm, and vesicular nuclei containing numerous lymphocytes within intracytoplasmic vacuoles. The histiocytes were strongly positive with S-100 protein by immunohistochemistry. This finding was concordant with RDD. The patient was treated by corticosteroids for two weeks and then lost to follow-up.

In December 2019, she presented to our department with worse inspiratory dyspnoea and a hoarse voice. In the physical examination, she was polypneic at 20 cycles/minute with sus sternal respiratory depression and stridor. We also palpated an axillary lymph node measuring 40-30mm. Pulmonary auscultation was normal; an electrocardiogram found a left branch block and a laryngeal nasofibroscopy examination found bilaterallesion had caused an airway obstruction at 70%. Computed tomography showed circumferential thickening in the subglottic region measuring 13 mm extended over 33 mm, narrowing the laryngeal pathway with compression of the cervical oesophagus (*Figs.1 and 2*). The biopsy of the axillary lymph node was performed. The histological finding showed that the nodal architecture was preserved with a diffuse infiltrate of histiocytes. The sinusoids contained numerous large histiocytic cells; the majority had smooth nuclear contours and abundant pale cytoplasm. Emperipolesis was seen as intact haematolymphoid cells floating freely in the cytoplasm of histiocytes. Immunohistochemical analysis revealed typical S-100 protein positive. The infiltrate was negative to CD1a and CD207 (unfortunately we did not have histological images since the biopsy was seen in a private laboratory and the histological images could not be provided to us). Corticosteroids were started as an emergency. The patient received high doses of steroids (1 mg/Kg/day). At 15 days of treatment, control laryngoscopy found a resolved tumour and the laryngeal lesion had disappeared. The patient was treated with high doses of corticosteroids for six weeks which was then progressively decreased. The outcome was favourable (the laryngeal lesion had disappeared under a physical examination and in tomography).

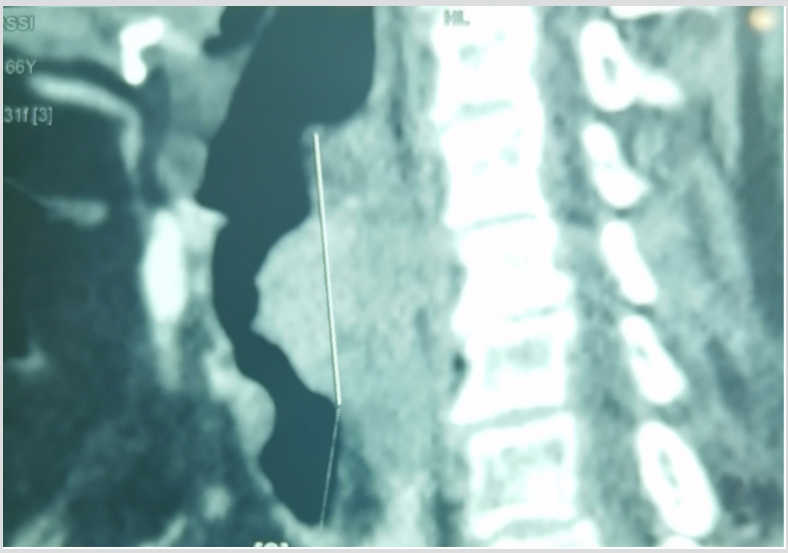

Figure 1. Computed tomography, sagittal section, revealing the occlusive lesion of the larynx measuring 3.7 centimetres

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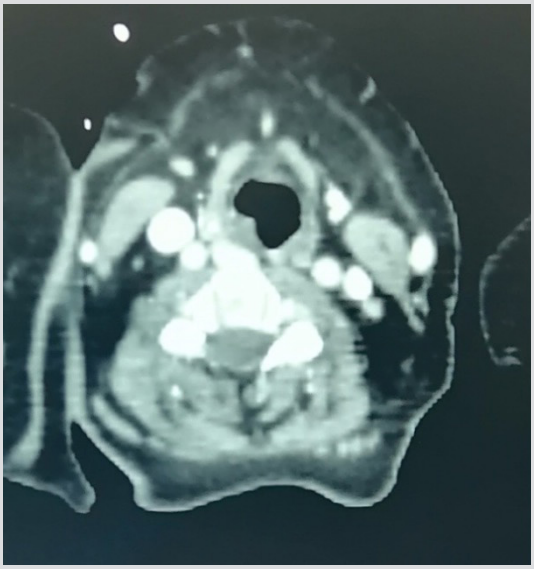

Figure 2. Computed tomography, axial section showing the obstructive lesion

DISCUSSION

RDD is a non-Langerhans cell histiocytosis characterised by accumulation of activated histiocytes in affected tissues. It occurs in isolation or in association with autoimmune or neoplastic diseases, and includes classic nodal and extranodal disease. It may be sporadic or familial [9,10]. Clinical manifestations in extranodal RDD patients depend on the location of disease. Laryngeal involvement is an uncommon extranodal site rarely affected, according to the literature[8,11], and fewer than 30 such cases reporting laryngeal involvement published[12] (*Table 1*). This localisation constitutes a diagnosis problem because of the frequency of malignant tumours in this region, which rules out biopsy; this can also often fail to provide a definite diagnosis[13]. In the majority of cases, lesions were unilateral or asymmetric nodular masses similar to our case[8]. Histological examination of extranodal RDD was characterised by the presence of an obvious fibrosis with fewer histiocytes. The immune histochemistry revealed that these cells were S-100 positive, CD68 positive, and CD1a negative; staining with GMS and PAS was negative[8,14,15]. RDD generally had a good prognosis, but laryngeal involvement is a dangerous location because it is life threatening. Dyspnoea due to occlusive laryngeal lesion sometimes indicates surgical intervention as the primary choice [16,17]. Glucocorticoids may be prescribed as the first-line therapeutic option for systemic treatment [8].Radiotherapy could be used in steroid resistant form [18,19], and chemotherapy was also prescribed [13,20]. In a series including 12 patients with laryngeal RDD [13], steroid therapy was used in five patients. Six patients were treated by laryngeal microsurgery under suspension laryngoscopy, three had laryngofissure, and three cases were treated with chemotherapy or radiotherapy, or follow-up observation. The outcome was unknown in three cases and good in the other cases; 20% of patients with extranodal RDD had spontaneous remissions, and 70% of patients require treatment because of disease in a vital organ that was involved [8,21].

CONCLUSION

Rosai Dorfman's histiocytosis is a benign disease characterised by clinical polymorphism. Its prognosis depends on the seriousness of the locations, particularly oropharyngeal involvement. Symptomatic localised disease is managed with surgical resection or radiation. Symptomatic disease as in the case of our patient is treated with glucocorticoids at high doses as the first-line therapy.

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	Age	Sex	Clinical presentation	Endoscopic findings	Treatment	Follow-up
Carpenter et al. 1978 (4)	44	Female	Nasal obstruction stridor Bilateral parotid swelling Upper and lower airway involvement Tracheo bronchial involvement Cervical adenopathy	Circumferential subglottic narrowing by erythematous granular tissue Erythematous, granular-appearing polypoid tissue extended from the subglottic area downwards for 3-4 cm, in the mid-trachea and just above the carina: island of polypoid tumefaction	Chemotherapy chlorambucil + prednisone	Regression of respiratory signs; disappearance of parotid enlargement and lymphadenopathy
Leighton et al. 1994 (22)	17	Male	Cough subglottic stridor	Tumour in the subglottis and the trachea	Tra cheotomy Suspension laryngoscopy operation	Unknown
Asrar et al. 1998 (23)	29	Male	Hoarseness Dyspnoea Neck mass	Tumour in the right glottic and subglottic	Tracheotomy, laryngofissure	Good
Hazarika et al. 2000 (24)	29	Male	Noisy breathing	Subglottic swelling with intact mucosa	Postoperative steroids and low-dose chemotherapy Tracheotomy, laryngofissure	The subglottic tumour was markedly regressed 6 months later
Aluffi et al. 2000 (5)	62	Female	Breathing difficulty Dysphagia Hoarseness of voice Stabbing pain in left half lymph node between the submandibular gland and the sterno cleidomastoid muscle	Concealed left vocal cord, a narrowing of the left piriform sinus, and a thickening of the left epiglottic fold with smooth mucosa covering	Excision of the neoplasm under general anaesthesia (+intended lateralisation and mild rotation of the remaining laryngeal entrance)	One-year postoperative follow-up: good outcome
Unal et al. 2003 (2)	15	Male	Difficulty in breathing and neck mass submandibular mass 5cm × 2cm Subglottic mass	Masses located on the left side of the nasal septum and nasal floor Subglottic mass narrowing the lumen covered with normal-appearing smooth surfaced mucosa	All the masses excised under general anaesthesia Neck mass easily dissected Nasal masses also dissected easily from overlying mucosa, and underlying septal cartilage and nasal floor Subglottic mass also completely excised endoscopically	After excision of subglottic mass, discovery of several small masses of the same appearance extending along the tracheal lumen Three months later the patient came back with respiratory difficulty and open tracheal surgery was suggested for removal of tracheal masses, but he did not accept the suggested treatment
Cossor et al. 2006 (19)	54	Male	Swelling of the superior aspect of right nostril	Polypoid mass below the right true vocal cord, encompassing approximately 80% of the proximal trachea in the subglottic area, obstructing the airway	Radiation therapy	Complete amelioration of the symptoms and at 16 months follow-up he had no evidence of recurrence
Talebi etal. 2007 (25)	68	Male	Sleep apnoea Dysphagia	Epiglottic pseudotumour	Resection of the epiglottic mass	Unknown
Tseng etal. 2010 (26)	55	Male	Noisy breathing Foreign body sensation	Left subglottic cricoid cartilage destruction	Chemotherapy (cyclophosphamide) +steroids	Good
Barbalho et al. 2010 (27)	58	Female	Dysphonia	Anulceron the right vocal fold and a decreased mucosal wave	Follow-up observation	Good; only minor synechiae in the glottis anterior commissure
Toguri et al.2011 (18)	92	Female	Stridor Dyspnoea	Glottic and subglottic lesions with significant airway obstruction	Suspension laryngoscopy operation, steroids, radiotherapy	Good
Illing et al.2012 (28)	45	Female	Recurrent dysphonia and airway obstruction	Mass lesion in the right vocal fold paraglottic space and subglottis	Radiotherapy Steroids	Good

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	Age	Sex	Clinical presentation	Endoscopic findings	Treatment	Follow-up
Fusconi et al.2013 (29)	40	Female	Hoarseness Dyspnoea	Subglottal sessile mass, all along and slightly posterior to the left side of the trachea, which reduced the tracheal lumen	Mass excised using laser	Good. No recurrence at 10 years follow-up
Gadde et al.2014 (30)	39	Female	Hoarseness Dyspnoea	Mass in the left vocal fold	Suspension laryngoscopy operation Steroids	Good
Swain et al.2015 (31)	42	Male	Dyspnoea Dysphagia	Epiglottic lesion	Tracheotomy, suspension laryngoscopy operation Steroids	Good
Ma et al.2015 (12)	67	Female	Hoarseness Dyspnoea Foreign body sensation	Right vocal cord and paraglottic space	Tracheotomy, laryngofissure	Unknown
Niu et al. 2017 (8)	27	Male	Hoarse voice	Glottis and subglottic region	Open surgery Tracheotomy Steroids	Stable
	34	Female	-	Subglottic region	Open surgery Tracheotomy Steroids	Stable
	39	Male	Hoarse voice	Glottis and subglottic region	Endosurgery ´2 Steroids	Tumour relapse aggravated laryngeal dyspnoea Tracheotomy 61 months after the diagnosis
	38	Male		Glottis and subglottic region	Endosurgery ´2 cladribine steroids	Tumour relapse Stable
	45	Female	Hoarse voice and suffocation	Glottis and subglottic region	Endosurgery Tracheotomy Steroids	Relieved
Xu et al.2018 (13)	51	Male	Progressive hoarseness for two months, and mild dyspnoea after activities and anterior neck mass for one month	A cauliflower-like neoplasm located on the left side of the glottis and the subglottic area	Minimal invasive surgeries combined with steroid therapy	Favourable
Wei et al.2021 (32)	39	Male	History of nasal obstruction for two years	Multiple submucous nodular lesions located at the nasal septum, the posterior region of the vocal cord, and subglottis	Endoscopic operations (in 2008, 2010, 2014, and 2016) and tracheostomy finally performed September 2016, thalidomide 100 mg/d combined with prednisone 40 mg/d started	After 20 months of treatment the laryngeal lesions greatly resolved on laryngoscopy
	26	Female	Hoarse voice for one year	Multiple lesions in the nasal cavity, nasopharynx, and subglottis	Prednisone 60 mg/day then thalidomide	Lesions stable on the laryngoscopy examination
	24	Male	Hoarse voice and progressing dyspnoea for five months	Severe restriction of the right vocal cord and glottic stenosis	Thalidomide 100 mg/d as first-line treatment	After six months: notable regression of the laryngeal lesion on the laryngoscopy examination

Table 1. Literature review of laryngeal Rosai-Dorfman Disease: 25 cases.

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