Laryngological presentations of Ehlers-Danlos syndrome: a case series of nine patients from two London tertiary referral centers

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Introduction

Ehlers–Danlos syndrome (EDS) is a heterogeneous heritable disorder of connective tissue characterised by hypermobility of the joints, skin hyperextensibility and tissue fragility. It does not have racial or gender predilection. The Villefranche classification divides it into six major forms: classic, hypermobility, vascular, kyphoscoliosis, arthrochalasia and dermatosparaxis[1], replacing the older nosology that described types I-XI.[2] Most patients have a normal or near-normal life expectancy, with variable morbidity, except the vascular type associated with the serious complications of spontaneous arterial rupture and visceral perforation.

Methods and Materials

Retrospective review of the case records of patients with EDS diagnosed by specialist rheumatologists presenting to the tertiary referral laryngology services of the two senior authors over the 3-year period 2012–2015.
A total of nine patients were identified, of whom seven were female.

Discussion

This is the first series to our knowledge to describe a range of potential presentations of EDS to the laryngologist. Limitations were due to retrospective nature of data collection.

In our series, clinical findings of EDS in the larynx and upper aerodigestive tract were quite subtle and included: hypotonia of musculature, incoordination or reduced mobility of vocal folds, and prolapse or subluxation of the arytenoids. GI endoscopy, radiological studies and electromyography were of limited use; a patient who underwent oesophageal manometry was found to have weak oesophageal peristalsis and stasis of food and fluid.

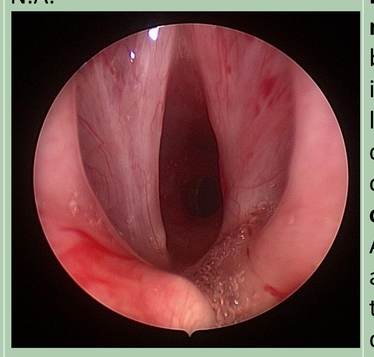
The commonest abnormal upper GI endoscopic findings in EDS are gastritis, oesophagitis or hiatal hernia,[4] and specific findings include oesophageal dilation, diverticula, and eosinophilic oesophagitis[5]. Oesophageal manometry may be more useful, as about 1/3 of EDS patients had abnormal motility or lower oesophageal sphincter pressures.[4]

The pathophysiology of dysphonia in EDS is likely multifactorial. Postulations include: incoordination or hypomobility of the vocal cords,[6] reduced mobility of the cricoarytenoid joint and loss of mucosal wave due to abnormalities of the collagen component of the deep layer of the lamina propria.[7]

Tissue fragility and tendency to form excessive granulation and scarring have also been noted.[8]

Laryngeal and upper digestive tract manifestations are very common in EDS – dysphagia occurs in 37–62%[7,8] and dysphonia in 28% of adults[7] with this syndrome. These may be their initial manifestations. It would be useful for laryngologists to be aware of the syndrome and its systemic manifestations, as well as the challenges in diagnosis and treatment.

Results

Patient characteristics	Presenting complaints	FNE and FEES findings	Other investigations	Management and outcome
Patient 1 Classic type	***Dysphagia*** Food getting stuck in throat - weak voice, - choking on swallowing liquids (three patients), - sensation of globus (two patients), - regurgitation of food (one patient), - odynophagia (one patient) - and nasal regurgitation (one patient)	"Baggy" hypotonic appearance of larynx and pharynx. FEES normal	TNO: Atonic oesophagus, normal gastro-esophageal junction (GEJ) Barium swallow: normal	Swallowing therapy
Patient 2 Hypermobility type		FNE normal, Reflux Finding Score less than 5. FEES slight residues with all consistencies, not significant	OGD normal	
Patient 3 Hypermobility type		FNE: posterior commissure swelling and erythema, Reflux Finding Score 7.	TNO: Mild esophagitis at the GEJ, small sliding hiatus hernia VFS normal	
Patient 4 Hypermobility type		FNE normal except for reflux.	Barium swallow normal	
Patient 5 Classic type	***Dysphagia***, weak voice. 10yrs prior had **hypermobility of hyoid bone**– lateral dislocation of laryngeal complex on head-turning. Worsened with hyoidectomy, improved with fascia lata sling. Recurred 5 years after.	FNE: saliva pooling, VC mobile. FEES - yoghurt failed to clear and induced coughing.	VFS -limited elevation of the larynx with failure of relaxation of cricopharyngeus	2 successful trials of Dysport (10 mouse units of abobotulinum toxin) into the posterior cricopharyngeus muscle. Underwent **open cricopharyngeal myotomy** with relief of dysphagia and an improvement in his EAT-10 score[3] from 33 to 10.
Patient 6 Hypermobility type	Fluctuating **hoarseness**. On examination, voice was Grade 1 with slight roughness (GRBAS 11000).	Flexible laryngoscopy showed a normal appearance of the vocal folds except for slight scissoring of the vocal cords.	N.A.	Voice therapy
Patient 7 Hypermobility type	Severe, chronic ***throat pain***, accompanied by mild hoarseness and vocal fatigue	No inflammation but bilaterally prolapsing arytenoids with normal vocal cord mobility	MRI and neurology referral: no abnormalities found	Speech therapy and pain clinic referral, with some symptomatic relief.
Patient 8 Hypermobility type (diagnosed 1month **after** laryngologic issues settled)	***Recurrent laryngospasm*** Intermittent episodes of choking on fluids and frequent attacks of "near-suffocation" triggered by emotion, exercise or respiratory tract infections	Right vocal cord immobility	Radiological and laryngeal electromyography investigations were normal. 24-hour esophageal pH testing and manometry revealed normal pH but weak or absent esophageal oesophageal peristalsis.	During a severe attack of laryngospasm, noted bilateral vocal cord immobility. Emergency microlaryngoscopy showed both cricoarytenoid joints severely subluxed with some fixation of the left cricoarytenoid joint. A **left posterior cordotomy and partial left arytenoidectomy** were performed with long-term relief of dyspnoea.
Patient 9 Classic type	***Progressive airway scarring*** History of likely idiopathic **subglottic stenosis** with multiple previous endoscopic airway procedures with the use of lasers and balloon dilatation. She had worsening effort tolerance.	Significant stenosis at the subglottis and upper trachea extending from 1 to 2.5 cm below the vocal folds. There was also a scar band extending from the posterior aspect of the right vocal fold to the left arytenoid (Fig. 1).	N.A.  (Fig. 1 Endoscopic view)	**Endoscopic laryngotracheal reconstruction** of the subglottic stenosis by means of stenosis resection and insertion of a temporary skin-covered laryngotracheal stent. The posterior commissure scar was resected by means of an open approach to place a **posterior cricoid cartilage graft**. Dyspnea resolved. A combination of difficult laryngoscopy and poor connective tissue support lead to three of her **upper teeth being lost** during endoscopy.

Conclusion

Ehlers–Danlos syndrome patients may present to the laryngologist with a variation in symptoms from dysphagia to dysphonia. Clinical findings may be subtle. Endoscopy and radiological investigations may be of limited value; however, oesophageal manometry may be considered in EDS patients presenting with dysphagia. Surgical treatment may be complicated by the predisposition for scarring.

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