

# Trachea Rupture in Tenascin-X-deficient Type Ehlers–Danlos Syndrome

Anna Besselink-Lobanova, M.D.,\*  
 Natasja J. G. Maandag, M.D.,†  
 Nicol C. Voermans, M.D.,‡  
 Henricus F. M. van der Heijden, M.D., Ph.D.,§  
 Johannes G. van der Hoeven, M.D., Ph.D.,||  
 Leo M. A. Heunks, M.D., Ph.D.#

**T**HE Ehlers–Danlos syndrome (EDS) is a heterogeneous group of inherited connective tissue disorders characterized by hyperextensible skin, hypermobile joints, and tissue fragility.<sup>1</sup> The revised classification of EDS in six major types is based on clinical and biochemical features and consists of major and minor diagnostic criteria.<sup>1</sup> The hypermobility type is the most common type of EDS (1 in 10,000–15,000), followed by the classic type (2 to 5 in 100,000). The vascular type (1 in 100,000–250,000) is associated with (dissecting) aneurysms, which may be life threatening. In 2001, a new autosomal recessive type of EDS caused by deficiency of tenascin-X was identified, which is characterized by joint hypermobility, skin hyperextensibility, and easy bruising.<sup>2</sup> Tenascin-X is a large glycoprotein prominently present in the extracellular matrix of various tissues, including the skin, joints, blood vessels, and muscle. It contributes to matrix stability and is possibly involved in collagen fibril formation, maturation, and maintenance.<sup>3,4</sup>

Numerous clinical features of EDS such as vessel fragility, poor skin healing, excessive bleeding, spontaneous pneumothorax, joint dislocation, mandibular dislocation during intubation, vertebral instability, valvular prolapse, poor response to local anesthesia, spontaneous dissections, and

ruptures of major vessels are relevant for anesthesiologists.<sup>5,6</sup> However, the complications related to anesthesiologic procedures in tenascin-X-deficient type EDS have not been reported in the literature. We describe postintubation tracheal rupture in a patient with tenascin-X deficiency.

## CASE REPORT

A 41-yr-old female patient (height 151 cm, weight 85 kg, body mass index 37.3 kg/m<sup>2</sup>) presented at our emergency department with a luxation of her left knee joint after minor trauma. Her medical history includes tenascin-X-deficient type EDS characterized by hyperextensible and velvety skin, hypermobile joints, easy bruising, musculoskeletal pain, and multiple (sub)luxations. In addition, she was known with adrenogenital syndrome, mild mitral valve prolapse with borderline pulmonary hypertension, and mild tricuspid regurgitation. In the previous years, she underwent multiple surgical procedures, mostly related to carpal tunnel syndrome and joint (sub)luxations.

Because of the severity of the current left knee luxation and intense pain, an arthroplasty was planned on the day of admission. Noteworthy, she reported a needle phobia, and therefore, previous surgery was performed with general anesthesia instead of using locoregional techniques.

The arthroplasty was performed with general anesthesia with a rapid sequence induction and intubation. After preoxygenation (end-tidal FiO<sub>2</sub> of 91%), 400 mg sodium thiopental and 150 mg suxamethonium were injected intravenously. Direct laryngoscopy showed a Cormack and Lehane grade 1 score. A Mallinckrodt Lo-Contour<sup>®</sup> Tracheal Tube 7.0 mm (Mallinckrodt Medical, Athlone, Ireland) with Mallinckrodt satin-slip stylet was prepared. The stylet was removed before passing the vocal cords. The endotracheal tube was advanced up to 22 cm from the teeth. Cuff pressure was measured immediately after intubation using a dedicated pressure-monitoring device (Rusch<sup>®</sup>, Endotest, Kern, Germany) and maintained at 25 cm H<sub>2</sub>O. Cuff pressure never exceeded 30 cm H<sub>2</sub>O. Patient was mechanically ventilated in assist-control mode: tidal volume, 500 ml; respiratory rate, 14/min; positive end-expiratory pressure, 5 cm H<sub>2</sub>O, and mean airway pressure was approximately 18 cm H<sub>2</sub>O. Peak airway pressure did not exceed 40 cm H<sub>2</sub>O any time during the operation. General anesthesia was maintained with sevoflurane and fentanyl. The course of the operation was uncomplicated and lasted approximately 45 min. During the emergence of anesthesia, she appeared

\* Critical Care Fellow, || Professor and Chair, # Staff, Department of Critical Care Medicine, † Resident and Staff, Department of Anesthesiology, ‡ Staff, Department of Neurology, § Staff, Department of Pulmonary Diseases, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.

Received from the Department of Intensive Care Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. Submitted for publication January 25, 2010. Accepted for publication March 25, 2010. Support was provided solely from institutional and/or departmental sources.

Address correspondence to Dr. Heunks: Department of Intensive Care Medicine (Route 631), Radboud University Nijmegen Medical Centre, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands. l.heunks@ic.umcn.nl. Information on purchasing reprints may be found at [www.anesthesiology.org](http://www.anesthesiology.org) or on the masthead page at the beginning of this issue. ANESTHESIOLOGY's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site ([www.anesthesiology.org](http://www.anesthesiology.org)).

bronchospastic and coughed several times. Subsequently, she developed impressive subcutaneous emphysema spreading from the face to the upper torso. Because of the severity of subcutaneous emphysema, she was not extubated but admitted to the intensive care unit. At that time, she was hemodynamically stable, and pulse oximetry showed normal oxygen saturation (>95%, while breathing 100% oxygen). Chest radiography at the intensive care unit showed massive subcutaneous emphysema, but a pneumothorax could not be confirmed (fig. 1). Subsequently, a thoracic computer tomography scan revealed widespread subcutaneous emphysema, severe pneumomediastinum, and a large bilateral pneumothorax (fig. 2). Immediately, chest tubes were inserted in both pleural cavities. Video bronchoscopy revealed a large tracheal rupture of the posterior wall (see Supplemental Digital Content 1, a movie showing a videobronchoscopic view of tracheal rupture on the posterior tracheal wall, <http://links.lww.com/ALN/A610>). The length of this defect was at least 4.0 cm, ending 2 cm proximal from the main carina (fig. 3).

The tracheal rupture was treated conservatively. She was reintubated using an oral endotracheal tube with the possibility of intermittent subglottic drainage. The cuff of this single lumen tube was positioned distal of the rupture, just above the main carina. Mechanical ventilation with low tidal volumes and low positive end-expiratory pressure was applied. Prophylactic antibiotics (cefotaxim and metronidazole) were administered.

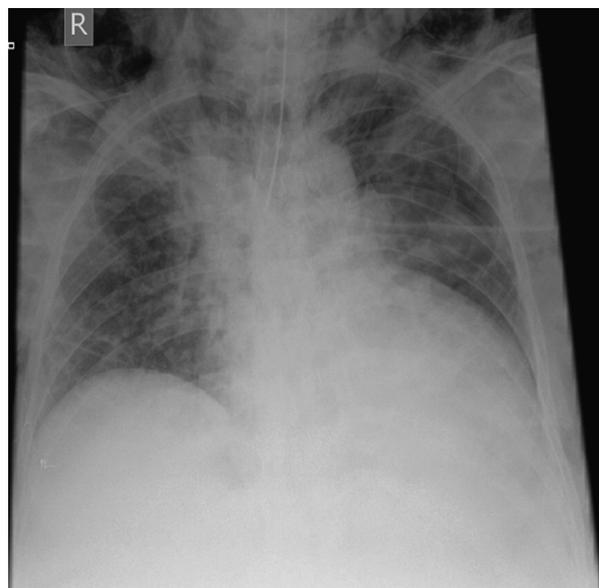
A follow-up bronchoscopy after 14 days revealed remarkable healing of the rupture (fig. 4; see Supplemental Digital Content 2, a movie showing a videobronchoscopic view of healed dorsal wall tracheal rupture, <http://links.lww.com/ALN/A611>). During the subsequent 5 days, the patient was weaned from mechanical ventilation and successfully extubated. Approximately 5 weeks later, she was reoperated on her left knee as planned, with general anesthesia without tracheal intubation. She was discharged to a rehabilitation center shortly thereafter.

## Discussion

We present a tenascin-X deficiency type of EDS patient with a rare complication from tracheal intubation. The development of tracheal rupture was unexpected as the tracheal intubation was easy (grade 1) and initially seemed uneventful.

Tracheal intubation is a routine procedure to aid surgery during general anesthesia. The incidence of iatrogenic injuries of the tracheobronchial tree after elective intubation is probably low,<sup>7</sup> and estimated at 1:20,000 during a 7-yr period survey,<sup>8</sup> with tracheal damage being more frequent after double lumen intubation (0.05–0.19%).<sup>9,10</sup>

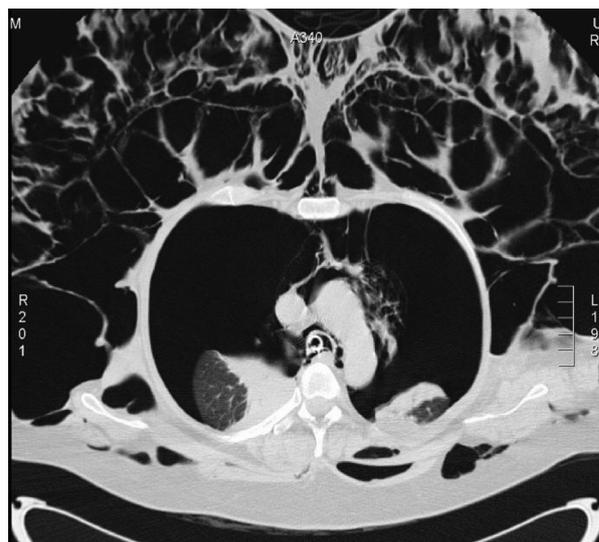
Both mechanical and anatomical risk factors have been recognized for the development of a postintubation tracheal rupture (table 1).<sup>9</sup> Patient height is not recorded in most studies, and a review by Minambres *et al.*<sup>9</sup> was unable to evaluate this. However, other authors suggest that short stature (height under 160 cm) and obesity result in an overestimation of the size of the tracheobronchial anatomy, resulting in the use of an oversized endotracheal tube, which can be a predisposing factor for a tracheal rupture.<sup>11–14</sup>



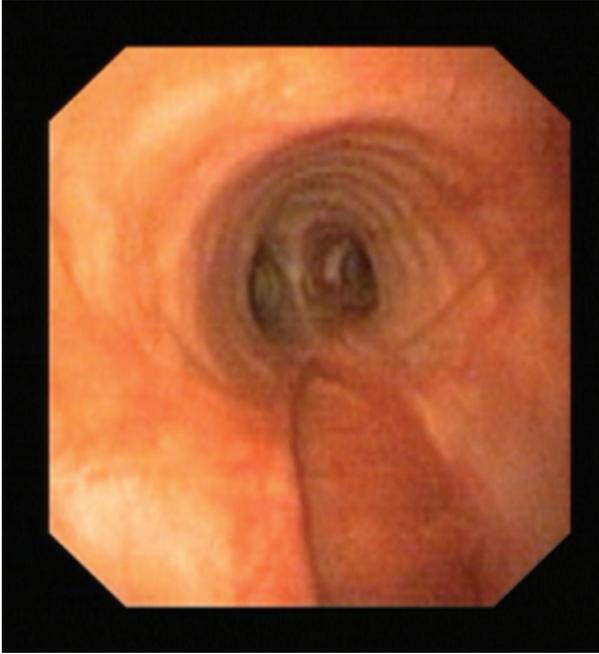
**Fig. 1.** Chest x-ray. Endotracheal tube in deep position with possible selective right main bronchus intubation. Massive subcutaneous emphysema. The right-sided diaphragm is visible, the left side is obliterated. No convincing evidence for pneumothorax except for the subcutaneous emphysema.

Today, a history of inherited connective tissue disorders is not a recognized risk factor for tracheal rupture after tracheal intubation. However, unexpected complications associated with anesthesia in EDS have been reported.<sup>5,15</sup> Furthermore, intubation may be difficult because of possible collapse of the upper airway as reported in a patient with the hypermobility type EDS.<sup>16</sup>

In our patient, several known risk factors for a postintubation tracheal rupture were present: female gender, short stature with obesity, chronic use of corticosteroids, an endo-



**Fig. 2.** Computer tomography scan at the level of the top of the aortic arch: bilateral pneumothorax. Extensive subcutaneous emphysema and pneumomediastinum. Endotracheal tube is visible in the trachea.



**Fig. 3.** Bronchoscopy shows a large tracheal rupture in the posterior wall of at least 4 cm extending up to 2 cm above the main carina.

tracheal tube at 22-cm depth, and coughing during the emergence from general anesthesia. Interestingly, this case report suggests that tenascin-X deficiency may be a risk factor for tracheal rupture. As mentioned, deficiency of tenascin-X alters the characteristics of the extracellular matrix, resulting in tissue fragility. Therefore, these patients may be prone to tracheal rupture after mild trauma, for instance induced by the endotracheal tube. It is unknown whether all types of EDS patients are prone to tracheal rupture. However, one



**Fig. 4.** Bronchoscopy reveals complete recovery of the rupture.

**Table 1.** Risk Factors for Postintubation Tracheal Rupture

Anatomic Risk Factors	Mechanical Risk Factors
Congenital tracheal abnormalities	Multiple forced attempts at intubation
Weakness of the pars membranosa of the trachea	Inexperienced healthcare professionals
Chronic obstructive pulmonary disease and other inflammatory lesions of the tracheobronchial tree	Use of endotracheal tube introducers who protrude beyond the tip of the tube
Diseases that alter the position of the trachea (mediastinal collections, lymph nodes, or tumors)	Overinflation of the cuff
Chronic use of steroids	Incorrect position of the tip of the tube
Advanced age	Repositioning the tube without deflation of the cuff
Female gender	Inappropriate size of the tube
	Significant cough and movements of the head and neck while the patient is intubated

Reprinted with permission from Minambres E, Buron J, Ballesteros MA, Llorca J, Munoz P, Gonzalez-Castro A: Tracheal rupture after endotracheal intubation: A literature systematic review. *Eur J Cardiothorac Surg* 2009; 35:1056–62.

case report described tracheal rupture in a type IV EDS patient.<sup>17</sup> In our opinion, the most likely scenario in our patient is that with the introduction of the endotracheal tube, the trachea was damaged. Because of the deep position of the endotracheal tube (fig. 1), the development of pneumothorax and subcutaneous emphysema was prevented. As patient recovered from anesthesia, started to breathe spontaneously, coughed while the cuff was deflated, the symptoms of trachea rupture became apparent.

In general, the challenging factors with general anesthesia in EDS are the potential collapse of the upper airway, tissue fragility, and cardiovascular abnormalities. Alternative anesthetic techniques may be considered in patients with EDS and tissue fragility, especially if there are also other mechanical and anatomic risk factors present. EDS-related factors challenging locoregional anesthesia are cardiovascular abnormalities, excessive bleeding, and a higher failure rate.<sup>10,18</sup>

We would like to make the following suggestions for anesthesia in patients with EDS complicated by tissue fragility. First, in an EDS patient with concomitant risk factors for postintubation tracheal rupture, alternative techniques should be considered (*i.e.*, use of a supraglottic device or

locoregional anesthesia). Second, if tracheal intubation is required, it must be performed by an experienced anesthesiologist, with correct tube size and depth. In addition, low positive-pressure ventilation especially during the emergence of anesthesia should be used. Third, peripheral regional anesthesia might be a good alternative option in selected patients. Recently, Wegener *et al.*<sup>10</sup> demonstrated the feasibility of ultrasound-guided peripheral nerve block in EDS patients. Although this seems to be a safe technique, any intervention in these fragile patients should be performed with extreme care. Finally, if tracheal rupture does occur, we recommend conservative treatment as the best approach in patients not requiring mechanical ventilation, for patients with scheduled extubation within 24 h or for patients with the ability to bridge the tracheobronchial rupture if mechanical ventilation is required.<sup>7</sup>

## References

1. Beighton P, De PA, Steinmann B, Tsipouras P, Wenstrup RJ: Ehlers-Danlos syndromes: Revised nosology, Villefranche, 1997. Ehlers-Danlos National Foundation (USA) and Ehlers-Danlos Support Group (UK). *Am J Med Genet* 1998; 77:31-7
2. Schalkwijk J, Zweers MC, Steijlen PM, Dean WB, Taylor G, Vlijmen IM, van Haren B, Miller WL, Bristow J: A recessive form of the Ehlers-Danlos syndrome caused by tenascin-X deficiency. *N Engl J Med* 2001; 345:1167-75
3. Egging D, van den BF, Taylor G, Bristow J, Schalkwijk J: Interactions of human tenascin-X domains with dermal extracellular matrix molecules. *Arch Dermatol Res* 2007; 298:389-96
4. Egging DF, van Vlijmen I, Starcher B, Gijsen Y, Zweers MC, Blankevoort L, Bristow J, Schalkwijk J: Dermal connective tissue development in mice: An essential role for tenascin-X. *Cell Tissue Res* 2006; 323:465-74
5. Lane D: Anaesthetic implications of vascular type Ehlers-Danlos syndrome. *Anaesth Intensive Care* 2006; 34:501-5
6. Dolan P, Sisko F, Riley E: Anesthetic considerations for Ehlers-Danlos syndrome. *ANESTHESIOLOGY* 1980; 52:266-9
7. Minambres E, Gonzalez-Castro A, Buron J, Suberviola B, Ballesteros MA, Ortiz-Melon F: Management of postintubation tracheobronchial rupture: Our experience and a review of the literature. *Eur J Emerg Med* 2007; 14:177-9
8. Borasio P, Ardissone F, Chiampo G: Post-intubation tracheal rupture. A report on ten cases. *Eur J Cardiothorac Surg* 1997; 12:98-100
9. Minambres E, Buron J, Ballesteros MA, Llorca J, Munoz P, Gonzalez-Castro A: Tracheal rupture after endotracheal intubation: A literature systematic review. *Eur J Cardiothorac Surg* 2009; 35:1056-62
10. Wegener JT, Frassdorf J, Stevens MF: Effective plexus anaesthesia in a patient with Ehlers-Danlos syndrome type III. *Eur J Anaesthesiol* 2009; 26:619-21
11. Schneider T, Storz K, Dienemann H, Hoffmann H: Management of iatrogenic tracheobronchial injuries: A retrospective analysis of 29 cases. *Ann Thorac Surg* 2007; 83:1960-4
12. Marty-Ane CH, Picard E, Jonquet O, Mary H: Membranous tracheal rupture after endotracheal intubation. *Ann Thorac Surg* 1995; 60:1367-71
13. Massard G, Rouge C, Dabbagh A, Kessler R, Hentz JG, Roeslin N, Wihlm JM, Morand G: Tracheobronchial lacerations after intubation and tracheostomy. *Ann Thorac Surg* 1996; 61:1483-7
14. Hofmann HS, Rettig G, Radke J, Neef H, Silber RE: Iatrogenic ruptures of the tracheobronchial tree. *Eur J Cardiothorac Surg* 2002; 21:649-52
15. Ishiguro T, Takayanagi N, Kawabata Y, Matsushima H, Yoshii Y, Harasawa K, Yamaguchi S, Yoneda K, Miyahara Y, Kagiya N, Tokunaga D, Aoki F, Saito H, Kurashima K, Ubukata M, Yanagisawa T, Sugita Y, Okita H, Hatamochi A: Ehlers-Danlos syndrome with recurrent spontaneous pneumothoraces and cavitory lesion on chest X-ray as the initial complications. *Intern Med* 2009; 48:717-22
16. Sood V, Robinson DA, Suri I: Difficult intubation during rapid sequence induction in a parturient with Ehlers-Danlos syndrome, hypermobility type. *Int J Obstet Anesth* 2009; 18:408-12
17. Nishiyama Y, Nejima J, Watanabe A, Kotani E, Sakai N, Hatamochi A, Shinkai H, Kiuchi K, Tamura K, Shimada T, Takano T, Katayama Y: Ehlers-Danlos syndrome type IV with a unique point mutation in COL3A1 and familial phenotype of myocardial infarction without organic coronary stenosis. *J Intern Med* 2001; 249:103-8
18. Dill-Russell P, Jones LS: Anaesthesia for caesarean section in a patient with Ehlers-Danlos syndrome and mitral valve prolapse. *Int J Obstet Anesth* 2001; 10:192-7