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CASE REPORT

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Idiopathic subglottic stenosis in a 32-year-old pregnant woman

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ABSTRACT

Diagnosis of subglottic stenosis remains greatly a challenge for physicians due to case rarity and presentation of symptoms imitating several other more prevalent medical disorders. Idiopathic subglottic stenosis most often occurs in previously healthy perimenopausal Caucasian women. Several cases have reported symptom progression and increased stenosis, during or in between pregnancies in younger women. The following case of a 32-year-old woman provides an example of significantly long duration from initial symptom onset to diagnosis of idiopathic subglottic stenosis. Additionally, the case illustrates how pregnancy complicates diagnosis and due to the potential risk of stenosis progression and complications during labour, the patient had to undergo surgery with balloon-dilation at week 17 of pregnancy.

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Introduction

The subglottic space is defined by the anatomical borders of the larynx, with the vocal cords as the upper border and the cricoid cartilage as the lower border [1]. Intraluminal obstruction in the subglottic space is termed subglottic stenosis (SGS). Symptoms of SGS develop gradually over time and include dyspnea, often during mild physical activity, coughing and wheezing or even stridor [2]. SGS severity is graded by the Cotton-Myer grading system into I (obstruction of lumen, 0–50%), II (obstruction of lumen, 51–70%), III (obstruction of lumen, 71–99%) and IV (total obstruction) [3]. Another grading system, i.e. the McCaffrey system, includes both anatomical position and length of the lesion [4]. The causes of SGS are numerous. The most common cause is iatrogenic stenosis due to tracheostomy and intubation [2]. SGS can also be seen in various diseases such as autoimmune disorders, i.e. granulomatosis with polyangiitis, infectious diseases, inhalational injury, side effect to radiation therapy, foreign body aspiration and many more [4,5]. Cases with unidentifiable cause are termed idiopathic subglottic stenosis (iSGS) with an annually incidence around 1 per 400,000 persons [6]. iSGS are predominately seen in previously healthy perimenopausal Caucasian women in ages 30–60 years, with a mean age of 50 [7]. This has led to proposed hormonal mechanisms in iSGS pathogenesis. An *ex vivo* study found differentially expressed hormone receptors, i.e. estrogen receptor 1 (ESR1), estrogen receptor 2 (ESR2) and progesterone receptor (PGR) in stenotic scar tissue from iSGS patients compared to healthy tissue in the same patients [8]. Other studies point towards immunological interactions between tracheal microbiota specifically Mycobacterium, Acinetobacter and Moraxella species and host immune respose, namely γδT-cells and IL-17 response initiating fibroblast proliferation [9,10]. The relative rarity of SGS and common symptoms of other disease gives rise to differential diagnostic challenges. Hence, the duration from symptom onset to diagnosis is often extensively long. Studies report a median time of 24–36 months from symptom to diagnosis, often due to a misdiagnosis of asthma [11,12]. The following case report prov ides an example of a significantly prolonged time from initial patient-physician-contact until final diagnosis and treatment, and how the disease severity progresses over time. It seems therefore important to increase awareness of this condition in physicians examining patients presenting with dyspnea.

Case report

Prologue

A 29-year-old woman was admitted to the acute ward due to increasingly dyspnea for the past days. The

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patient's dyspnea had been there periodically for almost 5 months. The dyspnea had suddenly progressed and was most present at night when lying down and was accompanied by cough. Upon admission, pneumonia or pulmonary embolism were the main diagnoses that were suspected. Admission blood tests were within normal range including a normal D-dimer and inflammatory parameters. A chest x-ray (Figure 1) showed no obvious pathology and the patient was discharged on the same day.

Two and a half years went by and the now 32-year-old woman was still experiencing progressive dyspnea and cough with occasionally expectoration. The patient was a previously healthy non-smoker. In primary care prior to referral to the asthma and allergy clinic the patient's symptoms were interpreted as asthmatic symptoms and the patient's lung function was assessed. Primary care spirometry showed normal dynamic lung volumes, forced vital capacity (FVC) and forced expiratory volume in 1st second (FEV1) with no reversibility. Chest x-ray and echocardiography were also normal. Despite normal lung function, the patient's symptoms progressed and treatment with low dose inhaled corticosteroid (ICS) was initiated. The treatment had no effect, and the patient was referred to the outpatient clinic for further examination.

Prior to first visit a mannitol test had been made in another asthma allergy clinic that proved to be negative. At the first visit, a series of tests including spirometry, bronchial provocation and airway resistance were performed in an attempt to diagnose asthma. The woman presented a spirometry within the normal range (Table 1). Flow (L/s)–volume (L) curve displayed in Figure 1. First measurement (blue curve) was separated from the rest with a plateau morphology and was thought to be an error or poor attempt. Furthermore, a direct bronchial provocation test with methacholine was performed at the first visit and turned out to be negative. Impulse oscillometry (IOS) showed increased total airway resistance R5Hzindicating an obstruction of the airways (R5Hz: resistance at 5 hz) and decreased X5Hz (X5Hz: Lung reactance at 5 hz) (Table I). The IOS was repeated and found a similar result. Blood tests included immunoglobulin E (IgE), specific IgE for most common aeroallergens and leucocyte count, including eosinophils. All blood tests were within the normal range. Fractional exhaled nitrous oxide (FeNO) was also within the normal range; seven parts per billion (ppb) (normal range < 25 ppb). A high-resolution computer tomography (HRCT) scan was proposed to further evaluate the airways and lungs; however, at this time, the patient was possibly carrying an early pregnancy, and therefore the scan was postponed.

Table 1. Spirometry and impulse oscillometry measurements at first, second and third visit. Bronchoscopy and flexible laryngoscopy were performed in between second and third visit. FEV1: forced expiratory volume in first second. Predicted values either by absolute or percentage presented in parenthesis. FVC: forced vital capacity. GA: gestational age. IOS: impulse oscillometry. R5: resistance at 5 hz. X5: lung reactance at 5 hz.

	1st visit – Early pregnancy GA: 1–3 weeks	2nd visit – Pregnant GA: 12 weeks	3rd visit – Pregnant GA: 17 weeks (1 week prior to endoscopic surgery)
FVC	4.47 (117%)	4.10 (108%)	4.29 (113%)
FEV1	3.42 (103%)	2.51 (76%)	2.88 (88%)
FEV1/ FVC index	0.76 (92%)	0.61 (73%)	0.67 (81%)
IOS, R5	0.77 (0.35)	0.89 (0.35)	–
IOS, X5	−0.36 (−0.02)	−0.31, (−0.02)	–

Second visit

The woman was now pregnant in the very end of first trimester (week 12). The patient's symptoms had progressed further. The patient experienced dyspnea in low-effort physical activity, such as standing up from a seated position. The patient's family, friends and colleagues were starting to comment on the patient's increasing shortness of breath. The patient's spirometry showed a close to stationary FVC, a significant decrease in FEV1 as well as a decrease in FEV1/FVC (Table 1). IOS measurements also indicated progression in pulmonary resistance (Figure 2). No reversibility was detected (Table 1). Flow-volume curve showed a maximum and constant flow around 2 L/s for the entire expiration (Figure 1). The flat, plateau-like, appearance of the Flow-Volume curve and progressive increase in airway resistance were highly suspicious of tracheal intraluminal obstruction. Hence, a bronchoscopy was requisitioned. Due to the symptom's severity and the ongoing pregnancy, a bronchoscopy was scheduled shortly after the second visit. Bronchoscopy showed an almost total obstruction of the subglottic area. After inserting the scope further down the trachea, a total obstruction was induced; the patient was gasping for air, and the bronchoscope had to be removed after approximately 15 s. A possible diagnosis of iSGS was made, and the patient was referred acutely to the department of otorhinolaryngology for further evaluation. Flexible laryngoscopy showed no abnormal findings in the pharynx, upper larynx and vocal cords. In the subglottic area, a grade II Cotton-Myer (51–70% obstruction) circumferential stenosis was observed. Due to the risk of further stenosis progression during pregnancy and potential life-threatening complications during labour,

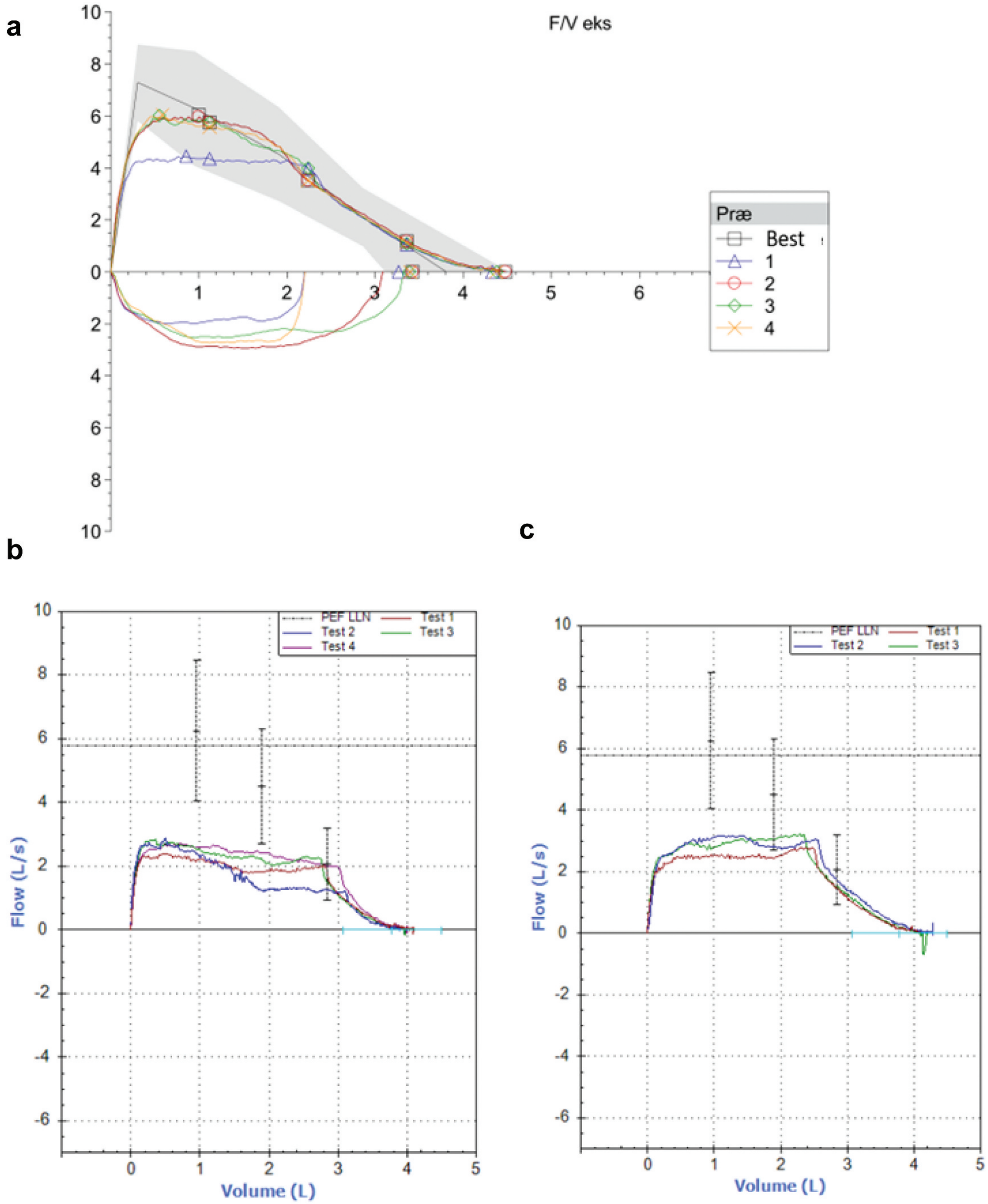
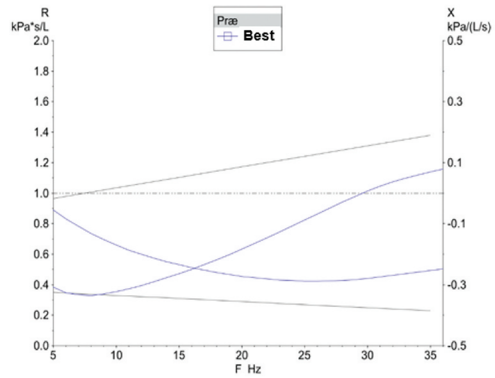


Figure 1. Flow-volume curves. Figure Ia–c: Flow-volume curves from first visit (a), second visit (b) and third visit (c). Inspiratory curves from second and third visits are unfortunately missing.

the surgical dilation had to be performed well before upcoming labour.

A third visit measuring spirometry was performed 1 week prior to surgery and showed stable to a minor improvement dynamic lung volumes, however, still noticeably worse than the first visit. During endoscopic surgery, the stenosis grade II was confirmed. Endoscopic surgery was performed in general anestesia under jet ventilation (Image 1). An endoscopic incision and balloon dilation were performed to expand and efface the stenotic area. Intralesional long-acting steroid injection was performed in three separate areas of the former stenotic area. The procedure was accomplished without complication in week 18 of pregnancy.

Impulse oscillometry



Resistance & reactance

		Pred	Best	%(B/P)	D-pred	Z-score	
R5Hz	kPa/(L/s)	0.35	0.89	254	-0.54	5.14	
X5Hz	kPa/(L/s)	-0.02	-0.31	1765	0.29	-2.77	
Fres.	1/s		29.60				
AX	kPa/L		5.13				
D5-20%	%		48.72				

Figure 2. Impulse oscillometry curve from 2nd visit.

Left x -axis: Resistance in kilopascal × seconds per liter. Right x-axis: Reactance in kilopascal per liter per second. Y-axis frequency in Hertz.

Left upper blue curve is the resistance/frequency curve. Lower gray line illustrates predicted re-sistance/frequency curve in healthy individual.

Left lower blue curve is the reactance/frequency curve. Upper gray line illustrates the predicted reactance/frequency curve in healthy individual. AX Reactance area. D5–20%: small airway index.

Fres: resonance frequency. R5: Resistance at 5 hz, total airway resistance. X5Hz: Lung reactance at 5 hz. %(B/P): Best/predicted ratio in percentage. Pred = predicted.

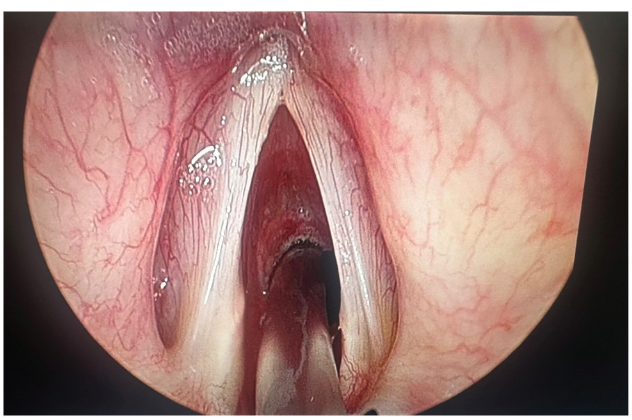


Image I. Endoscopic image showing the patients grade II SGS before incision. Jet ventilator catheter placed in laryngotracheal lumen.

Image II. Laryngoscopic image from case patient taken 2 months after endoscopic surgery. There is full remission of SGS and no post-surgical complications.

Epilogue

The now 33-year-old woman delivered vaginally a healthy normal weighing baby at term without complications during labour. Afterwards, the patient was followed up in the department of otorhinolaryngology. In Image II, an endoscopic image showed complete remission of the patient's SGS. Respiratory symptoms had also complete remission. Months later, symptoms had begun again, and the patient is currently being followed for relapsing iSGS.

Discussion

The case report provides an example of the challenging diagnostic process. Symptoms initially mimicking other diseases in an otherwise healthy patient. In this case, the flattened appearance of the Flow-Volume curve served as the final clue of SGS and led to the concluding bronchoscopy and laryngoscopy in the diagnosis of SGS. Similar cases of SGS with the characteristic Flow-Volume curve appearance have been reported [13,14]. The patient's dynamic lung parameters improved slightly between second and third visit. A feasible theory could be that there may be some severity variability in the patient's airway obstruction. There are two things that are supportive of this. First, the fact that the patient symptom burden varies with occasional exacerbations, i.e. the admission to the acute ward. Second, the Flow-Volume curve from the first visit contains one curve standing out from the rest (Figure 1).

The role of IOS in SGS diagnosis is not entirely investigated. A small study of 21 patients with confirmed tracheal stenosis showed only a weak correlation between X5 and tracheal narrowing ($p = 0.045$). The majority of patients in the study (90.5%) were patients with iatrogenic tracheal stenosis due to prolonged intubation [15]. IOS in aiding SGS diagnosis remains to be fully explored.

Other diagnostic modalities are advantageous in aiding physicians in diagnosing SGS. This includes radiologic modalities. A chest x-ray is of limited value; however, some case reports have been reporting use of it, but in all cases led to further investigation with more advanced radiologic modalities or endoscopy [16,17]. The sagittal neck x-ray may also be of some value, especially in pediatric population in respect to radiation exposure in young age [18], thus most times also lead to more diagnostic work up with greater sensitivity. Computer tomography (CT) scans and various modes including virtual endoscopy and multiplanar reformations are able to diagnose and grade SGS compatible to flexible tracheobronchoscopy [19]. The woman's, at the time, supposedly early pregnancy impeded a diagnostic work-up with the radiologic modality, thus a bronchoscopy and flexible laryngoscopy were performed.

Cotton-Myer grading system is a widely used grading system of SGS. It is developed and applicable for stenoses solely confined to the subglottic area. It is based on cross-sectional area reduction alone and does not take other complexities of lesions into account. This being length and anatomical positioning of stenosis. The McCaffrey grading system takes this in to accord as both length and involvement of upper trachea and glottis. Both grading systems are validated for an adult and pediatric population. A notable difference besides the above mentioned is that the McCaffrey system only significant benefit is the use as a predictor for a successful decannulation for intubated patients [20,21]. In regard to the case, the patient presents with an SGS confined to the subglottic area, thus the Cotton-Myer grading system is favourable.

Management of SGS includes various options, including both surgically invasive and minimally invasive endoscopic procedures that can be combined with topically applied mitomycin C or intralesional steroid injection. Conservative adjuvant treatment with anti-reflux therapy or ICS. The management is not internationally standardised and still debated. Recurrence of iSGS is quite high, ranging from 40% for open surgery and 80% for endoscopic surgery [7], and multiple treatments are often required. As small study of SGS of different etiologies found supportive evidence of endoscopic surgery followed by serial steroid injections in lowering recurrence rate and increasing surgery-free interval [22]. A larger multicenter prospective study of 810 iSGS patients found that laryngotracheal resection had the lowest recurrence (1.2%) rate compared to endoscopic surgery (28%). Recurrence rate of ISS for endoscopic surgery combined with adjuvant medical therapy was in between 12.4%. Steroid injection was not investigated in this study [23]. Endoscopic surgery was chosen in this case due to ongoing pregnancy.

There is quite noticeable decline in dynamic lung parameters in patient's first trimester, as FEV1 drops almost 1 L between first and second visit. This is also very apperent in Flow-Volume curve, as the plateau morphology emerges in the second visit. A few previous case reports have been reporting women with progressive worsening of symptoms during and in between pregnancies [24,25]. This may suggest that hormonal changes that occur during pregnancy and in post-pregnancy play a substantial role in iSGS pathogenesis. However, a study comparing ESR1/ESR2 and PGR expression in surgical specimens from pregnant and non-pregnant woman showed no difference in expression of hormonal receptors between the groups [26]. Differential expression of hormone receptor of iSGS patients compared to healthy individuals is, however, supportive of hormonal mechanisms in non-pregnant iSGS patients [8]. The tracheal microbiota and immune system are also theorized to play a role in iSGS pathogenesis [9]. Additionally, extraesophageal reflux has been suggested in stenosis formation of iSGS as pepsins were found in scar tissue from iSGS cases compared to healthy controls [27]. Dyspnea can be a symptom that occurs in late pregnancy itself. Pregnancy-related dyspnea could potentially mask symptoms of a previous asymptomatic young woman with subclinical SGS. Physicians may be alerted by disproportionately dyspnea, and especially wheezing and stridor in pregnant women, notably if these symptoms do not regress shortly after delivery. Management of SGS in pregnant women must be approached with a multidisciplinary team of otolaryngologists, pulmonologists, obstetricians and anaesthesiologists in determining risk of stenosis progression during pregnancy and risk of preterm delivery as reported in several cases [25,28].

Learning points of the case

- Flattened Flow-Volume curve is suggestive for upper airway obstruction
- Abnormal impulse oscillometry, a potential diagnostic clue along with spirometry.
- Pregnancy may lead to symptom progression and can prove challenging in diagnosis and management of treatment for SGS.
- When to suspect iSGS: Caucasian woman, in ages 30–60, with none to few other medical disorders.
- Time from symptom onset to diagnosis due to low disease incidence remains challenging for physicians.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Informed consent

Written informed consent for publication of this case report was obtained from the patient.

Abbreviations

CT	Computer tomography
ESR1	Estrogen receptor 1
ESR2	Estrogen receptor 2
FeNO	Fractional exhaled nitric oxide
FEV1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
GA	Gestational age
HRCT	High resolution computer tomography
LLN	Lower limit of normal
PGR	Progesterone receptor
ICS	Inhaled corticosteroid
IgE	Immunoglobulin E
IOS	Impulse oscillometry
iSGS	Idiopathic subglottic stenosis
Ppb	Parts per billion
PEF	Peak flow
R5	Resistance at 5 hertz, total airway resistance
SGS	Subglottic stenosis
ULN	Upper limit of normal
X5Hz	Lung reactance at 5 hertz

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References

[1] D'Andrilli A, Venuta F, Rendina EA. Subglottic tracheal stenosis. J Thorac Dis. 2016;8(Suppl 2):S140–7. doi: 10.3978/j.issn.2072-1439.2016.02.03

[2] Pasick LJ, Anis MM, Rosow DE. An updated review of Subglottic Stenosis: etiology, evaluation, and management. Curr Pulmonol Rep. 2022;11(2):29–38. doi: 10.1007/s13665-022-00286-6

[3] Myer CM 3rd, O'Connor DM, Cotton RT. Proposed grading system for subglottic stenosis based on endotracheal tube sizes. Ann Otol Rhinol Laryngol. 1994;103(4):319–323. doi: 10.1177/000348949410300410

[4] Aravena C, Almeida FA, Mukhopadhyay S, et al. Idiopathic subglottic stenosis: a review. J Thorac Dis. 2020;12(3):1100–1111. doi: 10.21037/jtd.2019.11.43

[5] Dablanca M, Maeso A, Méndez DDC, et al. Estenosis laringotraqueales de etiología autoinmune. Acta Otorrinolaringológica Española. 2017;68(1):38–42. doi: 10.1016/j.otorri.2016.01.002

[6] Maldonado F, Loiselle A, DePew ZS, et al. Idiopathic subglottic stenosis: an evolving therapeutic algorithm. Laryngoscope. 2014;124(2):498–503. doi: 10.1002/lary.24287

[7] Gelbard A, Donovan DT, Ongkasuwan J, et al. Disease homogeneity and treatment heterogeneity in idiopathic subglottic stenosis. Laryngoscope. 2016;126(6):1390–1396. doi: 10.1002/lary.25708

[8] Talatala ERR, Clark E, Ye W, et al. Localizing hormone receptor expression to cellular compartments in idiopathic subglottic stenosis. Laryngoscope. 2023;133(12):3506–3511. doi: 10.1002/lary.30856

[9] Marchioni A, Tonelli R, Andreani A, et al. Molecular mechanisms and physiological changes behind benign tracheal and subglottic stenosis in adults. IJMS. 2022;23(5):2421. doi: 10.3390/ijms23052421

[10] Gelbard A, Katsantonis N-G, Mizuta M, et al. Molecular analysis of idiopathic subglottic stenosis for mycobacterium species. Laryngoscope. 2017;127(1):179–185. doi: 10.1002/lary.26097

[11] Berges AJ, Lina IA, Chen L, et al. Delayed diagnosis of idiopathic subglottic stenosis. Laryngoscope. 2022;132(2):413–418. doi: 10.1002/lary.29783

[12] Wang H, Wright CD, Wain JC, et al. Idiopathic subglottic stenosis: factors affecting outcome after single-Stage repair. Ann Thorac Surg. 2015;100(5):1804–1811. doi: 10.1016/j.athoracsur.2015.05.079

[13] Pomerantz B, Pomerantz M, Finn A. Idiopathic subglottic stenosis in a young female patient. BMJ Case Rep. 2021;14(5):e241525. doi: 10.1136/bcr-2020-241525

[14] Verjans R, van Berkel S, Brandon T, et al. Idiopathic subglottic stenosis and the consequences in cardiopulmonary exercise testing. BMJ Case Rep. 2021;14(11):e242149. doi: 10.1136/bcr-2021-242149

[15] Linhas R, Lima F, Coutinho D, et al. Role of the impulse oscillometry in the evaluation of tracheal stenosis. Pulmonology. 2018;24(4):224–230. doi: 10.1016/j.pulmoe.2017.12.006

[16] Lee KH, Kang ES, Jung JW, et al. Use of the i-gel™ supraglottic airway device in a patient with subglottic stenosis -a case report-. Korean J Anesthesiol. 2013;65(3):254–256. doi: 10.4097/kjae.2013.65.3.254

[17] Seeli K, Ravi Kumar Angirekula V, Roberson D, et al. A case of subglottic stenosis due to an intra-cricoid abscess. Chest. 2023;164(4):A1110–A1111. doi: 10.1016/j.chest.2023.07.805

[18] Kakamad FH, Fatah M, Rashid R, et al. Challenges and successful management of subglottic tracheal stenosis in a 2-year-old child: a case report and a mini-review of the literature. Med Int (Lond). 2023;3(5):53. doi: 10.3892/mi.2023.113

[19] Morshed K, Trojanowska A, Szymański M, et al. Evaluation of tracheal stenosis: comparison between computed tomography virtual tracheobronchoscopy with multiplanar reformatting, flexible tracheofiberoscopy and intra-operative findings. Eur Arch Otorhinolaryngol. 2011;268(4):591–597. doi: 10.1007/s00405-010-1380-2

[20] McCaffrey TV. Classification of laryngotracheal stenosis. Laryngoscope. 1992;102(12):1335–1340. doi: 10.1288/00005537-199212000-00004

[21] Filauro M, Mazzola F, Missale F, et al. Endoscopic preoperative assessment, classification of stenosis, decision-making. Front Pediatr. 2019;7:532. doi: 10.3389/fped.2019.00532

[22] Wierzbicka M, Tokarski M, Puszczewicz M, et al. The efficacy of submucosal corticosteroid injection and dilatation in subglottic stenosis of different aetiology. J Laryngol Otol. 2016;130(7):674–679. doi: 10.1017/S0022215116001122

[23] Gelbard A, Anderson C, Berry LD, et al. Comparative treatment outcomes for patients with idiopathic subglottic stenosis. JAMA Otolaryngol Head Neck Surg. 2020;146(1):20–29. doi: 10.1001/jamaoto.2019.3022

[24] Miller EJ, Huning EY. Subglottic tracheal stenosis complicating pregnancy: a case report. Obstet Med. 2022;15 (3):205–207. doi: 10.1177/1753495X21990220

[25] Fang S, Pai BHP. Successful management of subglottic stenosis in pregnancy. BMJ Case Rep. 2021;14(3): e236466. doi: 10.1136/bcr-2020-236466

[26] Tapias LF, Rogan TJ, Wright CD, et al. Pregnancy-associated idiopathic laryngotracheal stenosis: presentation, management and results of surgical treatment. European Journal Cardio-Thoracic Surgery. 2021;59 (1):122–129. doi: 10.1093/ejcts/ezaa296

[27] Blumin JH, Johnston N. Evidence of extraesophageal reflux in idiopathic subglottic stenosis. The Laryngoscope. 2011;121(6):1266–1273. doi: 10.1002/lary.21776

[28] Hamersley ER, Perez AJ, Morrison MP, et al., Surgical treatment of symptomatic subglottic stenosis during the third trimester of pregnancy. Ear Nose Throat J. 2018;97 (4–5):E10–e12.