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Case report

TREATMENT OF PARADOXICAL VOCAL FOLD MOTION IN A 12-YEAR-OLD PATIENT WITH PATAU'S SYNDROME

Francesco Freni, Bruno Galletti, Viviana Nicastro, Pietro Abita, Annamaria Zagaria, Rocco Bruno, Francesco Galletti

Department of Adult and Development Age Human Pathology "Gaetano Barresi", Unit of Otorhinolaryngology, University of Messina, Italy

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ABSTRACT

We describe the case of a 12-year-old girl with paradoxical vocal fold motion (PVFM) secondary to partial Patau's syndrome, successfully treated with botulinum toxin A (BTX-A) injection to the vocal folds. We performed follow-up 1 and 3 months after the injection, with no relapse. Paradoxical vocal fold motion (PVFM) is a poorly understood disorder of episodic dyspnea. The aim of this case is to highlight the use of a mini-invasive surgical technique to treat PVFM in a patient otherwise forced to undergo a permanent tracheostomy, reducing the peri- and postoperative risks of its management.

1. Introduction

Paradoxical vocal fold motion (PVFM), also termed vocal cord dysfunction, is a poorly understood disorder of episodic dyspnea characterized by inappropriate vocal cord adduction during inhalation and potentially during exhalation. It can coexist or be confused with asthma and the symptoms are often acute in nature and can be quite variable in intensity and duration.[1,2] Although many patients with PVFM may have underlying psychological issues, there is emerging evidence to suggest that this entity is not psychogenic in every patient. Laryngeal irritants, exercise and laringopharyngeal reflux (LPR) have been identified as additional contributing factors in PVFM.[1,3]

The disorder was first described in 1842 by Robley Dunglsion who described laryngeal spasms induced by "hysteria". Literature from the 1970s further depicted a syndrome frequently mimicking asthma and carrying numerous misnomers including "Munchausen's stridor" and "factitious asthma". Rodgers and Stell first employed the more physiological terminology "paradoxical vocal cord movement" in 1978.[4]

The diagnosis can be made by fiber-optic laryngoscopy, which shows a paradoxical adduction of the vocal folds especially during inspiration with inspiratory stridor and respiratory distress.

Initial treatment of PVFM is conservative, consisting in reassurance, breathing techniques, drugs (such as benzodiazepines, ketamine, etc), helium-oxygen inhalation and non-invasive positive-pressure ventilation (C-PAP).

After failure of these kinds of treatments, invasive treatments can be taken into consideration ranging from BTX-A injection to the vocal folds to endotracheal intubation or tracheotomy.[5]

Patau's syndrome is a genetic disorder caused by the trisomy of the thirteenth chromosome (trisomy 13 syndrome), being the third most common autosomal chromosome trisomy, occurring in 1 per 5000 total births. Advanced maternal age is a risk factor for this pathology because of the increased frequency of nondisjunction in meiosis. This extra copy of chromosome 13 disrupts normal embryonic development and leads to multiple defects. The most common defects include the clinical triad microphthalmia, cleft lip/palate, and polydactyly. Heart defects (ventricular septal defect, atrial septal defect, tetralogy of Fallot, atrioventricular septal defect, and double outlet right ventricle) and central nervous system defects (alobar holoprosencephaly being the most common) are also commonly found in these patients. Trisomy 13 can also present in other genetic forms, including partial trisomy (in which the exuberant chromosome is incomplete), secondary to a chromosome translocation and as a result of mosaicism (when the trisomy cannot be found in the DNA of all body cells). The diagnosis of this condition can be made prenatally with chorionic villi sampling, amniocentesis or fetal free DNA analysis, supported by prenatal ultrasound showing holoprosencephaly or other central nervous system anomalies, facial anomalies, skeletal abnormalities, renal or cardiac defects, and growth restriction.

Corresponding author: Viviana Nicastro, *vivianica@hotmail.it*
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The prognosis for the complete trisomy 13 is extremely poor and patients surviving past infancy have a severe psychomotor disorder, failure to thrive, mental retardation, and seizures. Other genetic forms have a less critical presentation and patients can easily survive longer.[6-8]

We present the case of a 12-year-old girl with paradoxical vocal fold motion (PVFM) secondary to central nervous system disorders due to partial Patau's syndrome, successfully treated with botulinum toxin A (BTX-A) injection to the vocal folds, performed under general anesthesia through direct microlaringoscopy.

2. Case report

We present the case of a 12-years-old girl that came to our Pediatric Intensive Care Unit (P-ICU) from another hospital with a history of inspiratory stridor, dysphagia and signs of respiratory distress (episodic desaturation). The patient was affected by partial Patau's syndrome, a genetic disorder caused by partial trisomy of the thirteenth chromosome (13q-21.2). She presented multi-organ alterations which caused psychomotor disorder, epilepsy, chronic rhinosinusitis, sensorineural hearing loss and mental retardation due to hypotrophy of the left cerebral hemisphere (especially in the fronto-parietal-occipital cortex, as described by multiple magnetic resonances performed during patient's life) [9-10].

She arrived to the P-ICU with oro-tracheal intubation due to respiratory distress. The patient was mechanically ventilated with BiPAP (FiO_2 0,30; Ti 0,9; Pip 22; PEEP 6 ; frq 25). The Otolaryngology service was consulted and a flexible laryngoscopy was performed but, due to the intubation, no particular macroscopic abnormalities were found. Together with the P-ICU staff another flexible laryngoscopy was proposed, in which an extubation and further evaluation of the vocal plane was performed. During this evaluation, there appeared a presence of gastric secretions in the hypopharingeal and laryngeal space, aspirated with a channeled fiber-optic laryngoscope. After aspiration, the anatomic structures of the vocal folds and supraglottic larynx were explored, appearing normal. During inhalation though, a paradoxical adduction of the vocal folds was evidenced, reducing the respiratory space without its complete closure, with the conservation of a posterior diamond-shaped gap. Due to these findings, the patient was forced to be intubated again and maintained mechanical ventilation to avoid further episodes of desaturation, which were later documented even though the patient's airway were confirmed patent.

Allergologic tests and pneumologic examination were performed without showing any signs of allergic asthma or pulmonary dysfunction. After a review of the literature, the diagnosis of PVFM was suspected, supported by the normal abduction of the vocal folds. This vocal fold dysfunction was thought to be related to the chromosomopathy, due to the central nervous system abnormalities shown with magnetic resonances (chronic ischemic lesions in the corpus callosum and hypotrophy and cavitation in the white and grey matter of the frontal, occipital and parietal cortex, especially in the left brain hemisphere). An anti-reflux therapy was prescribed; the hypothesis of a tracheotomy was proposed to the parents who rejected it.

A laryngoscopic re-evaluation was performed 20 days after therapy, showing no signs of stasis of gastric secretion or GERD-related pharyngo-laryngopathy. During the examination, the diagnosis of PVFM was confirmed and, despite surgical tracheostomy, a conservative treatment based on injection of BTX-A was proposed and approved by the parents.

The patient was transported to the operating room of our ENT Unit. We performed, under general anesthesia, an injection of 0.075 ml of BTX-A at a concentration of 4UI/cc per vocal fold (in the lateral thyroarytenoid muscles) through direct microlaryngoscopy (Figure 1). Three days after surgery, the patient was extubated and evaluated, still demonstrating a paradoxical adduction of the vocal fold. She was intubated again and re-evaluated 8 days after the infiltration of BTX-A, demonstrating no signs of respiratory distress and inspiratory stridor. Finally, the patient was definitively extubated.

We performed two re-evaluations with flexible fiber-optic laryngoscopy, 1 and 3 months after surgery. The patient appeared asymptomatic during the examination, without other respiratory symptoms. We will perform the next follow-up 6 months after surgery.

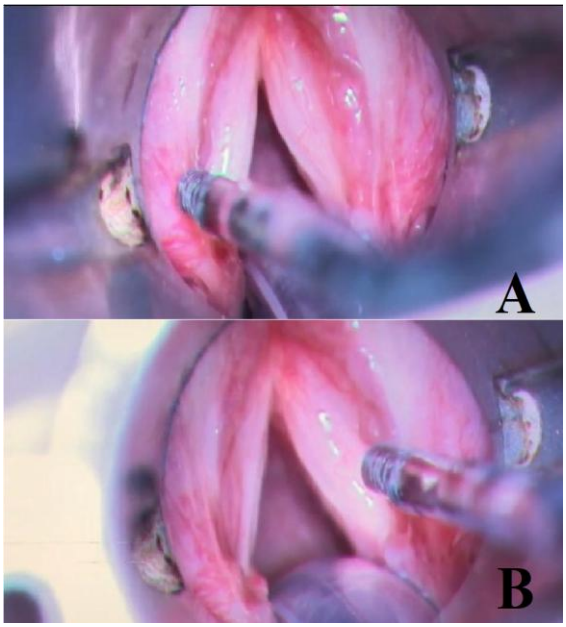

Figure 1. Injection of Botulinum Toxin A in both vocal fold in the lateral thyroarytenoid muscles.

3. Discussion

Malignant PVFM is a poorly understood disorder of episodic dyspnea characterized by inappropriate vocal cord adduction during both inhalation and exhalation, although most commonly observed during inhalation (as in our case study). The adduction results from a laryngeal muscles spasm, causing glottis and supraglottis airway obstruction. It is characterized by symptoms of respiratory distress (dyspnea and laryngeal stridor) and subsequent hypoxia. Its etiology is thought to be multifactorial with asthma, gastro-esophageal reflux and psychogenic disorders being the most common causes. Psychogenic disorders include depression, personality disorders, post-traumatic stress disorder or a history of childhood sexual abuse.[3] This condition is often misdiagnosed with asthma, which frequently coexists at diagnosis.

The treatment of asthma in these patients usually doesn't appear to give much response. The diagnosis remains complicated and seemingly more common after excluding the most typical causes of respiratory distress and needs to be established with a multidisciplinary approach (secondary to an ENT, pneumologic, speech therapy and radiological evaluation).

Flexible laryngoscopy remains the gold standard in diagnosing this condition, showing a paradoxical adduction of the vocal folds during inhalation. Vocal fold paralysis, glottic stenosis, subglottic or tracheal stenosis, tracheomalacia, laryngeal dystonia, and upper airway mass/lesion may have similar presentations to PVFMD and must be ruled out in the differential diagnosis.[2]

The nomenclature of this condition has not yet been confirmed nor agreed upon by the scientific community and finds its origin in the former etiologic hypothesis of a laryngeal spasm induced by hysteria (it is also known, in fact, as "Munchausen stridor", "factitious asthma", "emotional laryngeal wheezing", "irritable larynx syndrome", etc)[4,5,11]. Nowadays, the causes of this condition also comprehend organic diseases, such as Benign Rolandic epilepsy (BRE) (the most common epilepsy of childhood) described in at least one case in literature[12]. Our patient was affected by a partial form of Patau's syndrome, a genetic disorder in which epilepsy is commonly found. She has undergone numerous MRIs in her life which constantly showed an hypotrophy of the left cerebral hemisphere (especially in the fronto-parietal-occipital cortex), corpus callosum and brainstem, which could explain the presentation of the symptoms.

The treatment of PVFM consists mainly in conservative strategies such as speech therapy, breathing techniques, drugs like benzodiazepines (which have the potential risk of depression of the respiratory drive), ketamine (maybe associated with laryngospasm at high doses) and mechanical ventilation (BiPAP or C-PAP). Invasive treatments consist mainly of oro-tracheal intubation and tracheostomy[5]. In our case the patient's mental retardation and scarce collaboration excluded the potential use of any conservative treatment, leaving only invasive maneuvers as possible treatment scenarios. Considering the risks and difficulties in managing a tracheostomy, we decided to review the literature for considering a less invasive treatment for the patient and the possibility of injecting a small quantity of BTX-A was then proposed to the parents.

Injection of BTX-A in ENT field has been proven nowadays to be a safe and repeatable procedure to treat different kinds of diseases. In our Unit, for example, we used it to successfully treat facial sweating and redness during meals as a consequence of Frey's syndrome, a typical complication seen after parotidectomy[13]. Injection of BTX-A in the laryngeal muscles showed an excellent outcome in managing the respiratory distress symptoms and can also be performed after local anesthesia with an office-based trans-nasal approach through a channeled fiber-optic laryngoscope, having the aim of injecting the BTX-A in the thyroarytenoid muscles to provoke their temporary paralysis, relieving the patient from the respiratory symptoms[3]. However, the scarce collaboration of the patient forced us to perform surgery under general anesthesia. The review of the literature also showed that the efficacy of the treatment could last from 15 to 18 weeks,[14] with the possibility of repeating the treatment.

Authors of the literature concentrate their studies on the relieving effect BTX-A has on PVFM, without mentioning the delayed timing needed for the BTX-A to develop its effect. In our case, we concluded that a window period of 4 to 8 days (depending on the quantity and concentration of toxin injected) has to be considered for the toxin to perform its effect. We came to this conclusion because a fiber-optic laryngoscopy performed 3 days after the injection still showed no signs of symptom relief, which was then objectified 8 days after the injection.

In this case, this timing had to be considered for the fact that the patient's parents were very concerned about the efficacy of the treatment, so it was important to inform them that an apparent treatment failure in the first 4 days should be considered normal.

Our case report and experience show some important clinical implications since it considers another mini-invasive surgical technique to treat PVFM in a patient otherwise forced toward a permanent tracheostomy, reducing the peri- and postoperative risks of its management and relieving the parents to deal with another difficulty in caring for a compromised patient. PVFM is a less common disorder whose diagnosis is frequently delayed and difficult to be made, also requiring a multidisciplinary approach. The gold standard in the diagnosis is represented by direct fiber-optic laryngoscopy, which shows a paradoxical adduction of the vocal folds during inhalation. In our case, the management of this condition had the aim to perform a mini-invasive surgical technique to avoid the risks and complications of tracheostomy, yet helping the patient to manage the respiratory distress symptoms. BTX-A injection in the vocal folds is a relatively easy and repeatable technique which shows a great outcome and should always be considered in all patients who can't undergo non-invasive treatments. What surely has to be evidenced from our experience is the fact that BTX-A normally needs a window period before acting (in our case from 4 to 8 days after injection, considering the quantity of toxin injected). This statement was not taken under full consideration by most authors in the literature, but plays a central role in the management of the treatment's timing.

References

1. Palla J, Friedman AD. Paradoxical Vocal Cord Motion in Pediatric Patients. Pediatr Ann. 2016 May 1;45(5):e184-8.
2. deSilva B, Crenshaw D, Matrka L, Forrest LA. Vocal fold botulinum toxin injection for refractory paradoxical vocal fold motion disorder. Laryngoscope. 2019 Apr;129(4):808-811.
3. Montojo J, González R, Hernández E, Zafra M, Plaza G. Office-based laryngeal injection of botulinum toxin for paradoxical vocal fold motion in a child. Int J Pediatr Otorhinolaryngol. 2015 Jul;79(7):1161-3.
4. Smith B, Milstein C, Rolfes B, Anne S. Paradoxical vocal fold motion (PVFM) in pediatric otolaryngology. Am J Otolaryngol. 2017 Mar - Apr;38(2):230-232.
5. Denipah N, Dominguez CM, Kraai EP, Kraai TL, Leos P, Braude D. Acute Management of Paradoxical Vocal Fold Motion (Vocal Cord Dysfunction). Ann Emerg Med. 2017 Jan;69(1):18-23.
6. Hsu HF, Hou JW. Variable expressivity in Patau syndrome is not all related to trisomy 13 mosaicism. Am J Med Genet A. 2007 Aug 1;143A(15):1739-48.
7. Williams GM, Brady R. Patau Syndrome. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019-2019 Apr 4.
8. Watson WJ, Miller RC, Wax JR, Hansen WF, Yamamura Y, Polzin WJ. Sonographic detection of trisomy 13 in the first and second trimesters of pregnancy. J Ultrasound Med. 2007 Sep;26(9):1209-14.
9. Galletti B, Gazia F, Freni F, Sireci F, Galletti F. Endoscopic sinus surgery with and without computer assisted navigation: A retrospective study. Auris Nasus Larynx. 2019 Aug;46(4):520-525.

10. Gazia F, Abita P, Alberti G, Loteta S, Longo P, Caminiti F et al. NICU Infants & SNHL: Experience of a western Sicily tertiary care centre. Acta Medica Mediterranea. 2019, 35(2): 1001-7
11. Rosen CA, Mau T, Remacle M, Hess M, Eckel HE, Young VN, Hantzakos A, Yung KC, Dikkers FG. Nomenclature proposal to describe vocal fold motion impairment. Eur Arch Otorhinolaryngol. 2016 Aug;273(8):1995-9.
12. Gross JH, Bertrand M, Hirose K. Benign Rolandic epilepsy presenting like paradoxical vocal fold motion. Int J Pediatr Otorhinolaryngol. 2017 Nov;102:154-156.
13. Freni F, Gazia F, Stagno d'Alcontres F, Galletti B, Galletti F. Use of botulinum toxin in Frey's syndrome. Clin Case Rep. 2019 Jan 31;7(3):482-485.
14. van Esch BF, Wegner I, Stegeman I, Grolman W. Effect of Botulinum Toxin and Surgery among Spasmodic Dysphonia Patients. Otolaryngol Head Neck Surg. 2017 Feb;156(2):238-254.