

Life-Threatening Stridor in Xeroderma Pigmentosum Type A

Abstract

Vocal fold dystonia and total vocal fold paralysis in Xeroderma Pigmentosum Type-A (XPA) are rare clinical conditions that have been recently described in a few case reports from the Japanese literature. We report here an 11-year-old boy with XPA and seizures and a history of frequent emergency room (ER) visits to different local hospitals for recurrent inspiratory stridor that was treated as “croup” since the age of 10.

The child was brought to our ER for the first time with recurrent, severe stridor and was admitted as a severe case of “croup”. He was treated for approximately two weeks with only minimal improvement. Laryngoscopy showed normal vocal cord appearance with no signs of inflammation. Shortly after discharge, he was readmitted with episodic stridor, exacerbated by irritation, excitation and post-oral feeding. The stridor subsided completely during sleep. Repeated laryngoscopy was performed to investigate other potential causes of stridor.

Flexible rhino-laryngoscopy showed paradoxical vocal fold movement with glottic closure during inspiration and limited glottic opening upon expiration, which is consistent with laryngeal dystonia. This case report represents the history, physical examination and the follow-up findings in this case of XPA in a young boy with unusual presentation with stridor and rare association with vocal cord dystonia. Additionally, it illustrates the importance of proper examination and laryngoscopy in this fragile patient group for early diagnosis, proper treatment and prevention of life-threatening consequences.

Keywords: Xeroderma pigmentosum; Laryngeal dystonia; Stridor; Paradoxical vocal fold movement

Case Report

Volume 4 Issue 2 - 2016

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Received: March 20, 2016 | **Published:** April 13, 2016

Abbreviations: XPA: Xeroderma Pigmentosum Type-A; ER: Emergency Room; CF: Cystic Fibrosis; RSV: Respiratory Syncytial Virus; XP: Xeroderma Pigmentosum; PVFM: Paradoxical Vocal Fold Motion

Case Report

The patient was an 11-year-old Saudi boy who presented for the first time to the neuroscience center at 3 years of age as a referral for work-up of seizure disorder and ataxia. He was born by normal vaginal delivery without complications and had a normal early infancy. At 4 months of age, he became sensitive to sunlight with skin sunburns. His xerosis progressively increased with time. He then began to show milestone developmental delay; he did not smile until 5 months of age, did not roll over until 8 months and did not sit until 9 months. He had unsteady walk at 3 years of age with marked speech delay, uttering only a few words that were difficult to understand. Seizures developed at 3 years of age that were controlled well with anticonvulsants. The ataxia and regression of milestones progressed with time until he became totally bedridden. He had characteristic skin lesions in the form of diffuse skin freckling and telangiectasia with sunlight sensitivity. An EEG revealed severe generalized cortical dysfunction of nonspecific etiology. A brain MRI revealed

generalized brain atrophy.

A chromosomal study confirmed Xeroderma pigmentosum type A at 8 years of age. Reviewing his family history, his parents were first-degree cousins, and two younger brothers were diagnosed with a milder form of XPA. There was no family history of epilepsy. In the first presentation, the chief complaint was noisy breathing with shortness of breath associated with “cold” symptoms and a low-grade fever with no vomiting, diarrhea or seizure activity. His vitals were as follows: temperature 30°C, respiratory rate 28 per minute, oxygen saturation 95% on room air, heart rate 105bpm and blood pressure 100/60 mmHg. The patient appeared alert, mildly dehydrated and in mild respiratory distress with stridor.

A general examination (Figure 1) revealed microcephaly with no dysmorphic features, scleral telangiectasia, intact tympanic membranes and clear nose and throat.

He appeared to be mildly tachypnic. His neck was stiff with no lymphadenopathy or masses. A chest examination revealed good air entry bilateral, with no wheezing, rales or retraction. The cardiovascular examination was unremarkable. His abdomen was soft with no organomegaly.



Figure 1: Patient's appearance.

A neurological examination demonstrated spastic quadriplegia and brisk deep tendon reflexes along with contracted and fixed upper and lower extremities. The spine was stiff from the cervical to the lumbosacral segments. A skin examination displayed diffuse freckling and telangiectasia. There were no bed ulcers.

The laboratory findings and imaging studies are summarized as follows.

The venous blood gas data were pH 7.39, PCo₂ 41%, Po₂ 47%, bicarbonate 26 mmol/L and lactate 3.7 mmol/L. The renal panel and electrolytes data were Na⁺ 135 mmol/L, K⁺ 3.9 mmol/L, Cl⁻ 102 mmol/L, BUN 2 mg/dl, creatinine 19 μmol/L and an anion gap of 7. The bone panel data were phosphorus 1.53 mmol/L, alkaline phosphate 307 U/L, total protein 71 g/L, albumin 23.4 g/L, and calcium 2.51 mmol/L. The CBC data were WBC 9800/ml, hematocrit 32.4% and platelets 361,000/ml.

The blood and throat cultures were negative. The influenza A & B and RSV tests were negative. The chest and neck X-ray

studies were unremarkable. The laryngoscopic examination reported "normal" vocal cords. Based on the clinical findings, the preliminary diagnosis was croup. The patient was treated accordingly, with racemic epinephrine and IV fluid. His respiratory distress and stridor gradually improved and he was discharged home in five days in stable condition.

Ten days later, he came back to the emergency room with the same complaint of stridor and difficulty in breathing. Treatment was initiated again with racemic epinephrine and he was admitted to the pediatric ward to continue the same management.

During hospitalization, however, it was noticed that the stridor was triggered and exacerbated mainly by irritation and agitation and particularly during oral feeding time, and subsided totally during sleeping hours. The chest X-rays and all repeated laboratory work were within normal limits. The patient's O₂ saturation was normal, even during episodes of stridor.

A flexible, fiber optic rhino-laryngoscopic examination (Figure 2) showed normal vocal cord anatomy with no edema or mass. However, there was paradoxical vocal cord movement with glottic closure during inspiration (A) and limited glottic opening during expiration (B). These findings were consistent with laryngeal dystonia responsible for the recurrent episodes of stridor. The findings were discussed with the parents in detail and tracheostomy in the near future was advised. The family declined the procedure but agreed to continue follow-up with ENT, neurology and general pediatrics services in outpatient clinics. Follow-up laryngoscopic examinations (twice) within three months showed similar findings.

Six months later, the patient presented to the ER with severe stridor and life-threatening respiratory distress requiring intubation and PICU admission. Informed consent was obtained from the parents for tracheostomy, which was done without complications. The patient was extubated successfully. The patient was scoped again after tracheostomy to check for any changes. An additional decrease in vocal cord mobility to barely flickering movement was noted. The patient was discharged home with tracheostomy to follow-up closely.

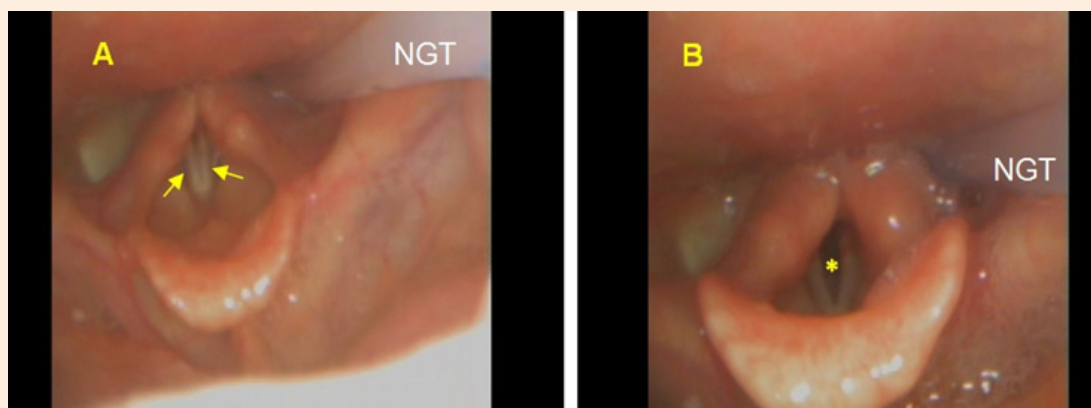


Figure 2: A: Fiber optic rhino-laryngoscopy view showing adducting vocal cords during inspiration (arrows). B: Partial abduction of vocal cords during expiration (*), with limited arytenoids movement. NGT- Nasogastric tube.

Discussion

Stridor is the distinctive, harsh and high-pitched sound resulting from the turbulent flow of air passing through a narrowed segment of the respiratory tract. It usually signifies the presence of upper airway obstruction and may progress to potential respiratory distress.

Stridor can be classified according to the age group. In early infancy, stridor could result from congenital laryngomalacia, vocal cord paralysis, subglottic stenosis, hemangioma, webs, cysts, and papilloma. In pediatric and adolescent age groups, the etiology of stridor differs and may be the result of juvenile onset of recurrent respiratory papillomatosis, foreign bodies, hypocalcemia, cystic fibrosis (CF) and Wagner's granulomatosis. Infectious diseases, commonly herpes simplex, candidiasis and infectious mononucleosis, may contribute to the etiology of stridor. Laryngotracheobronchitis (croup) caused by respiratory syncytial virus (RSV) and epiglottitis due to hemophilus influenza is the common etiology of stridor in infants and children. Stridor may result from neoplasms, such as Hodgkin's disease and thyroid masses. Myasthenia gravis may occasionally be associated with stridor [1].

Xeroderma pigmentosum (XP) is an autosomal recessive disease characterized by hypersensitivity to sunlight, abnormal pigmentation and a predisposition to skin cancer [2,3]. In addition to the cutaneous manifestation, neurological abnormalities (loss of hearing, tendon reflexes, walking impairment, and intellectual impairment) are seen in 20% of patients with XP [4].

Cell fusion analysis has identified seven complementation groups (A-G) of excision repair [5]. Patients with Xeroderma Pigmentosum group A (XPA) generally show the most severe symptoms and signs of the disease [6]. We described here a case of XPA with laryngeal dystonia that resulted in recurrent episodes of stridor and life-threatening respiratory distress requiring intubation and tracheostomy.

Laryngeal dystonia secondary to paradoxical vocal fold motion (PVFM) may be characteristic of this disorder. The vocal folds are innervated by the recurrent laryngeal nerves, which are branches from the vagus nerve originating from the medulla oblongata. During inspiration, the vocal folds should abduct. However, in some cases, such as our XPA patient, the opposite might occur and the patient will have adduction of the vocal folds during inspiration resulting in inspiratory stridor. The specific finding of PVFM is a relatively new clinical entity associated with XPA in the medical literature, with multiple attempts by researchers to explain its mechanism. PVFM has been defined by Andrianopoulos, et al. [7] as an "entity characterized by inappropriate closure of the vocal folds during inhalation, resulting in intermittent respiratory obstruction and stridor" [7].

It has been linked mainly to non-organic causes and psychiatric disorders. Mary JS, et al. [8] stated that the line differentiating between a functional or organic disorder is unclear [8]. Stephen Maturo, et al. [9] determined in their large case series of 59 cases of PVFM that the female to male ratio was 3:1 and that speech therapy was effective in 63% of cases. They reported that many of these cases might have an underlying psychiatric disorder

[9]. PVFM is still not fully understood, and many patients may carry the diagnosis of asthma. When compared with asthma, PVFM has a number of distinctive features, including inspiratory stridor, rather than expiratory wheezing, and the lack of a clinical response to bronchodilators or corticosteroids [9].

The neuropathological study of Røyttä M, et al. [10] showed "marked loss of neurons in the basal nucleus of Meynert, the substantia nigra, the cerebellum, medulla and spinal cord. Diffuse loss of neurons was noted in the cerebral cortex and in the deep cerebral nuclei" [10]. Rie Miyata, in his case series of three XPA patients in their teens with stridor and PVFM, proposed that this loss in the substantia nigra neurons found on autopsy of XPA patients was the explanation for the stridor. He attributed the stridor to the damage of the dopamine neurons in the substantia nigra, as in extrapyramidal disorders. Some improvement of the symptoms after administration of a low dose of levodopa was observed [11].

In our patient, levodopa was declined by the pediatric neurologist, as this treatment is still under clinical trials and is not approved by the corresponding medical societies.

Searching the literature on PVFM or stridor in XP patients, it was exclusively reported in XP type A. Only three papers were found. One paper described a case of total vocal cord paralysis in one XPA patient [12]. The other two papers presented cases very similar to our patient. Ayako Muto, et al. [13] reported three patients, while the other paper described three XPA patients with PVFM who were treated with levodopa [5]. All of these case reports are from Japan. All of these patients were in their second decade at presentation, with the youngest being 12 years and 3 months old [11]. Thus, our patient is the youngest to develop laryngeal dystonia due to PVFM in association with XPA, which began at the age of 10.

Summary

Laryngeal dystonia secondary to PVFM is a poorly understood condition that is life-threatening in XPA patients. To date, there is no definitive approved treatment for this disorder. The onset can be insidious and early in childhood. Laryngeal dystonia should be suspected in XPA patients who present with asthma- or croup-like symptoms that do not improve with standard treatment. Otolaryngology consultation is strongly recommended early in the presentation to assess the patient thoroughly with fiber optic laryngoscopy. Patients should be kept on close follow-up, as they might progressively deteriorate over time and require tracheostomy in order to secure the airway, as in our patient.

One final point that may deserve further discussion and additional research is whether PVFM in XPA patients could progress into total vocal fold paralysis, as found in the case reported by Tatsuyuki Ohto, et al. [12] and as observed clinically in our patient, who experienced a relatively rapid, progressive worsening of stridor over time into a life-threatening event.

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