

Waardenburg syndrome associated with laryngomalacia

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ABSTRACT

Waardenburg syndrome (WS) is a rare autosomal dominant condition characterised by sensorineural hearing loss, in conjunction with pigmentary abnormalities and defects of the neural crest-derived tissues. Depending on the additional phenotypic characteristics, WS is classified into four types, viz. WS1, WS2, WS3 and WS4. We report a 45-day-old male infant with WS1, who presented with inspiratory stridor associated with difficulty in respiration. Direct flexible laryngoscopic examination during evaluation confirmed laryngomalacia as the cause of the symptoms. The baby was managed conservatively and was discharged with appropriate advice to the mother, including the need for evaluation at regular intervals. There was gradual improvement in his symptoms, and by one year of age, he was completely symptom-free. To our knowledge, laryngomalacia as a part of WS, has not been documented to date in the English literature. We also briefly discussed the probable embryological basis for the observed association.

Keywords: hearing loss, laryngomalacia, respiratory distress, Waardenburg syndrome

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INTRODUCTION

We report a case of Waardenburg syndrome (WS) presenting with inspiratory stridor and laboured breathing secondary to laryngomalacia. To our knowledge, this congenital anomaly of the larynx has not been previously reported in association with the syndrome.

CASE REPORT

A 45-day-old male neonate, born to non-consanguineous parents, presented with difficulty in respiration with loud inspiratory noises for two days prior to admission. He was a vaginally-delivered, full-term neonate with satisfactory birth weight, length and head circumference. The mother's antenatal period and delivery were



Fig.1 Photograph shows a white forelock with dystopia canthorum and a broad nose with relatively anteverted nostrils.

uneventful. There was no history of fever, cough, runny nose or drooling of saliva from the mouth. The mother did not report difficult breastfeeding or episodes of choking and/or gagging in the infant. On examination, he was severely tachypnoeic with laboured breathing. Inspiratory stridor was audible. Auscultation revealed a clear chest with reduced air entry in both lung fields. The infant had a normal cry. The arterial blood gas values were normal at presentation. He was immediately laid prone in the cot, which remarkably reduced his distress. The air-entry to the lungs improved markedly. The oral cavity was normal, and no evidence of pharyngeal wall inflammation was found.

Formal direct laryngoscopic visualisation revealed an omega-shaped, floppy epiglottis with redundant aryepiglottic folds and prominent arytenoids bilaterally. There was no evidence of epiglottic inflammation or swelling. The subglottic area was normal on visualisation. The findings were consistent with the diagnosis of laryngomalacia. The facial features comprised a white forelock, dystopia canthorum (W index of 2), flattened nose bridge, bilateral blepharophimosis, slightly upturned nares and posteriorly rotated ears. (Fig. 1) Ophthalmological examination of the eye revealed

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segmental heterochromia of the left iris. Audiological assessment utilising the brainstem evoked response audiometry (BERA) employing monaural clicks at 110 dB and 100 dB stimulation in both ears, showed no identifiable BERA wave peaks at both sound intensities, suggesting a severe bilateral neurosensory hearing loss.

There was no history suggestive of familial childhood neurosensory hearing loss, maternal gestational infections due to cytomegalovirus, *Toxoplasma gondii*, rubella virus, *Treponema pallidum*, herpes virus, birth asphyxia, head trauma, postnatal pathological hyperbilirubinaemia, neonatal meningitis, and exposure to drugs causing otologic dysfunctions like aminoglycosides and diuretics. The findings were consistent with the diagnosis of WS1. The family and sibling history was negative. The radiographical skeletal survey, echocardiography and ultrasonography of the abdomen were normal. The karyotype was consistent with the normal male phenotype. The mother was counselled with the appropriate advice, and the patient was discharged after two days. He was followed up for one year, at the end of which the symptoms of laryngomalacia had subsided completely.

DISCUSSION

WS is a rare autosomal dominant condition, classically characterised by dystopia canthorum, broad nasal bridge, heterochromia irides, sensorineural deafness and white forelock. Four different types are known: Type 1 associated with dystopia canthorum; Type 2 without dystopia canthorum; Type 3 with all the characteristics of Type 1, plus hypoplasia and contractures of the upper limbs; and Type 4 associated with Hirschsprung disease.⁽¹⁾

The WS consortium⁽²⁾ proposed the diagnostic criteria for the diagnosis of WS in 1992. The major criteria include congenital sensorineural hearing loss, pigmentary disturbances of the iris, hair hypopigmentation, affected first-degree relative, and dystopia canthorum (W index > 1.95). The minor criteria include congenital leucoderma, synophrys or medial eyebrow flare, broad, high nasal root, hypoplasia of the alae nasi, and prematurely greying hair. The presence of one or two major and two minor criteria establishes the diagnosis of WS1. This present case met the abovementioned criteria for the diagnosis of WS1. Other features associated with WS include urinary system abnormalities,⁽³⁾ neural tube defects,⁽⁴⁾ Sprengel shoulder, cleft-lip or palate,⁽⁵⁾ facial nerve palsy and plicated tongue,⁽⁶⁾ dilated cardiomyopathy,⁽⁷⁾ and the absence of vagina and uterus.⁽⁸⁾

Laryngomalacia, implicated as the commonest cause for inspiratory stridor, affects either or both the epiglottis and the arytenoid cartilages. The epiglottis is usually elongated and curls on itself. Cross-sectionally, it is omega-shaped, and hence the term “omega-shaped epiglottis”, which is used to describe the epiglottis seen in this condition. Endoscopically viewed, the arytenoid cartilages are usually prominent and floppy, and are seen to prolapse over the larynx during inspiration. This inspiratory obstruction produces inspiratory noises, which may be high-pitched, coarse sounds resembling nasal congestion, or low-pitched stertorous noises. Laryngomalacia is usually a self-limiting condition, with most infants being symptom-free by two years of age.⁽⁹⁾ The condition is more common in infants with Down syndrome.⁽¹⁰⁾ Some other conditions that may be associated with laryngomalacia include diastrophic dwarfism, Marshall-Smith syndrome,⁽¹¹⁾ Larsen and Larsen-like syndromes,⁽¹²⁾ chondrodysplasia punctata,⁽¹³⁾ neonatal progeroid syndrome,⁽¹⁴⁾ Cohen syndrome⁽¹⁵⁾ and branchiootic syndrome.⁽¹⁶⁾

In our patient, we were able to exclude other relatively common conditions affecting the laryngopharynx. The conspicuous absence of features, such as fever, toxicity, drooling of saliva, altered cry, cough and nasal discharge, made acute laryngitis, croup and acute epiglottitis unlikely. Furthermore, improvement in clinical symptoms on assumption of the prone posture and the typical laryngoscopic findings confirmed the presence of laryngomalacia. WS remains, at the fundamental level, a disorder of the abnormal neural crest cell differentiation and migration. In addition to forming the sensory ganglia, neural-crest cells differentiate into sympathetic neuroblasts, Schwann cells, pigment cells, odontoblasts, meninges and mesenchyme of the pharyngeal arches. During the development of the larynx, the cartilages (thyroid, cricoid and arytenoids) and the intrinsic muscles originate from the mesenchyme of the fourth and sixth pharyngeal arches.⁽¹⁷⁾ Thus, both pigment-producing cells and laryngeal cartilages have a common source of origin, which is the neural-crest cells; aberrant differentiation and migration of the neural-crest derived cells may thus explain the occurrence of laryngomalacia in WS.

In conclusion, we report, for the first time, laryngomalacia occurring in association with WS in a neonate. Formal flexible bronchoscopic examination should be carried out in such infants for adequate diagnosis so that the parents may be counselled on the potentially-dramatic presentation of this otherwise self-limiting and benign condition.

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