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The G syndrome/Opitz oculo-genital-laryngeal syndrome/ Opitz BBB/G syndrome/Opitz-Frias syndrome

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Abstract
We report on a family exhibiting a range of congenital anomalies consistent with the G syndrome of Opitz. Three members of the family had laryngo-tracheo-oesophageal clefts, one of which succumbed. There was a strong family history of perinatal mortality on the maternal side of the family. We note also the paucity of reported cases of this syndrome in the otolaryngological literature and stress the necessity of early diagnosis in the management.

Key words: G syndrome, BBB syndrome, hypertelorism, laryngo-tracheal cleft, hypospadias, Opitz-Frias syndrome

Introduction

The G syndrome and BBB syndrome were both described by Opitz and his co-workers in 1969 and considered as separate entities (Opitz *et al.*, 1969). They used the letter 'G' and the acronym BBB to represent the initials of the family name of the patients who originally presented with these syndromes. Such is the overlap between the two syndromes that recently they have been treated as variants of the same syndrome, namely the oculo-genital-laryngeal syndrome or Opitz BBB/G syndrome (Cappa *et al.*, 1987). Affected individuals share a wide range of developmental anomalies with variable severity of expression. Almost all patients have hypertelorism with distinctive facies and posterior rotated ears. Dysphagia is universal with laryngo-tracheal clefting occurring in approximately 30 per cent of cases. Hypospadias has been reported in almost all cases but was not a feature in the family we describe. Less common manifestations include palatal and lip clefts, high tracheal bifurcation, duodenal stricture, imperforate anus, lung hypoplasia, cardiac abnormalities and gall bladder agenesis (Funderbunk and Stewart, 1978). Inheritance is thought to be autosomal dominant with incomplete penetrance. There is predominant male sex limitation and minimal expression in carriers (Little and Opitz, 1971). Perinatal mortality in these patients approaches 30 per cent, invariably due to recurrent aspiration following a delay in diagnosis.

Case reports

Case 1

A two-day-old male infant was transferred to our unit because of respiratory distress. He was born after 42 weeks of gestation and the pregnancy was uneventful. At birth he experienced respiratory distress necessitating ventilation. He was extubated after 48 hours but again developed respiratory distress. Repeated attempts at extubation over the next 10 days failed. The infant had also had difficulty in feeding from birth with episodes of cyanosis and choking when given food. He was managed with nasotracheal and nasogastric intubation. Recurrent respiratory tract infections were managed with continuous positive airway pressure (CPAP) at four hourly intervals.

Abnormal features noted at birth included marked hypertelorism, low and posterior rotated ears, flattened nasal bridge and widely spaced anterior fontanelle.

Chest X-ray, barium swallow, sweat test, imunoglobulins and chromosome analysis were all normal. Bronchoscopy and oesophagoscopy revealed a marked laryngo-tracheomalacia which had failed to improve as shown on repeat endoscopic follow-up. Tracheoplexy was performed which relieved the malacia but he continued to have respiratory distress on extubation and recurrent aspiration pneumonia.

Endoscopy at the age of one year and eight months revealed a laryngo-tracheo-oesophageal cleft. This was a type 3 cleft as described by Benjamin and Inglis (1989) extending to and involving the first three tracheal rings. This was repaired via a left lateral pharyngostomy incision. The child made an excellent post-operative recovery and commenced vocalizing for the first time following closure of the tracheostomy. He had no further problems with aspiration pneumonia during 10 years follow-up.

Case 2

This infant, born in 1988, is a first cousin of *Case 1*. He was admitted to the neonatal intensive care unit shortly after delivery for investigation of respiratory distress. Facial anomalies recognized at birth included hypertelorism, flattened nasal bridge, posteriorly rotated ears and widened anterior fontanelle.

Endoscopy at two months revealed a type 2 laryngo-tracheo-oesophageal cleft which was treated initially by tracheostomy and a gastrostomy feeding tube. Repair of the cleft was undertaken at five months via the left lateral approach. Post-operative recovery was excellent with normal development of feeding and vocalization. The child was followed up for five years and continued to do well.

Case 3

This infant, born in 1981, was an older brother of *Case 1*. He had a similar presentation of respiratory distress from birth, requiring repeated ventilation. Facial anomalies included hypertelorism, low set ears, wide anterior fontanelle and a broad nasal bridge.

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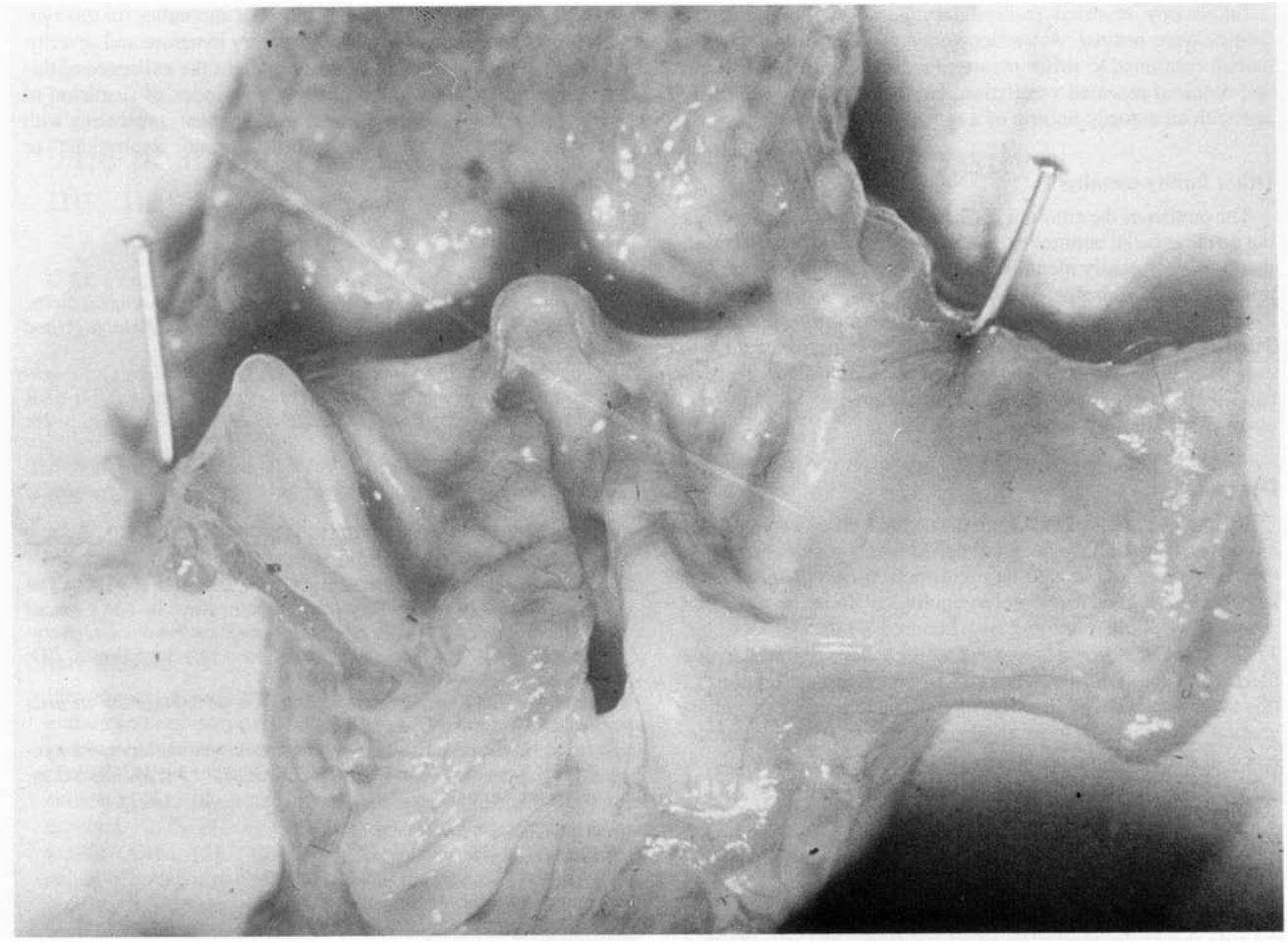

FIG. 1
Autopsy specimen of *Case 3* demonstrating type 3 laryngeal cleft.

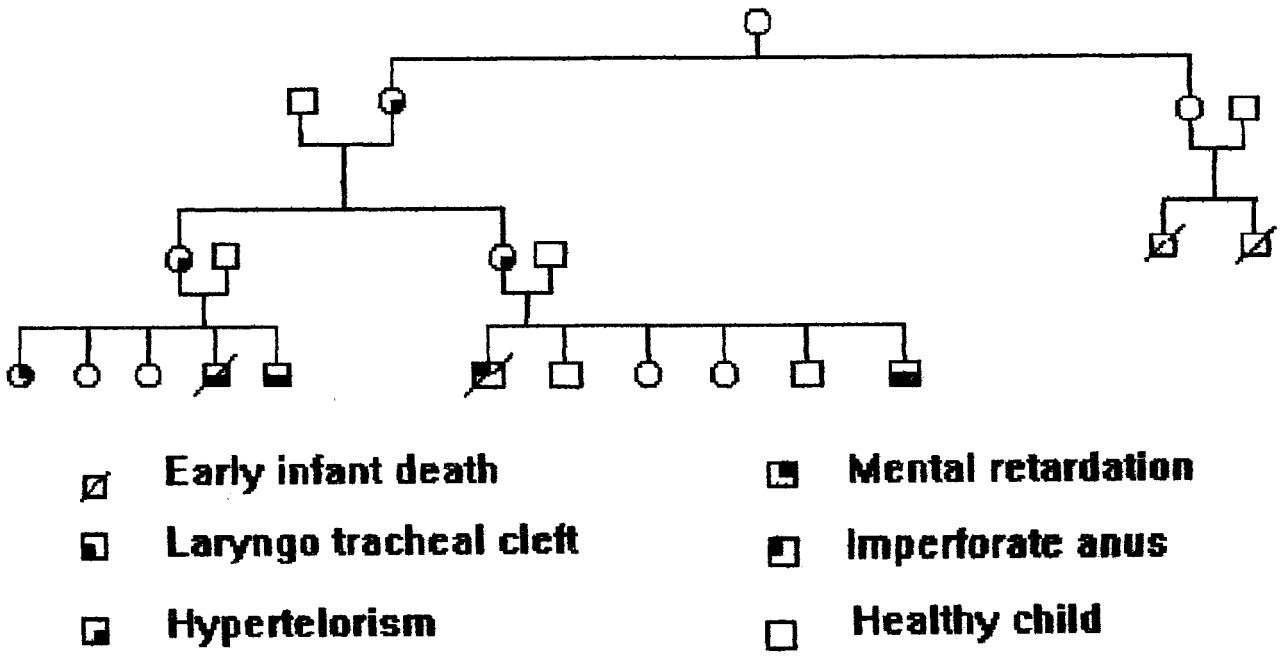

FIG. 2
Family pedigree.

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Endoscopy revealed marked laryngomalacia and contrast studies were normal. A tracheostomy was performed but the patient continued to suffer recurrent respiratory tract infections and required repeated ventilation. He died at seven months of age with an autopsy finding of a type 3 cleft (Figure 1).

Other family members

The mother of the children in *Cases 1* and *3* had hypertelorism but no other facial anomalies. A female sibling of these two children was profoundly mentally retarded but had none of the features of the G syndrome. The mother of *Case 2* also had marked hypertelorism and had lost a child with multiple congenital anomalies while undergoing surgery for an imperforate anus in the past. A maternal aunt also lost two male children in the perinatal period over 40 years ago. The pedigree of the family is given in Figure 2.

Discussion

To date 143 cases of the G syndrome have been described, the majority of which have been published in the genetic literature. Over 140 cases of isolated laryngo-tracheal-oesophageal clefts have been described in the otolaryngological literature since first reported by Richter almost two hundred years ago (Richter, 1772). The G syndrome however has rarely been reported in this literature. Clearly an awareness of the characteristic features of this syndrome will aid in early diagnosis and hence early intervention. The clinician must also be aware of the potential recurrence of the syndrome in further offspring.

Laryngo-tracheal clefts are frequently difficult to diagnose and often missed at endoscopy if the presence of the defect is not suspected. Contrast studies often fail to delineate the fistula due to approximation of the edges of cleft and maybe of little value.

We also feel it is necessary to point out the difficulties in the nosology of this syndrome. Sedano and Gorlin (1988) favoured the title the oculo-genito-laryngeal syndrome of Opitz. Such a title would exclude our family as genital abnormalities were not a feature in the group reported. We feel it is unwise to apply unduly strict criteria in the designation of anomalies for this syndrome as the anomalies present may vary in nature and severity.

The purpose of this report is to highlight the existence of this syndrome. Clinicians should have a high index of suspicion of laryngo-tracheo-oesophageal clefting in patients presenting with hypertelorism, dysphagia and recurrent aspiration or pneumonia.

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