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Studies of Malformation Syndromes VID: The *G* Syndrome. Further Observations*

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Abstract. An anatomic study of the organs of a 2-day-old female infant with severe repiratory manifestations of the *G* syndrome is presented. This case represents the third affected infant and first affected female of the J family. The first 2 male siblings were reported in previous communications. The developmental defects in this case include: failure of closure of the laryngotracheal groove, a high carina, hypoplasia of the left main stem bronchus, complete absence of the left lung, lack of major fissures of the right lung, a tracheo-esophageal fistula, agenesis of the gallbladder, and a stricture of the duodenum.

Key words: *G* syndrome — Malformation syndrome — Autosomal dominant inheritance — Laryngotracheal malformation — Duodenal malformation — Congenital absence of gallbladder.

The *G* syndrome was first described by Opitz *et al.* [3] in 4 male siblings (the *G* family) as a syndrome of multiple congenital anomalies consisting of a characteristic facial appearance, a defect of the esophagus and swallowing mechanism with regurgitation, a hoarse cry, minor anomalies of the ears, hypospadias with descended testes and an occasional imperforate anus [1, 2]. Only males, in those cases previously described, have

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been affected severely enough to cause death. This patient (the third affected infant of the J family [1, 2]) is the first known lethally affected female with the *G* syndrome. A detailed post mortem examination is included to compare her malformations with those previously reported in her brothers and other males with the *G* syndrome.

Case Report

This female infant (patient 3 of the J family) was the product of the mother's third pregnancy [2] and was delivered on 16 October 1973 by cesarean section because of a double footling breech presentation, decreased fetal heart rate (60/min) and a prolapse of the cord. Two previous pregnancies had resulted in seriously affected males with the *G* syndrome. This pregnancy was complicated by polyhydramnios and premature labor. At birth the child required bulb suction and oxygen by mask.

On admission to the intensive care nursery at St. Mary's Hospital Medical Center, Madison, Wisconsin, she was noted to have marked respiratory distress with flaring of the nares, intercostal retraction, tracheal tugging, inspiratory stridor and a loud expiratory wheeze. Breath sounds were markedly decreased over the entire left hemithorax. Direct laryngoscopy showed "a small epiglottis, a normal or slightly large entrance to the esophagus and normal vocal cords". Metabolic acidosis was treated with sodium bicarbonate. Chest roentgenograms showed a homogeneously opacified left hemithorax and a right hemithorax with a granular pattern, and failure of gas to pass beyond the duodenum. During passage of a nasogastric tube for gastric decompression the patient experienced respiratory arrest following which she was supported on a ventilator. Repeat roentgenograms were compatible with either aspiration or hyaline membrane disease and antibiotic treatment was begun.

During the second day of life blood gas analysis indicated severe acidosis. Cardiac arrest occurred on 18 October 1973, following several episodes of bradycardia.

Autopsy

The external appearance was unremarkable with the exception of a shortened lingual frenulum. The external genitalia were normal.

The crown-heel length was 49 cm, head circumference 34 cm, chest circumference 27 cm, abdominal circumference 24 cm, and body weight 2450 g.

The larynx was hypoplastic; failure of closure of the laryngo-tracheal groove had resulted in the absence of a partition between the larynx and esophagus. This had resulted in a single cavity from the epiglottis and hypopharynx superiorly to the trachea and esophagus inferiorly. A probe-patent tracheo-esophageal fistula was present 1.5 cm below the hypoplastic larynx (Fig. 1). There were only 9 tracheal

Fig. 1. Posterior view of the (opened) hypoplastic esophagus with failure of closure of the laryngo-tracheal groove resulting in a continuous opening between the trachea and esophagus. Also note the presence of a probe in the patent tracheo-esophageal fistula (arrow)

Fig. 2. Hypoplastic left main stem bronchus and complete absence of the left lung. The right lung lacks major fissures. Note network of shallow sulci covering the surface of the right lung

Fig. 1

Fig. 2

rings associated with a high carina. The left main stem bronchus was hypoplastic and ended blindly after a distance of 1 cm. The left lung was totally absent. The right lung showed no evidence of major fissures, but a reticulated system of shallow sulci was present over the entire surface of this lung (Fig. 2).

The solitary right lung was diffusely atelectatic; histologic studies showed hyaline membrane deposition in numerous alveolar ducts and a minimal amount of aspiration.

The cardiovascular system was normal.

There was complete absence of the gallbladder. The stomach was moderately dilated. The superior portion of the duodenum was folded tightly upon itself and was fixed firmly in that position by the peritoneum, thus preventing the passage of a flexible, small caliber probe which indicated obstruction at this site and resulting dilatation of the duodenum proximal to this constricted segment.

The urinary system was unremarkable. No other anomalies were found.

Discussion

The mother of this infant has given birth to two other infants, both males, with the *G* syndrome.

Patient 1 was the male product of a normal gestation, labor and delivery. He had a severe form of the *G* syndrome and died at 4 months of age. Patient 2 was stillborn at term. His *in utero* death was discovered 4 days before planned delivery. Details of these two siblings were reported by Gilbert *et al.* [1] and by Little and Opitz [2].

The mother herself shows manifestations of the condition. During infancy she experienced considerable stridor, but no swallowing difficulties are recalled. Roentgenograms during childhood demonstrated hypoplasia of the left lung. Presently she has audible stridor with cyanosis and dyspnea at rest. Until the birth of this infant she was the only reported female affected and till then the *G* syndrome was thought to be the result of an autosomal dominant mutation predominantly confined in expression to the male. Because of her manifestations the hypothesis was revised to include the occasional occurrence of rather serious pulmonary malformations in female heterozygotes [1]. The birth of this severely affected female now suggests an autosomal dominant mode of inheritance particularly since she manifests many of the characteristic malformations of the respiratory tract which had been observed previously only in affected males.

This infant (patient 3 of the J family) was found to have a short trachea, high carina, hypoplastic left main stem bronchus, complete absence of the left lung, lack of major fissures of the right lung and the characteristic closure defect of the laryngotracheal groove. The respiratory tract involvement was similar to that observed in her brothers. Genito-urinary tract defects were lacking in this infant. Hypospadias has been a consistent finding in affected males some of whom also had a bifid

scrotum with descended testes. She had no congenital cardiac malformations.

Additional malformations not previously observed in the G syndrome were agenesis of the gallbladder and a duodenal stricture.

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