Brief Clinical Report

Tetralogy of Fallot in Three Sibs

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We report on three sibs (2 boys, one girl) with tetralogy of Fallot from non-consanguineous parents. The first child died during corrective surgery in 1972 from irreversible right ventricular failure. Corrective surgery was successful in the 2nd son and the daughter. The occurrence of tetralogy of Fallot in 3 sibs suggests a recessive gene.

KEY WORDS: familial, autosomal recessive inheritance, non-consanguineous

INTRODUCTION

The incidence of congenital heart defects is approximately 4/1,000 live births [Ferencz et al., 1985]. The most common cardiac anomaly causing cyanosis is tetralogy of Fallot, representing 4 to 7.5% of all forms of congenital heart defects [Mitchell et al., 1971; Campbell, 1972; Boughman et al., 1987]. Various mechanisms of inheritance with varying risk of recurrence were suggested for tetralogy of Fallot. There is evidence for multifactorial determination [Boon et al., 1972], as well as reports suggesting Mendelian inheritance [Lynch et al., 1966; Friedberg, 1974; Jones and Waldman, 1985; Der Kaloustian et al., 1985].

We present a family in whom 3 of 5 children were diagnosed with tetralogy of Fallot without other malformations.

CLINICAL REPORTS

Patient 1

The son was born at term after a normal pregnancy, as the first child. Birth weight was 2.75 kg, length 53 cm. The mother was 20 years old and the father 37 years old at the time of birth. They are nonconsanguineous. Apart from recurrent infections, his early infancy was normal. At age one year, the presence of a cardiac anomaly was suspected. A loud systolic murmur was present on auscultation without cyanosis or dyspnea. Bilateral cryptorchidism was noted. The diagnosis of tetralogy of Fallot with pulmonary valve hypoplasia (Miller-Lev-Paul syndrome [Miller et al., 1962]), and a right aortic arch (Table I) was confirmed at cardiac catheterization. At age 12½ years corrective surgery was attempted. The patient died intraoperatively from irreversible right ventricular failure.

Patient 2

Patient 2 was born as the third child following a normal pregnancy. Birth weight was 3.25 kg. Early infancy was normal. At age 16 months he was admitted to the hospital with cyanotic spells resulting in loss of consciousness for 2 to 5 minutes. He had a moderate generalized cyanosis and a loud systolic murmur with maximal loudness in the region of the left 3rd and 4th intercostal spaces. Cardiac catheterization confirmed the diagnosis of tetralogy of Fallot with a right aortic arch (Table I).

At age 6 years 7 months corrective surgery was performed. Now, at age 23 years he has severe pulmonary valve regurgitation and mild peripheral pulmonary stenosis (Table I). A pulmonary valve replacement is planned.

Patient 3

The daughter was born at term as the fourth child, following a normal pregnancy. Birth weight was 3.55 kg, length 49 cm. She had peripheral cyanosis at birth. At age one year reduced exercise tolerance and central cyanosis were apparent. At age 2½ years, she was admitted to the hospital with generalized cyanosis, dyspnea on exertion, and clubbing. There was a 3/6 systolic murmur in the region of the left 3rd and 4th intercostal spaces. Cardiac catheterization confirmed the diagnosis of tetralogy of Fallot (Table I) and a Blalock-Taussig shunt was performed.

At age 4 years one month, cardiac catheterization was repeated because of shunt dysfunction with failure to thrive, cyanosis, and severe tachydyspnea (Table I). At age 5½ years, surgical correction was performed. Postoperative cardiac catheterization showed a residual pulmonary stenosis and a small residual ventricular septal defect (Table I). The patient is now 19 years old and asymptomatic.

DISCUSSION

A study by Boon et al. [1972], in which the families of 106 patients with a tetralogy of Fallot were evaluated, showed a recurrence risk of 1%. The tendency of familial
aggregation was notable. Friedberg [1974] described a family with tetralogy of Fallot, in which 4 patients, in 3 successive generations, had various grades of pulmonary obstruction, from a mild stenosis to pulmonary atresia. Jones and Waldman [1985] reported an autosomal dominant syndrome of characteristic facial appearance, preauricular pits, fifth finger clinodactyly, and tetralogy of Fallot. Six patients in 3 generations showed various malformations. Three patients in 2 generations had a tetralogy of Fallot.

Lynch et al. [1966] presented 2 children with tetralogy of Fallot, one of whom (male) was psychomotorically retarded with a chromosomal mosaic (46 XY/45 X). The sister showed no symptoms of Ullrich-Turner syndrome and a chromosome analysis was not performed. It was discussed whether the mosaic result and the cardiac anomaly were promoted by a common occurrence after fertilization, or, in view of the sister, whether a recessive gene was responsible for the tetralogy of Fallot, which then promoted the mosaic result. Der Kaloustian et al. [1985] described a family in whom 2 sisters had tetralogy of Fallot with pulmonary valve atresia. The parents were first cousins. There was no history of other affected relatives. A recessively inherited type of tetralogy of Fallot was suggested.

In the family presented here, 3 of 5 children had nonsyndromal Tetralogy. Consequently a chromosome analysis was not performed. Neither of the parents had cardiac disease.

The occurrence of tetralogy of Fallot in 3 sibs suggests a recessive gene. Variable expression of tetralogy reported here (one patient with Miller-Lev-Paul syndrome) and also by Friedberg [1974] does not contradict monogenetic inheritance.

The right aortic arch in 2 of our patients is not an unusual finding considering that 25% of all patients with tetralogy of Fallot have this association [Rao et al., 1971; Rees and Somerville, 1969].

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REFERENCES


