Fraser syndrome in a 96-year-old female

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Abstract

Fraser syndrome is an autosomal recessive disorder in which the life expectancy is <1 year. The main features are cryptophthalmos, ear, nose and skeletal malformations, syndactyly, laryngeal stenosis and malformation of the uro-genital system, lungs, liver and central nervous system (CNS). We report the clinical, laboratory and post-mortem findings of this condition in an elderly woman aged 96 years. She is the oldest known patient with Fraser syndrome.

Keywords: Fraser syndrome, cryptophthalmos, syndactyly, elderly

Case history

A 96-year-old widowed woman was admitted from a residential home complaining of increasing unsteadiness over the previous 3 days. She described having had a simple fall 7 days before, which required numerous stitches to the head. The following week she developed a poor appetite and had minimal fluid intake. Her medical history revealed that she had had operations as a child to correct a cleft lip and palate and also to correct webbed fingers. She had had no subsequent hospital admissions and was not on any regular medications. There was no family history of consanguinity or of congenital abnormalities.

The patient was born when her mother was aged 38. She was totally blind, had a normal intellect and attended a special boarding school for the blind where she learned to read and type Braille. The majority of her life was spent in various homes. She developed several hobbies and had a friendly and likeable personality. At the age of 76, she married another elderly resident of the home and was widowed 10 years later.

On clinical examination, she was noted to have turricephaly (pointed head) and bilateral cryptophthalmos (a developmental anomaly in which the skin is continuous over the eyeballs without any formation of eyelids) (Figure 1). Other facial abnormalities included a low hairline, broad nose with depressed nasal bridge, low-set ears and hypertelorism (increased distance between the two eyes). There was extensive syndactyly (webbing/fusion) in hands and feet (Figure 2). No focal neurological deficits were evident although it was noted that the patient wore a hearing aid and had a high-pitched voice. She was cognitively intact and scored the maximum of 10 points on the 10-point abbreviated mini-mental test score. On catheterisation, it was noted she had no vagina.

Blood investigations revealed raised inflammatory markers and mild renal impairment (CRP 33, urea 12.1, creatinine 142). Urine dipstick showed proteinuria and microscopic haematuria. She was commenced on a course of intravenous fluids and ciprofloxacin for treatment of a presumed urinary tract infection. However, during the following few days, she became progressively more lethargic and unsteady. A computerised tomography scan of the head was arranged on day 7 to exclude a subdural haematoma. This showed a normal brain but in addition it revealed the presence of small, calcified eyes and multiple skull defects (see Appendix 5 in the supplementary data available on the journal website http://www.ageing.oxfordjournals.org/). The patient continued to gradually deteriorate and died 25 days after admission with no specific cause of death identified.

A post-mortem was undertaken to delineate the extent of her congenital abnormalities. Internal findings included three circular bony defects in her skull covered by thick dura, a normal brain, partially fused lungs with incomplete fissures, an abnormally lobulated liver, a single left kidney and ureter and a normal bladder. She had no ovaries, uterus or vagina. For illustrations of some of the post-mortem findings, please see the supplementary data available on the journal website (http://www.ageing.oxfordjournals.org/).

Discussion

The congenital features described in this patient are consistent with Fraser syndrome. George Fraser first reported two
siblings with features of this autosomal recessive syndrome in 1962 [1]. A review of 124 cases of cryptophthalmos [2] led to the definition of the major and minor diagnostic criteria for Fraser syndrome (Table 1). Two major criteria and one minor criterion or one major and at least four minor criteria are required for a diagnosis of Fraser syndrome.

This patient had three major criteria (cryptophthalmos, syndactyly and abnormal genitalia) and five minor criteria (malformations of the nose and ears, cleft lip and palate, skeletal defects and renal agenesis).

A recent review [3] showed that the majority of the deaths in Fraser syndrome occur in the first week of life and ∼50% are stillbirths. The commonest causes of death are central nervous system (CNS) malformations, laryngeal stenosis or atresia, respiratory insufficiency, obstructive uropathy or bilateral renal agenesis. To our knowledge, there have been fewer than 10 reported cases of a patient fulfilling the diagnostic criteria for Fraser syndrome and surviving over the age of 20 years [3].

This lady is the oldest known case of Fraser syndrome, and it is unclear exactly how or why a person with such gross malformations has survived longer than other patients with this syndrome. At her birth, 96 years ago, the average life expectancy for a healthy baby girl was only around 50 years. It is hardly possible that Fraser syndrome could have given her a survival advantage. The absence of life-threatening malformations, especially CNS malformation, was certainly an important factor.

**Key points**

- Fraser syndrome is a rare congenital abnormality causing death at typically <1 year of age. Only known patient to have survived so long.
- There are well-documented major and minor criteria which should be considered in patients born with cryptophthalmos.

**Conflicts of interest**

There are no conflicts of interest.

**References**


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