

Case Study

Cystic fibrosis co-existing with trisomy 21

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Abstract

Previous reports of children with co-existence of cystic fibrosis and full trisomy 21 suggest a very poor prognosis, with the majority of cases dying in infancy and the oldest reported survivor being 6 years of age. We report the case of a young man with genetically confirmed trisomy 21 and homozygous for the F508del cystic fibrosis mutation. Despite the diagnosis of cystic fibrosis being delayed until the age of 2 years he has transitioned to adult services and is now 25 years of age. Currently he has poor lung function and a continuous ambulatory oxygen requirement. © 2010 European Cystic Fibrosis Society. Published by Elsevier B.V. All rights reserved.

Keywords: Trisomy 21; Cystic fibrosis

1. Introduction

Reports of cases of children with both trisomy 21 and cystic fibrosis are rare in the literature [1–3]. The documented outlook has been extremely poor, with three such children dying as infants, another before the age of two and the oldest reported survivor aged six years and eleven months [1–3].

A further single case report of an 8% mosaic trisomy 21 and cystic fibrosis has been reported and was making good clinical progress at age seven [4].

The current available literature thus suggests a very poor prognosis for full trisomy 21 co-existing with cystic fibrosis.

We report a case of genetically proven full trisomy 21 with cystic fibrosis (genotype homozygous F508del mutation), who with cystic fibrosis centre care, has survived through childhood and transitioned to the adult cystic fibrosis clinic. He is now twenty five years old. This case will help inform antenatal and postnatal counselling given to parents of babies in whom these two lifelong medical conditions are found to co-exist with regard to prognosis and management.

2. Case report

A diagnosis of trisomy 21 was made shortly after birth, on the basis of clinical features, and was subsequently confirmed as full trisomy 21 by chromosomal analysis. He was adopted and first became unwell with two chest infections requiring hospital admission between the ages of 21 and 26 months.

He was noted to have offensive fatty stools and had faltering growth. He was diagnosed with cystic fibrosis at just over 2 years of age on the basis of a positive sweat test (sodium 106 mmol/L and chloride 140 mmol/L, with 309 mg of sweat) and started on regular pancreatic enzymes, vitamins and prophylactic trimethoprim. Faecal chymotrypsin was low at this time, pancreatic insufficiency was later confirmed by faecal elastase of 5 µg/g stool (normal range >200 µg/g). At the age of 2 and a half *Pseudomonas aeruginosa* was cultured from a cough swab sample and he received a 10 day course of intravenous gentamicin.

He had a full assessment at our centre at the age of 3 years and was already noted to have digital clubbing and evidence of chronic changes on chest X-ray. Cough swab showed a heavy growth of *Staphylococcus aureus* and *Haemophilus influenzae*, and he was changed to prophylactic flucloxacillin and prescribed a treatment course of amoxicillin.

Clinically he improved dramatically on pancreatic supplementation and remained under regular medical follow up by his

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Table 1

Previously published case reports of children with probable co-existent trisomy 21 and cystic fibrosis. Not all cases are genetically confirmed.

Reference	Method of trisomy 21 diagnosis	Method of cystic fibrosis diagnosis	Outcome
Milunsky [1]	Clinical features	Older sibling had CF, sweat test	Died 10/52
Milunsky [1]	Clinical features	Sweat test, absence of pancreatic enzymes in stool, post mortem	Died 22/12
Milunsky [1]	Chromosomes	Sweat tests, (pancreatic sufficient)	Alive at publication (age 6 years)
Vetrella et al. [2]	Unclear	Sweat test, absent pancreatic enzymes in duodenal secretions	Died day 49
Kruger et al. [3]	Chromosomes	Sweat test, genetic — homozygous F508del mutation	Died at 6/12
Saglani and Bush [4]	8% mosaic	Genetic — homozygous F508del mutation	Alive at publication (age 7 years)

district hospital, with intermittent reviews at the Leeds Regional Cystic Fibrosis Centre.

At the age of 10 years he had increasing chest symptoms and grew *P. aeruginosa* again, and had two courses of intravenous anti-pseudomonal antibiotics. He continued to have productive cough with FEV1 47% predicted, but was enjoying life and attending mainstream school. A further unsuccessful attempt at eradication was made with oral ciprofloxacin and nebulised colomycin despite this chronic *P. aeruginosa* infection developed.

At transition to adult services aged 18 years, spirometry demonstrated a FEV1 of 1.46 (46% predicted) and FVC of 2.48 (73% predicted). Over the following seven years, FEV1 slowly declined to 20% predicted. With regular intravenous antibiotics every 3 to 4 months lung function remained stable for over 2 years. More recently he has required long term oxygen therapy. MRSA was eradicated from sputum. Following a discussion with both the patient and his parents, a collective decision not to proceed with referral for transplantation was made.

3. Discussion

We are aware of five previous cases of children with cystic fibrosis and trisomy 21 reported in the literature, as well as a child with 8% mosaic trisomy 21 (see Table 1). Whilst both conditions in isolation are relatively common (UK incidence of cystic fibrosis 1:2415 live births [5] and of trisomy 21, 1:1100 live births [6]), the expected incidence for both to co-exist in the United Kingdom would be approximately 1:2,650,000. Thus we would only expect to see a case with cystic fibrosis and trisomy 21 every 3–4 years in England and Wales (using the 2008 birth rate). [7] The reported outlook for patients with full trisomy 21 and cystic fibrosis has been very poor (Table 1).

As children with trisomy 21 are reported to have elevated sweat osmolality, it is important to confirm the diagnosis of cystic fibrosis by genotype if possible. [8]

Our case is the longest reported survivor with genetically confirmed cystic fibrosis and trisomy 21. As he was diagnosed with cystic fibrosis at the age of 2 years on the basis of symptoms, and developed chronic *P. aeruginosa* infection at the age of 10 years, it would be hoped that outcomes for children diagnosed with CF through newborn screening who have trisomy 21 and who are treated comprehensively from diagnosis may be better still.

In summary, despite the previous literature suggesting a very poor prognosis, we can report a patient who has transitioned to adult care with co-existing trisomy 21 and cystic fibrosis. We hope that this will help paediatricians when counselling parents regarding prognosis and management in the future.

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