TRISOMY 21, CHOLELITHIASIS AND POSITIVE SWEAT TEST AT INFANT - DIAGNOSTIC DIFICULTY

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Abstract

A 5 month old female infant was admitted to hospital for evaluation of a particular phenotype. The particular phenotype was assimilated to a Langdon-Down syndrome The kariotype has confirmed a structural chromosomal abnormality of robertsonian translocation type between acrocentric chromosomes 21 and 22, and a numerical chromosomal abnormality consistent with a total trisomy 21 type, the cytopenic formula being: 46, XX, -22, +21, trob (21;22). The echocardiography, revealed a common atrioventricular canal in its complete form. An abdominal ultrasonographic scan was also performing, showing the gallbladder, which exhibited three hyper echoic image. The sweat test was positive. The genetic test for cystic fibrosis was negative. The conclusion is, if it is about comorbidity trisomy 21 and cystic fibrosis, or sweat test could be fals positive in trisomy 21.

Key words: trisomy 21, cystic fibrosis, cholelithiasis

Case presentation

In October 2008, a 5 month old female infant was admitted to the II[nd] Pediatric Clinic for evaluation of a particular phenotype.

The particular phenotype assimilated to a Langdon-Down syndrome was observed at birth, and also a cardiac murmur was noted, labeled initially as a ventricular septal defect. The parents were reticent about medical problems evidenced and did not follow the recommendations linked to the med of additional evaluation. About 10 days prior to current admission, at an ultrasonographic examination, the presence of a cholelithiasis is evidenced, and this prompted the admission to our clinic for evaluation. The clinical examination at admission revealed an average general status, a weight of 5000g, a length of 59 cm, a cranial perimeter of 40 cm, a thoracic perimeter of 38 cm a particular phenotype (Mongolian epicanthic skin folds, eyelid slit, small, low-seat ears, hypertelorism, epicanthus, a slightly open mouth with tongue protrusion, a single palmar flecxion crease = simian crease, a groove between the great toe and the second toe = the sandal sign), pale in teguments, a globally reduced subcutaneous tissue, a generalized muscle hypotonia, more marked on axial groups, no pathological change in lungs at auscultation, a telemid systolic murmur of III-IV/VI degrees on the entire cardiac area, with interscapulovertebral and axillary irradiation, a normal time of capillary re-coloring, a well-beating peripheral pulse, abdominal hypotonia with right abdominis diastasis, liver and spleen within normal limits, spontaneous miction with no signs of meningeal irritation.

We were facing an infant with a particular phenotype, with clinical characteristics of Langdon–Down syndrome, with a cardiac murmur attributable to the malformative complex, usually accompanying this syndrome. Associated to this is the diagnosis of cholelithiasis.

Lung X-ray evidenced a global cardiomegaly and a paramediastinal opacity in the upper right area, relatively homogenous and well circumscribed (a possible condensation process, or an adenopathy), with a bilateral paramediastinal alveolar interstitial infiltrate (fig 1). The sweat test was positive; initially the concentration of NaCl was 86 mmol/l, later 98 mmol/l (normal values: < 40 mmol/l-negative; < 40/60 mmol/l-inconclusive; > 60 mmol/l-positive). An echocardiography, revealed a common atrioventricular canal in its complete form and a mild/moderate pulmonary hypertention; an abdominal ultrasonographic scan was also performing, showing normal results except for the gallbladder, which exhibited three hyper echoic image which a maximum diameter of 0,5mm, a result confirmed also by a magnetic resonance cholangiography, where several millimetric images were seen, very likely due to a biliary microlithiasis. The kariotype has evidenced a structural chromosomal abnormality of robertsonian translocation type between acrocentric chromosomes 21 and 22, and a numerical chromosomal abnormality consistent with a total trisomy 21 type, the cytopenic formula being: 46, XX, -22, +21, trob (21;22) – fig 2.

The genetic (molecular) test for cystic fibrosis was negativ for the 29 most common mutations for Central–Western European Area (the Elucigene CF 29 Kit).

The subsequent positive diagnosis was as follows: Trisomy 21 (Langdon-Down syndrome), common atrioventricular canal in complete form, cystic fibrosis, and cholelisthiasis.

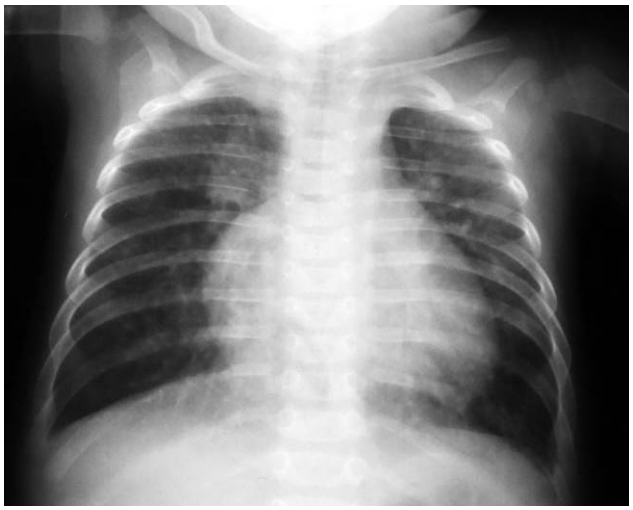

Fig 1. The lung X-ray.

Fig 2. The kariotype.

In favor of cystic fibrosis diagnosis are pleading two markedly positive sweat test the failure to thrive, and the likelihood that mutations which make up the genotype could not be identified with the aid of the Elucigene CF 29 Kit, as well the presence of cholelithiasis (although the cholelithiasis usually is not a rapidly progressing developmental event beginning in infancy; as a matter of fact, it isn't mentioned in guides for the performance of sweat test).

The arguments against the diagnosis of cystic fibrosis are the following: a negative genetic test and a possibility of a false-positive sweat test. Among the disease in which the sweat tests may be false-positive one can mention: a severe malnutrition, celiac disease, mucopolysaccharitoses, hypothyroidism, pseudohypoaldosteronism, diabetes insipidus, HIV infection, as well as Down syndrome. In this regard, there are several European reports on cases, going up to 2001-2002, referring to isolated cased of Down syndrome with a positive sweat test, without statistical consideration though (the mosts extensive communication can be found in Pedriatrics in 1968, reporting on 3 such cases).

Concerning the cholelithiasis, the following issues emerge: is it a developmental complication in the context of cystic fibrosis (the arguments against are presented above), is it a part of 6% of the cases of trisomy 21, appearing through hypotonia of excretory bile ductile or has it an independent cause). Among causes of biliary lithiasis in infants one cite the hemolytic anemia, parental nutrition, familial or anatomical cholestasis, and transiently, following ceftriaxone administration.

The evaluation and the prognosis for this child depend on two major things: a surgical correction of congenital cardiac abnormality, and, if the suspicion of cystic fibrosis is confirmed, the development of respiratory disease influences the vital prognosis.

The particularity of this case consist, on one hand, in the rarity on the chromosomal abnormality involved, the robertsonian translocation representing a very small percentage (2,5-4%) of the integrality of abnormalities presented in the Down syndrome and, on the other hand, Down syndrome - cystic fibrosis - cholelithiasis, three independent or interconnected clinical situations.

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