Case Report
Genetic findings in a child with deferential abnormalities. From surgery to clinical genetics

Fernando Rivilla*
Division of Pediatric Surgery Hospital, Universitario Ramony Cajal. Ctra, Colmenar Km.9.1. Madrid 28035, Spain

Abstract
A male 14 months old had deferential abnormalities during orchidopexy. The genetic study demonstrate cystic fibrosis (∆F508 / ∆F508). A literature review of the genetic alterations observed in patients with congenital unilateral and bilateral absence of the vas deferens was underwent as well as the role of cystic fibrosis trans membrane conductance regulator gene on fertility.

INTRODUCTION
Congenital disorders of the vas deferens are an autosomal recessive disease and occur in 1–2% of infertile men [1]. However, it is well known that most patients with cystic fibrosis (CF) and infertility appears in 98% of cases due to obstructive abnormalities such as congenital bilateral or unilateral absence of the vas deferens (CBAVD and CUAVD respectively), which determine the hypo or azo ospermic appearance [1,2].

This finding is related to alterations in the cystic fibrosis trans membrane conductance regulator gene (CFTR). Based on the observed genetic defects in this gene, different CF variants has been described [3,4]. Classical, non classical and disorders related with CFTR gene with an involvement of a single organ disorders, such as the CBAVD [2,5] or CUAVD [6,7] as it has been demonstrated in our patient.

Moreover, it is believed that CFTR gene influences other aspects of reproduction, such as spermatogenesis [8,9] and semen viscosity [10]. It is described more difficulty obtaining high quality semen samples and a less success in procedures of assisted reproduction [11,12]

CASE REPORT
It is reported the case of a male. At birth a healthy boy with a non palpable right testicle in scrotum were explored. He was referred to pediatric surgery outpatient clinic. Decisions on surgery were delayed until a spontaneous descent of the right testicle at one year of age. At 14 months the physical examination was similar to that described at birth. According to surgical protocol in our Institution and with the agreement of parents, an orchidopexy was performed. During surgery, the right testicles were located in middle third of inguinal duct, consistency and gross appearance were normal with a dissociation epididimo-testicularis and without evidence of vas deferens. (Figure 1). An orchidopexy were performed according to Murphy procedure in a day surgery bases. No left testicle surgical exploration was underwent due to a correct anatomical location. It is unknown whether there is a contralateral vas deferens agenesia.

The postoperative genetic studies demonstrate a cystic fibrosis (∆F508 /∆F508), classical form in homozygosis. No other structural organic malformation was founded. Parents by history were not known to be consanguineous.

The postoperative first year follow up has been uneventful except by difficulty in weight gain and one episode of Pseudomonas aeruginosa Pneumonia treated early without complications recorded.

DISCUSSION
Deferential abnormalities and specially CBAVD is a common
finding in patients with severe CF genotype (98%), although it is not a major signs of the disease. However, it has been described several cases diagnosed casually during childhood, especially during inguinal surgical procedures such as herniorrhaphy and orchidopexy [13,14] as the patient reported here. In fact, it has been suggested in CF a higher incidence of inguinal hernia, hydrocele and cryptorchidism [15]. If it is discovered in a child during surgery is highly recommended to discard CF at any age and some others genitourinary malformations such as the more common renal agenesis [16-18]. Moreover when a child with CF should be operate with those conditions parents must be advised about the possibility to find deferential abnormalities.

Patients with fortuitous finding during surgery can have an asymptomatic CF with homozygosis mutations of CFTR gene or a middle mutation with a partial function of the gene. In the last, a high genetic heterogeneity has been described in literature [16,19-21]. Most are heterozygous, with other mild or severe mutation and the genotypes more frequently found are ΔF508/ST and ΔF508/R117H. However, ST polymorphism penetrance is incomplete [22] and seems to be determined by the number of sequential repetitions of thymine and guanine [23,24]. On the other hand there are important geographical differences [21] although the spectrum and frequency distribution of CFTR gene mutations in most patients of European descent or other countries may not be the same for all countries or ethnicities [25]. By contrast, forms ACBCD / ACUCD with renal agenesis not appear to be related to alterations in the CFTR gene or CF [6,17,19].

Although CBAVD patients are able to have children using intra cytoplasmic sperm injection, they will experience a higher risk than normal of having a child with CF. Assuming a risk of 1/25 of the partner being a CF carrier, and the affected male having a chance of 0.5 of transmitting the mutant CFTR gene to the child, the combined risk of a CBAVD-affected couple having a CF child is 1/100 [21]. The partner of the CBAVD patients should be tested for CFTR mutations and dear genetic counselling should be provided. Furthermore, commercial test detect the most frequent mutations and not all mild genetic variations. Thus, only they detect alterations in 60% of cases of CBAVD [21,25]. It has been proposed, although there is no consensus, that in CF patients with CBAVD or CUAVD, is highly recommended a familiar genetic counseling [25,26].

Concerning the importance of CFTR gene on fertility, it seems also to play roles in different stages. First during embryonic development of vas deferens [26]. It has also been observed an increased expression of the gene during spermatogenesis [9,10] with a lower maturation of spermatides in testicular biopsies from patients with mutations 5T of the CFTR gene [8]. In addition, it has been suggested that this gene regulates the viscosity of seminal fluid and may have a role in the maturation of sperm in vitro [11], which has caused a min or success of artificial reproduction procedures [8-10].

Finally, it should be emphasized the importance of the diagnosis of CF in patients with incidental findings CBAVD or CUAVD during surgical exploration of the inguinal area and the genetic counseling of family.

REFERENCES


