Bladder exstrophy (BE) is a serious closure defect of the fetal abdominal wall of unknown pathogenesis. In Spain, a prevalence of 1:35,597 live births has been recorded, similar to that described worldwide, being more frequent in males. It is part of a spectrum of wall closure defects, ranging from epispadias as the mildest form to cloaca exstrophy as the most severe form.

BE is produced by a migration defect of the cells of the infraumbilical mesenchyme that will result in the inferior abdominal wall, genital tubercles and pubic branches. The mesoderm fails to interpose between the superficial ectoderm and the bladder portion of the cloaca (endoderm), producing the fusion of the abdominal wall with the anterior bladder wall, which causes evertion of the posterior bladder wall, and the mucosa is exposed.

It is accompanied by low umbilical cord insertion, separation of the pubic bones, and rudimentary, flattened urethra; the bladder neck is hypoplastic. In men, the penis is flattened and small, with divergent corpora cavernosa, the urethra is open dorsally, and thus a severe epispadias is formed, although cases with normal penis have been described. The girls have a bifid clitoris accompanied or not by vaginal intercourse and a bifid uterus. In addition, the association of skeletal and intestinal malformations is common.

The hormonal environment has a fundamental role in embryonic cell differentiation and differentiation at all levels. For example, dihydrotestosterone (DHT) is indispensable for the complete development of the male external genitalia.

It is presented to a newborn with complete bladder exstrophy, whose development may have been influenced by the presence of a 5-reductase type II inhibitor, which prevents the conversion of testosterone to DHT.

It is a male newborn, the sole child of the third pregnancy of young, non-consanguineous parents. At week 30 of gestation, maternal autoimmune hypothyroidism was detected and controlled with levothyroxine at 50 mg/day. In recent weeks, he has presented gestational diabetes treated with dietary measures, without the need for medication. The father had been taking finasteride (5 mg/day) for 2 years for chronic prostatitis. It was not possible to specify the length of time during which sexual intercourse persisted after conception.

The eutocic delivery occurred at the 40th week of gestation. The weight of the newborn was 2,730 g (P10-25), and a length of 47.5 cm (P25). He had low umbilical cord insertion; solution of continuity of the infraumbilical skin, through which the mucosa of the bladder wall was everted; penis, flattened and short, with severe epispadias. The left teste was palpated in the scrotal pouch and the right in the inguinal canal. It associated indirect bilateral inguinal hernias, and in the examination of associated malformations only a pubic diastasis was found. The ultrasound and functional renal study was normal.
Finasteride is a specific inhibitor of 5-alpha reductase type II, an enzyme that metabolizes testosterone to DHT. It works by competing with testosterone for 5-alpha reductase, to which it joins forming a stable complex of prolonged half-life (approximately 30 days). Since DHT is the main stimulus for the development of male external genitalia in the embryonic phase, numerous safety trials of the drug have been conducted to test the effects that its administration to pregnant females of different animal species may have on the development of male fetuses.

In these studies, with very high doses, there have been dose-dependent alterations of genital development such as hypospadias, decrease in the size of the prostate and seminal vesicles, reduction of anogenital distance, [falos planos no tubulares], or small-sized, hypoplastic scrotums and balano-prepucial adhesions.

The technical data sheet of the drug insists that it is absolutely contraindicated in a pregnant woman, or with a possibility of becoming pregnant. It even warns about the potential risk for male fetuses, due to the absorption of the compound transcutaneously if a pregnant woman handled a tablet with the damaged coating.

The old drug information sheet warned that a pregnant woman, or a woman planning a pregnancy, should not have contact with the semen of a male being treated, as small concentrations of the compound may be found in the semen of treated healthy males (up to about 20 ng of finasteride/ml of ejaculate), but this warning no longer appears in subsequent editions of the information sheet.

In the case presented, it is difficult to estimate the concentration that the drug has been able to reach in the embryo, since the precise time of exposure is not known, nor studies on the amount that can be eliminated by seminal route a patient with chronic prostatitis, nor if this concentration would be sufficient to influence the levels of DHT of the embryo. On the other hand, BE affects many structures of different embryonic origin, in addition to the genitals, so it is not possible to establish a causal relationship between congenital malformation and finasteride, especially considering alterations in the closure of the abdominal wall have not been described in premarket trials of the drug.

Despite the low probability that the malformation is due to finasteride, the suspicion of adverse reaction was promptly reported to the Spanish Pharmacovigilance System. To date, no similar case has been reported, although it is true that the relationship between BE and exposure to finasteride could go unnoticed, since the medical history of newborns does not usually ask about the treatments the father receives. In any case, as this is the first time that this coincidence has been communicated, it will be necessary to take account of it in the future and to communicate it if it is repeated. In addition, when suspected congenital malformations, especially genital development (including micropenis, testicular maldescensus, hypo- or epispadias, etc.), both obstetricians and neonatal pediatricians should begin to ask not only for the medication that the mother has received during pregnancy, but also for the one that the father has received.