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Newborn with incarcerated inguinal hernia and complete androgen insensitivity syndrome

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ABSTRACT

Disorders of sex development represent a large and heterogeneous group of diseases that have an important impact on physical and mental well-being of patients and their families. An early diagnosis and a multidisciplinary approach are fundamental to guarantee the highest standard of care.

We describe a case of complete androgen insensitivity syndrome (CAIS) in a six-days-old female newborn brought to our Emergency Department for intestinal occlusion due to an incarcerated inguinal hernia. During the operation, male-appearing gonads were identified in both inguinal canals and the histology confirmed the testicular features. Blood tests validated the diagnosis.

The diagnosis of CAIS is usually made during elective inguinal hernia repair or for delayed puberty. To our knowledge, this is the first case diagnosed in a neonatal urgent setting. Being able to immediately recognize this clinical picture, it allowed us to offer the best standard of care for the patient and the family.

1. Introduction

The disorders of sex development (DSD) are considered a rare disease and they may be found as a feature of a genetic syndrome or as a newly characterized condition [1]. The overall prevalence of DSD is 1 in 4000 born alive and the most common cause of ambiguous genitalia in XX females is congenital adrenal hyperplasia [2]. Another notable cause is androgen insensitivity syndrome (AIS). The pathogenesis of AIS is based on various mutations on the androgen receptor that range from complete insensitivity (CAIS), with primary amenorrhea in female adolescent without genital ambiguity, to a partial mutation of the receptor (PAIS) with various androgen effects and partial virilization [3].

We report a case of complete androgen insensitivity syndrome diagnosed during an emergency operation for incarcerated inguinal hernia in a six-days-old female newborn. To our knowledge, this is the first case reported in literature of presentation and diagnosis of this rare disease in a newborn.

2. Case report

A term six-days-old child presented at our Pediatric Emergency Department with a history arisen the same day, when she started refusing milk and, after few hours, developed signs of bowel occlusion. She was thus admitted to the Emergency Department of a local hospital. Her past medical history consisted in an apparently healthy pregnancy and a normal perinatal life. The day of the presentation, the child developed initially a fatigue during feeding and then a progressive decline of general conditions, characterized by irritability and biliary vomits. An abdominal radiography was performed, showing a bowel occlusion. Therefore, she had a surgical referral: the abdomen was referred as tender, the external genitalia appeared feminine (Fig. 1) and a swelling in the right groin region was detected. As any attempt of reduction of the hernia was unsuccessful, the child was transferred to our Department. An ultrasound exam of the inguinal region completed the clinical evaluation confirming the presence of intestinal loops incarcerated in the groin.

Due to the impossibility to reduce manually the intestinal loops and the overall clinical condition of the neonate, we decided to proceed with a surgical exploration. After the opening of the inguinal canal, we reduced the intestine in the abdomen and we detected the presence of an anomalous appearing gonad, similar to a testicle (Fig. 2). We thus explored the contralateral inguinal canal where we found an identical

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anatomical situation. Since the intraoperative scenario was unexpected, we contacted the on-call Endocrinologist that suggested a bilateral biopsy of the gonads. At the end of the operation, a complete exploration of the perineal region was performed confirming a normally located urethra and anus and a small vaginal pouch, with a length of approximately 1 cm (Fig. 3).

The following day, we performed a complete abdominal ultrasound which described the absence of the uterus and the presence of dysgenetic residuals of the Mullerian ducts. Furthermore, the baby underwent a complete hormonal work-up: 17OH-Progesterone 41.7 nmol/L (0.20–3.20), LH 0.1 U/L (female 0.7–20), FSH 0.3 U/L (female 2–12), 17 Beta estradiol 35 pmol/L (female 183–734), Testosterone 1.50 nmol/L (0.07–0.17), Androstenedione 1.3 nmol/L (1.4–11.9), DHT 0.73 nmol/L (0.08–1.26), DHEA 1.1 μmol/L (0.9–11.7), Inhibin B 148 ng/L (0–111), anti-Mullerian hormone 39.7 μg/L (0.02–3.39). These results show elevated levels of androgens suggesting the diagnosis of an androgen insensitivity syndrome. After the achievement of a full enteral feeding, the baby was discharged from the hospital and then followed-up in the outpatient clinic.

The pathology report confirmed the presence of testicular parenchyma consisting of seminiferous tubules with either irregular shape or without lumen, and isolated germ cells. Within the samples, interstitial Leydig cells were not found. Finally, the diagnostic confirmation was obtained through genetic tests: standard karyotype that showed a genotype 46, XY and a molecular analysis that showed a mutation c.2338C > T p.(Arg780Trp).

3. Discussion

As stated in the Consensus Statement published by Hughes et al., in 2006, the term “disorders of sex development” refers to all the congenital conditions in which development of chromosomal, gonadal or anatomical sex is atypical. The same authors stressed the concept that

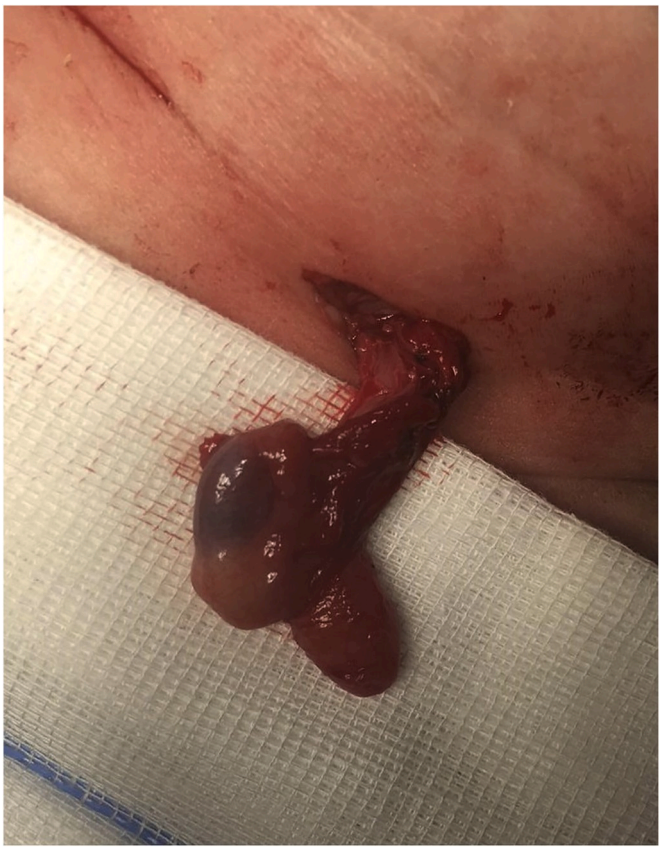

Fig. 2. Male appearing gonad found at the opening of the right inguinal canal.

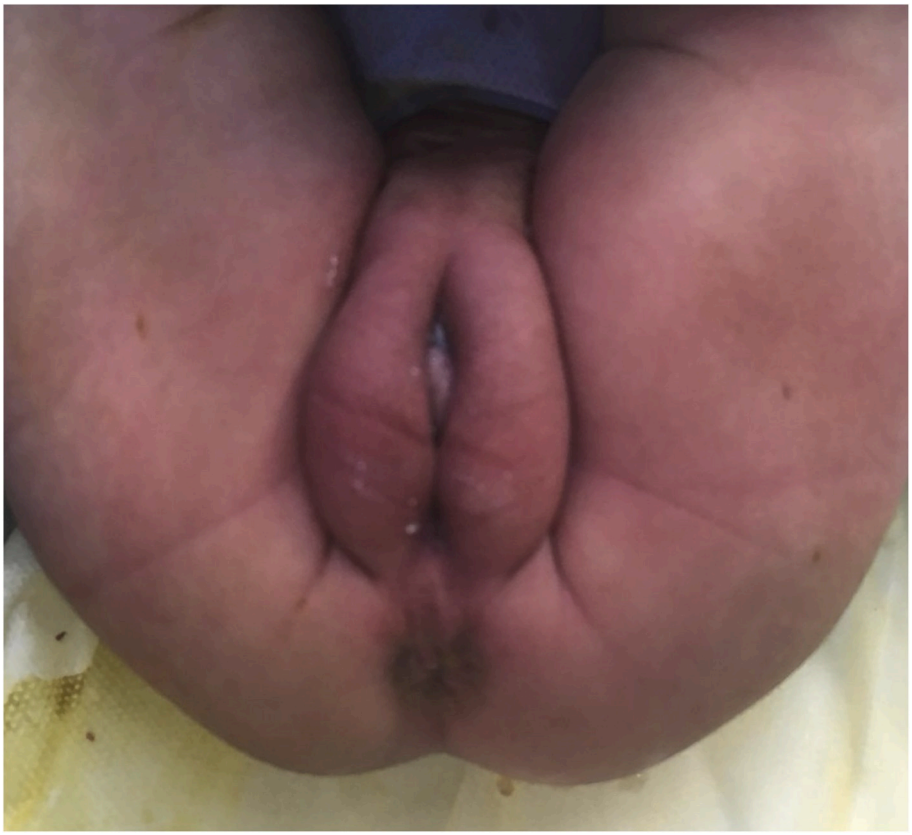

Fig. 1. Normal appearing female external genitalia at the preoperative evaluation.

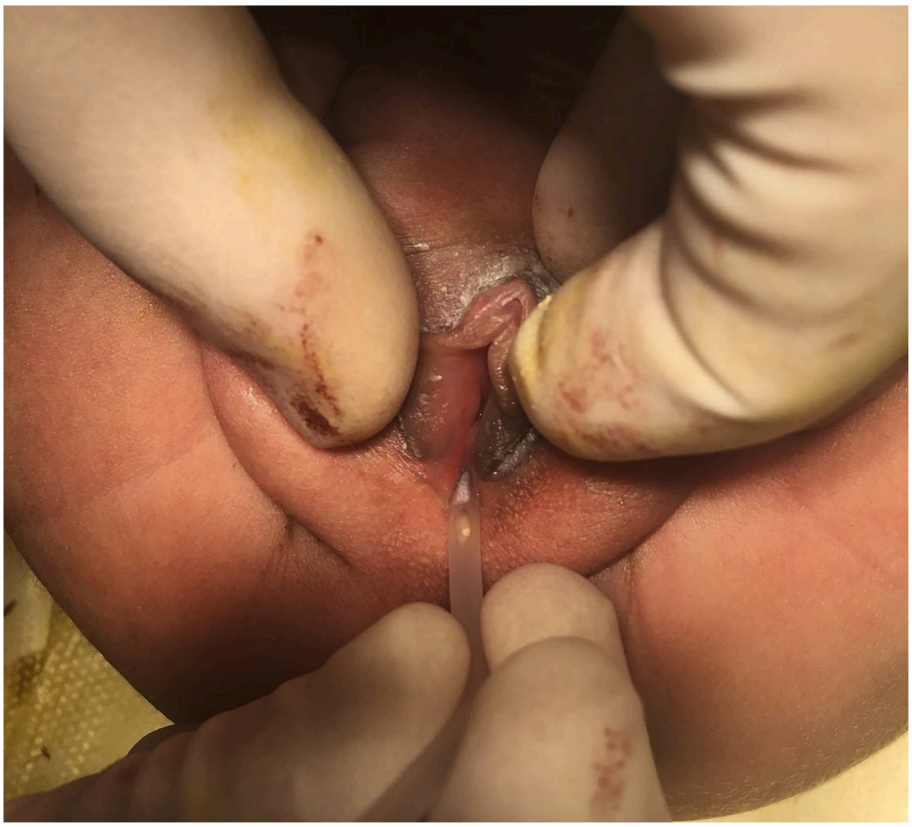

Fig. 3. Evaluation of the vaginal pouch at the end of the operation.

genital ambiguity should be never posed, by itself, as a final diagnosis but it constitutes a finding during a clinical exam, on which basis a proper assessment is performed to obtain a specific diagnosis [4].

Despite having obtained in the last years, a deeper knowledge of the genetic background and the molecular pathways causing a DSD and its clinical manifestation, these improvements should be necessarily related to ethical issues regarding sex assignment at birth and the patient concerns on sex determination [5].

The diagnosis of DSD with apparently normal external genitalia is usually delayed till the puberty age when it is diagnosed following investigations for primary amenorrhea. In particular, CAIS is usually diagnosed in teenager girls phenotypically appearing as females, with fully developed secondary sexual characters [3].

To our best knowledge, our report is the first one describing the diagnosis of a CAIS in a setting of urgency in a six-days-old newborn. The only other article describing the diagnosis of a CAIS in a case of incarcerated inguinal hernia, referred to a 12-years-old girl [6]. In this report, the authors describe the content of the inguinal hernia as a twisted testicle that was removed because of the lack of revascularization after de-rotation; after the exploration of the contralateral inguinal region, they found a testicle with a normal vascularization that was also removed. The histologic description of the two gonads reported in the article is similar to our case, confirming the typical alterations that can be found in a dysgenetic gonad.

Patients with androgen insensitivity syndrome may have an increased risk of germ cell tumors [7], therefore in the Consensus Statement of the European Society for Paediatric Endocrinology the authors suggest the removal of the testes in patients with CAIS and PAIS to prevent malignancy in adulthood. However, given the reported low rate of malignancy before puberty, today it seems reasonable to delay gonadectomies until puberty [8]. This choice allows the achievement of a spontaneous puberty thanks to the process of aromatization of androgens and enables patients to participate to the decisions regarding their therapeutic course (namely to agree on the testicle removal). According to the most recent data reported in literature [7], we performed a fixation of the gonads in the inguinal canals as they appeared macroscopically normal, in order to allow an easier clinical and ultrasonographic follow-up evaluation.

Despite the proper treatment being postponed till the pubertal age, the early diagnosis enabled us to guarantee a multidisciplinary approach since the neonatal period. This specific aspect is fundamental dealing with patient with DSD, as the optimal care for these children requires an experienced multidisciplinary team in a tertiary care center, including pediatric endocrinologists, psychologists, psychiatrists, geneticists, surgeons, urologists, gynecologists and social workers, with the first included since the beginning of the treatment of the child and the last introduced in the following years [9]. This aspect is also highlighted in the open letter to the Council of Europe written by the European Society for Paediatric Urology where they describe the importance of “multidisciplinary patient - and family - centered care” [10]. Support groups also play an important role in the delivery of care to DSD patients and their families and they also claim the importance of an active role of the patients in the decision [9].

We therefore recall the importance to consider the large group of disorders of sex development while examining or treating a small child even when dealing with common pathologies and to undertake the necessary investigations even in an urgent setting.

4. Conclusions

We report this case of CAIS diagnosed in a newborn of six days of life to highlight the possibility to diagnose a rare disease even in an urgency setting, as the case of an incarcerated inguinal hernia. Considering the disorders of sex development, an early diagnosis is the best achievement in a newborn with either ambiguous or normal genitalia.

Contributions

The authors contributed equally.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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