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VANISHING TESTES SYNDROME: A LONGITUDINAL REVIEW/STUDY

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ABSTRACT Vanishing testes syndrome (VTS) is a rare congenital disorder with bilateral anorchism where both testes are absent at birth with normal male external genitalia. A longitudinal research was carried out on a case of an 18 years old male, presented with incomplete secondary sexual characters and absence of testes where semen analysis showed aspermia. Hormonal analysis revealed high gonadotrophins and very low testosterone even after HCG stimulation test, suggestive of castrate level and total absence of testicular tissue. Karyotyping confirmed his 46XY status. Ultrasound /CT/MRI abdomen and pelvis did not give any information regarding testes or its remnants. CT guided aortorenogram showed agenesis of gonadal arteries which confirmed absence of testicular tissue after the 1st trimester. It was concluded that there should be a proper standard protocol for the management of patients who have empty scrotum.

KEYWORDS : Anorchia, castrate state, aspermia, vanishing testes, empty scrotum, MIS.

INTRODUCTION

There is a controversy surrounding the optimal management of the testicular remnants associated with the vanishing testes syndrome. Some urologists advocate the need for surgical exploration, whereas others believe this is unnecessary. These differing opinions are based on the variable reports of viable germ cell elements found within the testicular remnants. To better understand the pathology associated with this syndrome and the need for surgical management, the experience regarding the incidence of viable germ cell elements within the testicular remnant was observed.

Gender differentiation results from the interaction of hormonal and genetic factors. According to the sex chromosomes of the individual and the effect of transcriptional factors, testes or ovary develop from the embryonic bipotential gonads.[1]

During foetal development, testes develop in abdominal cavity and migrate to scrotum spontaneously. Descent is complete in 90% at birth, 98% at 1 year and 99.7% by puberty. Prevalence of congenital bilateral anorchia is 1 in 20,000 males. Under the normal circumstances testicular functions cover two phases of reproductive system: embryonic and adult phase. Embryonic testes contribute virilisation of Wolffian ducts which develop into epididymis, vas deferens, seminal vesicle and also induce formation of male external genitalia i.e. phallus and scrotum along with Mullerian ducts regression which form uterus, fallopian tubes and upper ½ of vagina in female. The adult testes are responsible for the spermatogenesis and steroidogenesis governing the further reproductive life in a male. A VTS phenotypically male presents with bilateral anorchia.[2]

Merry et al (1997) reviewed anatomical and histological findings in 105 vanishing testes. Records of 2,509 boys with 3,064 cryptorchid testes treated at a hospital between 1969 and 1995 were reviewed. Results showed that 691 (23%) testes were clinically impalpable. Exploration in these 691 impalpable testes revealed absent testes in 144 (21%). In 39 (27%) of the 144 absent testes, there was complete agenesis of testes along with the epididymis and vas deferens whereas 105 (73%) were associated with blind-ending cord structures – the vanishing testes. The site of blind-ending cord structures in 105 vanishing testes was intra-abdominal in 22 (21%), inguinal canal in 62 (59%), superficial inguinal ring in 19 (18%) and scrotum in 2 (2%). Histological information was available in 47 vanishing testes and revealed vas, epididymis, or both in 32 (68%), fibrous/vascular tissue in 11 (23%) and testicular cords in 4 (9%). Dystrophic calcification and/or haemosiderin were present in 7 (15%). It was concluded that the incidence of vanishing testes in boys with non-palpable testes is over twice the incidence of testicular agenesis. The most common site of blind-ending cord structures is distal to the internal inguinal ring. The finding of viable testicular tissue at the end of the attenuated cord structures in 4 of their patients, and also reported in other series, suggests that inguinal exploration should be carried out in all patients who on laparoscopy are found to have cord structures entering the internal ring.[3]

The present case is a type of bilateral anorchia, which required workup to establish the aetiology and to avoid patient's fear of developing malignant transformation in future, in case of hidden /ectopic or with any remnant of testicular tissue.

As for the management of cases of non-palpable testes on physical examination, most surgeons opt for laparoscopic exploration as the primary intervention. The laparoscopy is followed by inguinal exploration in cases where spermatic vessels are seen passing through internal inguinal ring.[4,5] The surgical literature regarding TRS emphasizes the importance of identifying the vascular supply and drainage of the gonad. This is due to the fact that the testes cannot be present in absence of testicular vessels and also because the vein and pampiniform plexus almost always indicate the location of the testes, even though the vas deference and the epididymis are present.[6]

OBJECTIVE

The main purpose of the study was to clear the confusing state that appeared regarding the gonadal tissue, because every new consultant had different views about the location of testicular remnants. Hence a prospective longitudinal study was taken up to find out the exact status of testes and to decide future line of management.

RESULTS AND INTERPRETATION

This 18-year young boy with normal birth was detected to have empty scrotum at the age of 1 year. At this stage he was treated with injection human chorionic gonadotropin (HCG) 1000 IU, subcutaneously, biweekly for 6 months. At 3 years of age he was diagnosed as bilateral cryptorchidism and underwent ? orchidopexy. At 3 ½ years repeat USG of scrotum and lower abdomen concluded absence of testes at both sites.

At 12 years of age, repeat USG created a doubt of visualization of the right testis in the scrotum and an endocrinologist diagnosed this as dysgenetic gonads. At that time levels of gonadotrophins were very high at -FSH 80 miu/ml (N 1.4-18.1) and LH of 40 miu/ml (N 0.1-6) and testosterone level was very low at 30 ng/dl (N 241-827). CT abdomen and pelvis at the age of 17 years concluded absence of

structure simulating a testis in abdomen, pelvis, perineum and inguinal canal bilaterally.

At the age of 18 years, the patient was presented to the human fertility research centre for the first time. The review of history, previous investigations and examination confirmed absence of testes but had very poor androgenization and low sexual maturating rating (SMR-Grade 1) {figure-1}. His phallus and scrotum were developed but pubic hair growth and pigmentation were of hypogonadic range.

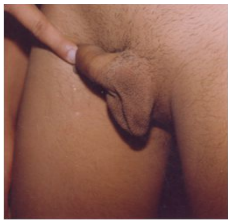

Figure-1 Empty scrotal sacs of the patient

His latest investigations revealed that there was no semen emission. Hormonal analysis showed TSH 1.22 miu/ml (N 0.5-4.5), FSH 88miu/ml), LH 40 miu/ml E2-<10 pg/ml (ND-56), CEA<1.20 ng/ml (N l 0-5), β HCG-<2 miu/ml (N 0-3). On HCG stimulation test there was no increase in testosterone level from the base value 34.31 ng/dl. His karyotyping was of normal male pattern i.e. 46 XY. Lastly a new technique Abdominal CT angiogram (aortogram and renal angiogram) confirmed suboptimal/unremarkable bilateral testicular arteries (figure-2). Ideally by 1 year of age testicular arteries cross external inguinal ring and reach scrotal sacs.

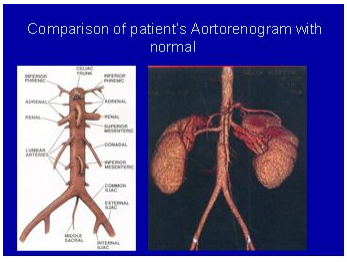

Figure-2 Comparison of the normal Aortorenogram with patient's Aortorenogram.

The patient was treated with long acting testosterone undecanoate 1000 mg (4ml) deep IM at D1, D45, D90, and then repeated every 3 months which is still continuing. After 6 months of therapy, he developed good androgenization. He was also advised prosthetic testicle implants for cosmetic purpose and his maintenance testosterone levels raised up to 587.83 ng/dl, FSH and LH level declined to normal range.

DISCUSSION

In an XY male, during embryonic development, under the genetic influence of testes defining factor-TDF gene, bipotential gonadal ridge differentiates in to testes. In testes, sertoli cells appear at 6-7 week of gestation and produce Mullerian inhibitory substance (MIS) that is responsible for Mullerian ducts degeneration. At 8-9 weeks, another component of testes called Leydig cells originate and secrete embryonic testosterone, which virilises Wolffian ducts. Then under the influence of 5 α- reductase enzyme, testosterone gets converted into di-hydrotestosterone (DHT) and develops prostate, urogenital sinus and male external genitalia, which gets completed by 12-13 weeks of foetal life.[7]

In the present case, empty scrotum was detected at 1 year of age and later the absence of testes was confirmed by various investigations. There were two possibilities that either testes did not develop at all or they had developed during embryonal stage and vanished later on. Normal development of phallus and scrotal sac suggests that there was survival of testes up to 12-13 weeks of gestation age.

At 1-year age he had empty scrotum and later on no testes were detected which suggest that after 14 weeks of intrauterine life testes had regressed and then vanishesd. Abdominal aorto-renogram had shown absence of testicular arteries bilateraly thoughout their course, confirmed absence of any remnant of testes.

There are 3 variants of congenital bilateral anorchism:

1. If before 8 weeks testicles fail to develop, then there is no secretion of MIS and the baby will have female genitalia (XY female). This is known as pure gonadal dysgenesis or Swyer syndrome.
2. If between 8 and 10 weeks the testes are lost, then the baby will have ambiguous genitalia.
3. If after 12-14 weeks the testes start regressing then the baby will be born with normal male external genitalia, i.e. scrotum and penis, but without testicles. This condition is called 'Vanishing Testes Syndrome'.

Aetiology of this disorder remains unclear. It may be caused by mutation, teratogen, bilateral tortion, trauma, infection, or vascular agenesis during developmental period after 14 weeks of gestation.[9] In our case vascular agenesis seems to be the cause of anorchia. During the early foetal stage (before 12 weeks) a testis derives its nourishment from several small branches arising from aorta which later on develop into gonadal arteries.

Storm et al. (2007) conducted an institutional review board-approved, retrospective review of all consecutive patients undergoing exploration for a non-palpable testis at Eastern Virginia Medical School and Geisinger Medical Centre between 1994 and 2006. Patients who were found to have spermatic vessels and a vas deferens exiting a closed internal inguinal ring were included in this analysis. It was found that fifty-six patients underwent removal of the testicular remnant. Patients' age ranged from 11 to 216 months. In 8 of the specimens (14%), they identified viable germ cell elements. In an additional 4 patients (7%), they identified seminiferous tubules without germ cell elements. It was identified that a significant number of testicular remnants associated with the vanishing testes syndrome can harbour viable germ cell elements or seminiferous tubules. The exact fate of these residual elements remains unknown. However, there may exist the probability of malignant transformation. Given the potential for malignant degeneration, they believed that these remnants should be removed.[8]

Some studies show that the loss or absence of testicles can have negative psychological effects on adult men or children. Therefore, surgery for testicular prosthesis implantation is a solution that minimizes psychological consequences of the absence of the testicle in the scrotum, providing similarity in size, weight and appearance of natural testicle.[9]

Furthermore, one should consider the possibility of orchidopexy and testicular prosthesis implantation to minimize the risk of testicular torsion of the viable tissue and negative psychological effect.[10]

Therefore, the present case is of high importance for management of patients who present themselves with empty scrotum. The first step is to confirm presence or absence of testes in inguinal canal, pelvic areas and abdomen. When testes are not traceable at any location by various investigations, it needs to establish absence of testicular artery by abdominal aorto-renogram. In such cases any invasive procedures like histopathology, venogram, laparoscopy to detect testes is not advisable, as this can be done using various non-invasive techniques.

CONCLUSION

VTS can be under-diagnosed by clinicians because it is a rare entity. In the present case also multiple visits to paediatricians, surgeons, urologist, radiologist and endocrinologist failed to establish the phenomenon of vanishing testes in early embryonic life, which is evidenced by the presence of normal development of phallus and scrotum. Agenesis of testicular arteries suggested lack of further development of testes after the first trimester.

Hence, now the patient will be free from the fear of future potential of having malignant transformation in abdominal testicular tissue. He must receive lifelong testosterone replacement and can plan his married life as an absolute infertile male. In this way a fractured male reproductive system can be repaired.

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