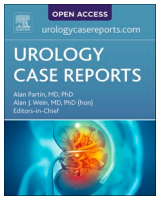
Urology Case Reports 56 (2024) 102803

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: www.elsevier.com/locate/eucr



Oncology

Testicular tumor in a case of, undescended testes, persistent mullerian duct syndrome and transverse testicular ectopia: Report of a case and review of the literature

Haytham Araibi

Urology and Kidney Transplantation Department, Ibn Senna Hospital, Sudan Medical Specialization Board of Urology, University of Khartoum, Faculty of Medicine, Anatomy Department, P.O BOX 102, Qasr Street, Khartoum, 11111, Sudan

ARTICLE INFO

Keywords:
Testicular tumor
Persistent mullerian duct
Transverse testicular ectopia
Disorder of sexual differentiation

ABSTRACT

A 20-year-old with normal male body features and secondary sexual characteristics presented with a right testicular swelling. Imaging revealed a right testicular mass, leading to a diagnosis of classical seminoma. During inguinal orchiectomy, a solid testicular mass was found on the right side along with two spermatic cords, one attached to the mass and the other to a structure resembling a testes. Examination showed the presence of other testes and a rudimentary uterus, indicating a rare case of a testicular tumor coexisting with undescended testes and transverse testicular ectopia (TTE) in a Pseudohermaphrodite with "persistent mullerian duct syndrome" (PMDS).

1. Introduction and literature review

Disorder of sexual differentiation (DSD) is one of the rarities in medicine. Inspite of that, the physician or the operating surgeon, should always consider them between the lists of the possible differential diagnosis. The condition named "persistent mullerian"s duct syndrome" (PMDS) – is a one type of "Disorders of Sexual Differentiation" (DSD). It is diagnosed when the mullerian duct structures identified, in otherwise phenotypically and genetically normal man.[1] Thought to result from absence of mullerian duct inhibiting factor synthesis or release, or from a defect in its receptor.[2] It was firstly reported in 1939 by Nilson,[3] consequently additional cases has been added to literature since then. The number of reported cases today reached the 150 cases.[2] The condition has many sub-types, one of them called "Hernia uteri inguinalis "-PMDS type 1 – is one of the rarities, when the mullerian duct structures descend within the hernia sac, as it is in our case[4]

On the other hand, the disorder of "Transverse Testicular Ectopia" (TTE), is one form of undescended testes, when both testicles descended in the same inguinal canal. It was firstly reported by Von Lenhossek in 1886,[5] and up to date,a total of 260 cases were reported. The combination of both (TTE) and (PMDS), is even more rare, to our knowledge, about only 57 cases has been reported.[6]

Three different sub-types of the condition has been identified, type –one – associated with inguinal hernia (40–50 %), type –two- by PMD structures (as in our case) (30 %), and type –three- with other congenital anomalies, such as,hypospadias, pseudohermaphrodism and scrotal abnormalities.

The gene "SRY box transcription factor" (SOX 9) is the testicular gene responsible for the production of "Anti mullerian hormone kinase "(AMH kinase), which is responsible for regression of the mullerian duct structures at approximately the 8 weeks gestation.[7] The molecular regulation of this, is that, there are two receptors for (AMH kinase) (serine/threonine). Type two identifies the ligand specificity, and type one fires signaling cascades.[8]

The presentation of the condition in male patient could be in one of the following forms:

1 Testes is in the position of the ovary, and the inguinal sac is empty (60–70 %).
2 One testes in inguinal canal with attached mullerian duct structures (Hernia uteri inguinalis 30-20 %).
3 Both testes in the same inguinal canal, in one processes vaginalis – (TTE – represents about 10 %) - as in our case.

In the first both testes and PMD structures are impalpable inside the abdomen, with empty scrotal sac, in the second there is cryptorchidism in one side with PMD structures within it in the same hernia sac, lastly the last type both testicles with PMD structures are in the same hernia

E-mail address: araibi85@yahoo.com.

https://doi.org/10.1016/j.eucr.2024.102803
Received 17 June 2024; Received in revised form 9 July 2024; Accepted 14 July 2024
Available online 18 July 2024

sac.[9]

2. Case presentation

2.1. History of present illness

The case involves a 20-year-old male with missed undescended testes (UDT). The patient experienced gradual onset right scrotal swelling over six months, which increased in size without pain or tenderness. Additionally, a swelling in the right inguinal area was noted, correlating in size with the scrotal mass, which was also painless. The patient reported significant weight loss. Family history includes a brother diagnosed with testicular malignancy at 24 years, treated successfully with surgery and chemotherapy. There was no systemic symptoms of infection or distant metastases. The physical examination revealed a large scrotal mass on the right side measuring 10 × 6 cm, with a hard consistency, irregular margin, and no tenderness. The spermatic cord was separately palpable, but the proximal part and epididymis could not be differentiated from the mass, while the overlying scrotal skin appeared normal. Additionally, multiple enlarged firm right inguinal lymph nodes of variable size were found, fixed and not tender to palpation. On the left scrotum, no testes were palpable, but the scrotal skin appeared well developed.

2.2. Laboratory tests

Test	Value	Reference range
CBC – Hemoglobin	12.0 mg/dl	13–17 mg/dl
RFT – Creatinine	0.9 mg//dl	0.7–1.3 mg/dl
S.urea	12 mg/dl	17–43 mg/dl
LFT – ALT/AST/ALP	all within normal limit	
S.billirubin	1.1 mg/dl	0.3–1 mg/dl
PT	13 seconds	12.3–15.1seconds
APTT	32 seconds	30–40 seconds
Urine general: Pus		
Pus cells	0–5	0–5
RBCS	<5	0–5
Tumor markers:		

(*continued on next page*)

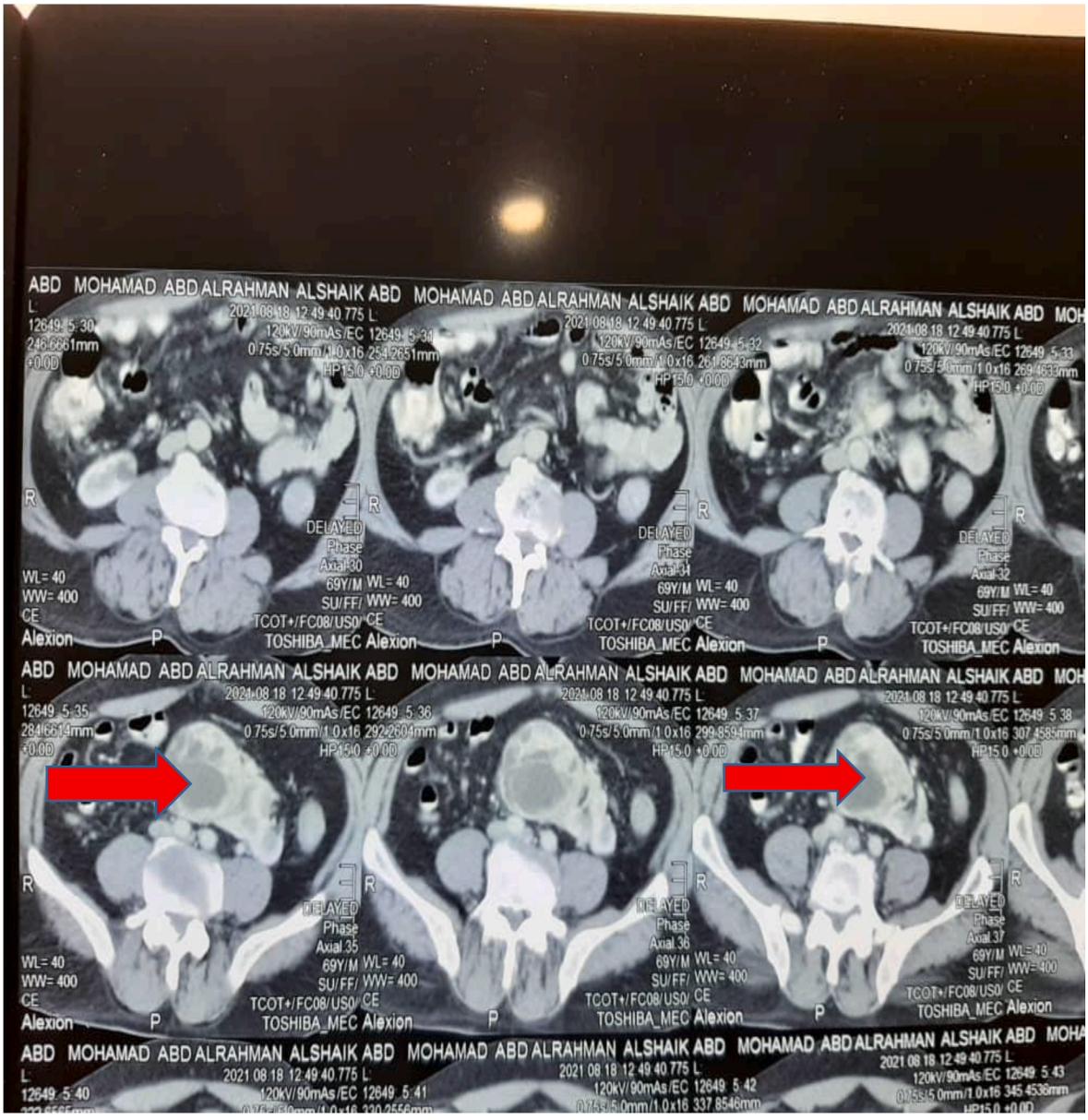


Fig. 1. Axial views of the CT scan abdomen and pelvis with IV and Oral contrast. Showing huge heterogeneous solid retroperitoneal par aortic lymph nodes mass with Central necrosis.

(*continued*)

Test	Value	Reference range
AFP	25 Ug/L	>40 Ug/L
LDH	3 IU/L	105–233 IU/L
B-HCG	5 µkat/L	<5 µkat/L

2.3. Imaging studies

2.3.1. Ultrasound

- Testes identified at the mid inguinal canal about (3 × 2 × 3 cm).
- Right hemi scrotum showed hypo echoic complex solid mass, with central cystic component (8 × 10 × 4 cm).
- About five separate enlarged lymph nodes in the Right inguinal region, the largest measuring (2 × 2 × 3 cm) with surrounding fluid.
- Mild amount of peritoneal ascites between the bowel lobes.

2.4. CT scan abdomen and pelvis

With IV and Oral contrast. Showing the RT heterogeneous Testicular mass and Huge Heterogeneous solid retroperitoneal. Par aortic lymph Nodes mass with Central necrosis (Figure-1).

2.5. MRI abdomen and pelvis

- Testes located at the distal inguinal canal (3.3 × 2.2 × 3.2 cm) of low signal intensity on T1W1 and T2W1, heterogeneous enhancement and restricted diffusion on DW1.
- Right hemi scrotum showed peripherally enhancing complex mass, with central non enhancing component, representing tissue necrosis (2.7 × 2.3 × 2.1 cm).
- Multiple enlarged lymph nodes in the Right inguinal region, the largest measuring (8.4 × 11.5 × 5.5 cm) restricted on DW1 **(**Figure-2**).**

On the bases of the previously mentioned history, physical examination, laboratory and imaging findings, the decision was made for operative treatment. The patient received Neoadjovant chemotherapy according to the Standard Regimen.

2.6. Operative findings

- Right side inguinal incision made, inguinal approach to the spermatic cord used. At the opening of the inguinal canal two separate spermatic cords identified, one is related to the mass and the other to an organ looked like testes identified in the distal inguinal canal (unfortunately, even this was completely encased by the tumor). After extensive discussion with the two most senior urologists of the unit, final decision was made to excise the whole mass, including the second testes attaching to the mass. The two spermatic cords was firstly ligated and excised, before the whole mass been removed. (Figure-3).

2.7. Histopathology results

2.7.1. Macroscopic appearance

Scrotal tissue weight 300 gm. , composed of three different structures, right spermatic cord of 3 cm length + scrotal sac looks like uterus 4 cm maximum diameter + right testes 3cm + left testes 1.5 cm + well circumscribe mass of 8 cm length maximum diameter.

2.7.2. Microscopic examination

One testes showed malignant neoplasm composed of sheets of uniform tumor cells divided into poor demarcated lobules by delicate fibrous septa with lymphocyte and plasma cells. The tumor cells are large, round, polyhedral with distinct cell membranes, abundant clear cytoplasm, large central nuclei, and prominent nucleoli. Focal necrosis noted, there is evidence of per tumor lymph vascular invasion and intratubular germ cell neoplasia. The surgical cut edge and spermatic cords are free of neoplasm the features are consistent with classical seminoma, the other testes is atrophied and involved with the neoplasm. Microscopy of hernia sac showed uterus, lined by atrophic endometrium **(Figure-4).**

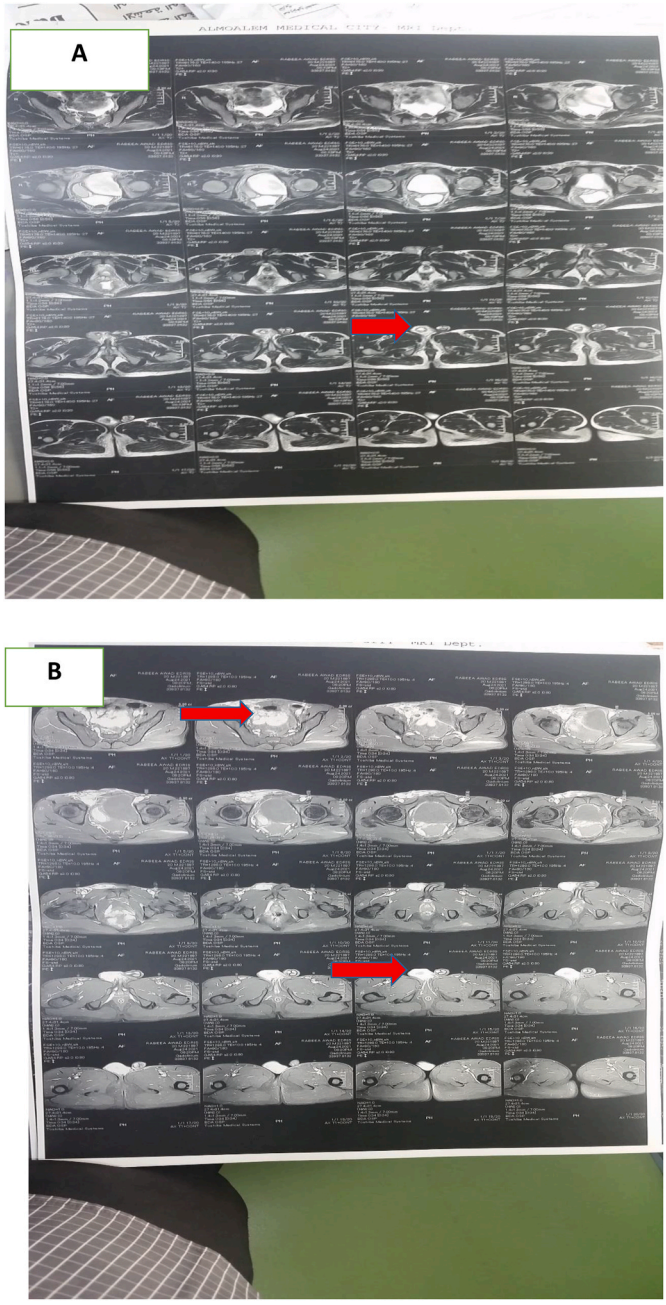


Fig. 2. Axial views of the MRI scan abdomen and pelvis with contrast. Showing the RT low signal intesity (T1W1-T2W2) testicular mass and huge heterogeneous solid retroperitoneal par aortic lymph nodes mass with Central necrosis.

3. Discussion

The definition of true hermaphrodite is when both testes and ovaries are located in the same individual.[10] In contrast female

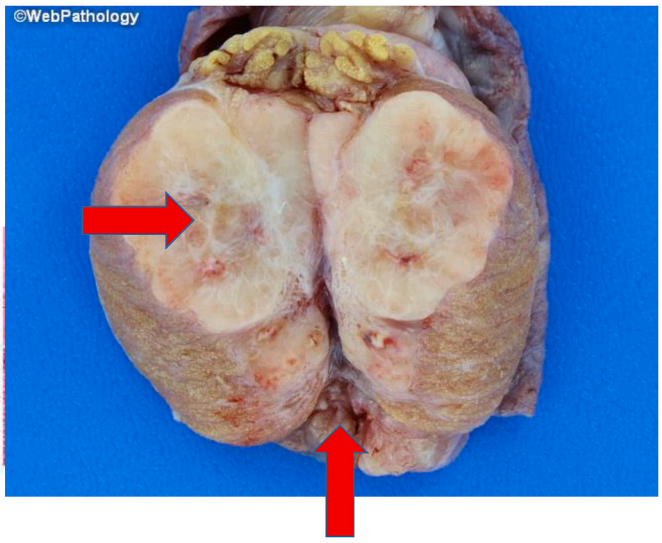


Fig. 3. Gross Specimen of the RT testicular exophytic whitish mass typical of Seminoma (300 gm), with sperrmatic cord (3cm), scrotal sac (looks like Uterus, 4cm), and LT testes impeded within the tumor (1.5cm).

pseudo-hermaphroditism, the gonads are ovaries and the external genitalia shows musculinic properties. Male pseudo-hermaphroditism, the gonads are testes, but the internal genitalia failed to develop.[11] The presentation of male pseudo-hermaphroditism varies: 1- fully developed masculinized external genitalia and uterus (as in our case) 0.2- poorly developed external genitalia 0.3- Equivocal developed external genitalia[12]

Male pseudo-hermaphroditism could passed undetected till adulthood.[13] PMDS is a subtype, in which mullerian duct structures persist. The first to report it, was Nelson in 1939.[3] some of the cases are found to have familial association[2]

The causative factor of the condition is thought to be a defect in mullerian inhibiting factor (MIF), which is released by sertoli cells of the testes and leads to mullerian duct structures regression. The defect could be in the factor itself or its receptor. The condition is also associated with cryptorchidism, as it seems that, the MIF also affect the process of testicular descend.[2] So the individual will be phenotypically male subject, with normally developed external genitalia, but with fallopian tubes,uterus, upper vagina as internal genitalia and secondary sexual characteristics.[4]

The PMDS could present in either phonotypical male or female. When the patient is phenotypically male-represents about 80–90 %, it could be either: 1- Unilateral cryptorchidism and contra-lateral inguinal herniation, this is further could be one of following types: 1-cryptorchidism with ipsilateral uterus and fallopian tube descend (uterine inguinale) 2- herniation of both testes, uterus and fallopian tube in the same inguinal canal (crossed testicular ectopia).[4] 2- When the patient is phenotypically female represents about 10–20 %, there will be bilateral cryptorchidism, when both testes are fixed at the site of ovaries and connected to the round ligament.[4] Other classification of TTE is that.

1 Type −1, accompanied by hernia (40–50 %)
2 Type-2, associated with PMDS (30 %)
3 Type-3 –associated with other congenital anomalies (hypospadias, cryptorchidism, scrotal abnormalities)20 %[14]

A condition known as mixed gonadal dysgenesis, is a disorder of abnormal sex chromosomes characterized by ambiguous genitalia with unilateral testicle and contralateral streak gonad, in addition to PMDS in the same side.[15]

The condition is usually an intra-operative diagnosis, but it could be detected by U/S, CT scan and MRI. The prognosis depends on the condition of the testicular tissue and the close proximity between the vas difference and fallopian tube[1]

The risk of malignancy of the an undescended testes associated with PMDS is 7–35 % more than that of normal population, (as in our case). There are multiple reported cases of seminoma, embryonal carcinoma, yolk sac tumor and teratoma. Perkmen[16] reported three cases of malignancy associated with PMDS (two was seminoma and the other showed mixture of both seminoma and teratoma). However the tumor related to mullerian duct structures are very rarely detected. As it is expected the rate of infertility is high, with azoospermia in semen analysis.[2,4]

The mode of surgical treatment entitles, to try to preserve the testicular tissue, by fixing the testes to the scrotum (orchidopexy), this is usually combined with removal of mullerian duct structures, separating it from the vas difference. PMDS is only removed if it intervenes with the process of orchidopexy, as it is thought, that this may endanger the

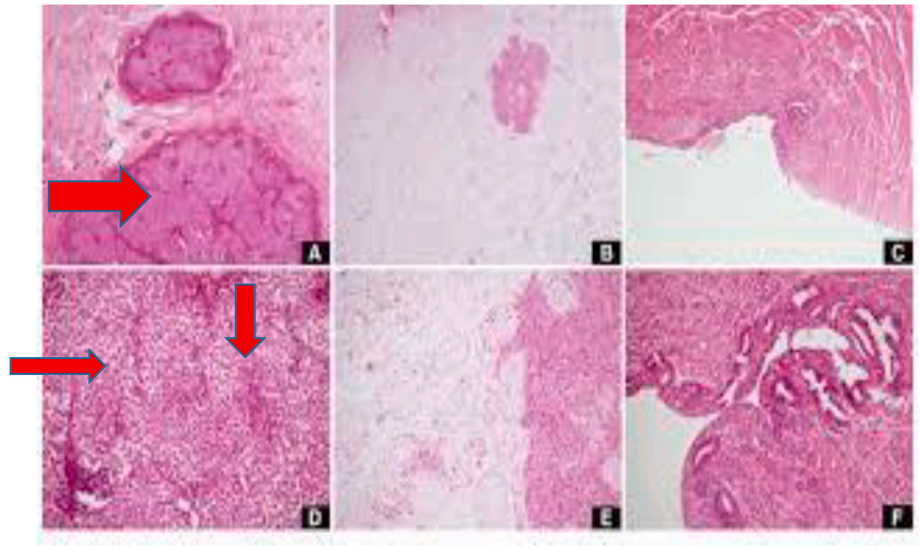


Fig. 4. Microscopic slides of the histopathological specimen, showing Sheets of uniform tumor cells, divided by poorly demarcated lobules of fibrous septa with lymphocytes and plasma cells. Tumor cells are large, round and polyhedral with distinct cell borders, abundant clear cytoplasm large Central nuclei and prominent nucleoli. Central necrosis identified with Evidence of lymph vascular invasion and intratubular germ cell neoplasia.

vessels of spermatic cord. In case of TTE, the other testes could be brought through crossing the root of the penis or through *trans*-septal approach.[17] This surgery should be attempted as early as possible to try to retrieve fertility.[2,4] The risk of malignant transformation of the testes increased in intra-abdominal location compared to inguinal position, as a result an undescended testes found in the inguinal canal could be safely brought to scrotum. In our case, the condition is unfortunately different, as both testes are found in one inguinal canal, and the tumor of one testes infiltrating the other, so the decision was made to remove both of them enblock.

4. Conclusion

The condition is usually diagnosed intra-operatively, with the subsequent risk of crypt orchid testes to become malignant is about 18 % (embryonal carcinoma, seminoma, yolk sac tumor, and teratoma). All effort should be done to preserve functional testes, with the ideal operation is bilateral orchidopexy.[18] The division of the PMD structures is not advised unless it prevents the orchidopexy. Again in case of TTE the ectopic testes could be placed in the contralateral scrotal sac by crossing the root of the penis, and if this is impossible, it could be placed in the retro peritoneum.[17,19]

CRediT authorship contribution statement

Haytham Araibi: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Data curation, Conceptualization.

Declaration of competing interest

I hereby declare that I have no conflict of interest with the journal, publisher, or reviewer. This statement is directed to the chief editor in charge.

References

1. Yuksel B, Saygun O, Hengirmen S. Persistent müllerian duct syndrome associated with irreducible inguinal hernia, bilateral cryptorchidism and testicular neoplasia: a case report. *Acta Chir Belg.* 2006;106(1):119–120.
2. Prakash N, Khurana A, Narula B. Persistent Müllerian duct syndrome. *Indian J Pathol Microbiol.* 2009;52(4):546.
3. Nilson O. Hernia uteri inguinalis bein Manne. *Acta Chir Scand.* 1939;83:231–249.
4. Renu D, Rao BG, K Ranganath N. *Indian J Radiol Imag.* 2010;20(1):72.
5. Von Lenhossek M. Ectopia testes transverse. *Anat Anzeiger.* 1886;1:376.
6. Ferri M, Ansari S. (PMDS) associated with transverse testicular ectopia. *Can J Urol.* 1999;6(5):865–867.
7. Taguchi O, Cunha GR, Lawrence WD, Robboy SJ. Timing and irreversibility of Müllerian duct inhibition in the embryonic reproductive tract of the human male. *Dev Biol.* 1984;106(2):394–398.
8. Klatte T, Seitz C, Waldert M, et al. Features and outcomes of renal cell carcinoma of native kidneys in renal transplant recipients. *BJU Int.* 2010;105(9):1260–1265.
9. Imbeaud S, Rey R, Berta P, et al. Testicular degeneration in three patients with the persistent müllerian duct syndrome. *Eur J Pediatr.* 1995;154(3):187–190.
10. Ceylan K, Algun E, Gunes M, Gonulalan H. True hermaphroditism presenting as an inguinal hernia. *Int Braz J Urol.* 2007;33:72–73.
11. Stern O, Vandervort W. Testicular feminization in a male pseudohermaphrodite: report of a case. *N Engl J Med.* 1956;254(17):787–790.
12. Shojai AR, Patil KK, Kulkarni V. Obstructed hernia in male intersex. *Bombay Hosp J.* 2004;46(4).
13. Michiels I, Peperstraete L, De Wever I, Gruwez J. Inguinal hernia repair leading to the diagnosis of internal male pseudohermaphroditism. *Acta Chir Belg.* 1984;84(4):255–258.
14. Gauderer MW, Grisoni ER, Stellato TA, Ponsky JL, Izant Rj Jr. Transverse testicular ectopia. *J Pediatr Surg.* 1982;17(1):43–47.
15. Robboy S, Bentley R, Russell P, Anderson P, Fox H, Wells M. *Pathology of abnormal sexual development. Haines and Taylor Textbook of Obstetrical and Gynecological Pathology*. fifth ed. Philadelphia: Churchill Livingstone; 2003:1217–1219.
16. Berkmen F. Persistent müllerian duct syndrome with or without transverse testicular ectopia and testis tumours. *Br J Urol.* 1997;79(1):122–126.
17. Telli O, Gökçe Mİ, Haciyev P, Soygür T, Burgu B. Transverse testicular ectopia: a rare presentation with persistent Müllerian duct syndrome. *Journal of clinical research in pediatric endocrinology.* 2014;6(3):180.
18. Farikullah J, Ehtisham S, Nappo S, Patel L, Hennayake S. Persistent Müllerian duct syndrome: lessons learned from managing a series of eight patients over a 10-year period and review of literature regarding malignant risk from the Müllerian remnants. *BJU Int.* 2012;110(11c):E1084–E1089.
19. Esteves E, Pinus J, Maranhão RFdA, Abib SdCV, Pinus J. Crossed testicular ectopia. *Sao Paulo Med J.* 1995;113:935–940.

Abbreviations and acronyms

AMH: antimullerian hormone
CT scan: Computer Tomography
DW: diffusion weighted
H&E: haematoxylin and eosin
LT: left
MRI: Magnetic Resonance Imaging
PMDS: persistent mullerian duct syndrom
RT: right
SOX9: SRY-related HMG-box gene
TTE: transverse testicular ectopia
U/S: ultrasound