

“RADIOLOGICAL EVALUATION OF AMBIGUOUS GENITALIA WITH VARIOUS IMAGING MODALITIES “

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Abstract:

Disorders of sex development (DSDs) are congenital conditions in which the development of chromosomal, gonadal, or anatomic sex is atypical. These can be classified broadly into four categories on the basis of gonadal histologic features: female pseudohermaphroditism (46,XX with two ovaries); male pseudohermaphroditism (46,XY with two testes); true hermaphroditism (ovotesticular DSD) (both ovarian and testicular tissues); and gonadal dysgenesis, either mixed (a testis and a streak gonad) or pure (bilateral streak gonads). Imaging plays an important role in demonstrating the anatomy and associated anomalies. Ultrasonography is the primary modality for demonstrating internal organs and magnetic resonance imaging is used as an adjunct modality to assess for internal gonads and genitalia. Early and appropriate gender assignment is necessary for healthy physical and psychologic development of children with ambiguous genitalia. Gender assignment can be facilitated with a team approach that involves a pediatric endocrinologist, geneticist, urologist, psychiatrist, social worker, neonatologist, nurse, and radiologist, allowing timely diagnosis and proper management. We describe case series on ambiguous genitalia presented to our department who were evaluated with multiple imaging modalities.

Key words: ambiguous genitalia , ultrasound ,Computed Tomography scan , Magnetic Resonance Imaging

CASE 1 -

- A 39 year Married male patient presented with change in voice , cyclical pain abdomen in the suprapubic region and right iliac fossa and Bleeding from external genitalia on and off. on physical examination Absent right Testicle since birth & enlarged both breast with absent male pattern of hair distribution.

- Hormonal investigations revealed elevated FSH (2.55 mIU/micro L) , decreased testosterone(6.6 micro g/micro L) ,Leutinisig Hormone (LH) - 2.8 mIU/micro L,estradiol- 41 micro g/micro L and karyotyping- 46xx- normal female.
- On ultrasonography there was a Midline well defined thick walled fluid filled pear shaped structure behind Urinary Bladder (fig 1)and anterior to rectum. Another fluid filled thick walled structure noted to the right of above mentioned lesion with low level internal echoes (fig 2).
- CECT showed Fairly defined heterogeneous enhancing soft tissue attenuation mass in right side of the pelvis, antero- lateral to recto sigmoid and posterior to the bladder with enhancing solid component displacing the iliac vessels laterally(fig. 3).Left testis- normal in size and attenuation. Right testis not visualized in the scrotal sac and in other abdominal sites(fig 4 & 5).
- Intra-Operative Findings showed uterus and bilateral fallopian tubes with right ovarian lesion which were removed and confirmed histopathologically.(fig 6 & fig 7)

Case2:

- An 18 year old boy with history of pain in left inguinal region from 6 months and absent left testis since birth came for contrast computed tomography(CECT). On examination he is tall built with sparse hair on chest , enlarged breast and hypoplastic right testis.
- Laboratory examination revealed estradiol to be on higher end of the marginal values(41.5pg/ml), decreased testosterone levels(1.67pg/ml). Rest of the investigations were normal.
- Karyotyping revealed 46 XX.
- On CECT , A tubular enhancing soft tissue attenuating lesion noted in left inguinal canal(fig 8) . A thick peripherally enhancing cystic lesion with a speck of wall calcification was noted in left leftparavesicle space superior to above said tubular lesion (fig 9). Left hemiscrotum was empty(fig 10)
- These lesions were sent to Histopathological diagnosis after laparoscopic removal. Left ovarian cyst with seminoma in undescended testis was diagnosed.

CASE 3:

- 18 year old boy with history of haematuria for a period of one month , loss of appetite and loss of interest in school academics came for ultrasonography. On general examination he was tall built with coarse hairs and had feminine voice.
- Laboratory examination revealed elevated Follicular stimulating hormone(FSH)(69.81mIU/ml), LH (47mIU/ml), normal Human chorionic gonadotropin (HCG) & AFPlevels ,
- Elevated Estrogen& decreased testosterone levels were observed.
- Ultrasonography abdomen revealed left testis as hypoplastic (measuring 1.2x2.0 cm) and right empty scortum with absent corpora spongiosum. A pear shaped structure with fluid fluid level was noted on to right of bladder

in pouch of Douglas with a heterogeneous vascular structure extending to involve bladder lumen and protruding into it(fig 11).

- Multiple oval to round enlarged pelvic and para aortic lymph nodes were also noted. Bilateral hydronephrosis was also noted
- On Contrast enhanced computed tomography absent testis on right side with non enhancing left testis and aoblong elongated pear shaped structure was noted on to right of bladder with heterogeneously enhancing lesion lower one third of the structure eroding the bladder wall and protruding into the lumen and causing bilateral uterovesical junction obstruction (fig 12 & fig 13)
- On MRI the lesion in lower one third of pear shaped structure showed heterogenous enhancement with diffusion restriction (fig 14 & fig 15). Multiple nodular enhancing lesions on T1& T2 weighted imaging showing diffusion restriction was noted in bilateral lungs with diffusion restriction in the lesion present in pouch of Douglass.(fig 16).
- Karyotyping revealed mixed gonadal dysgenesis with 50% 45 XX and 50% being 45XY.
- Histopathological diagnosis was given as poorly differentiated malignant tumor .

Figures :



Fig 1.



Fig 2.

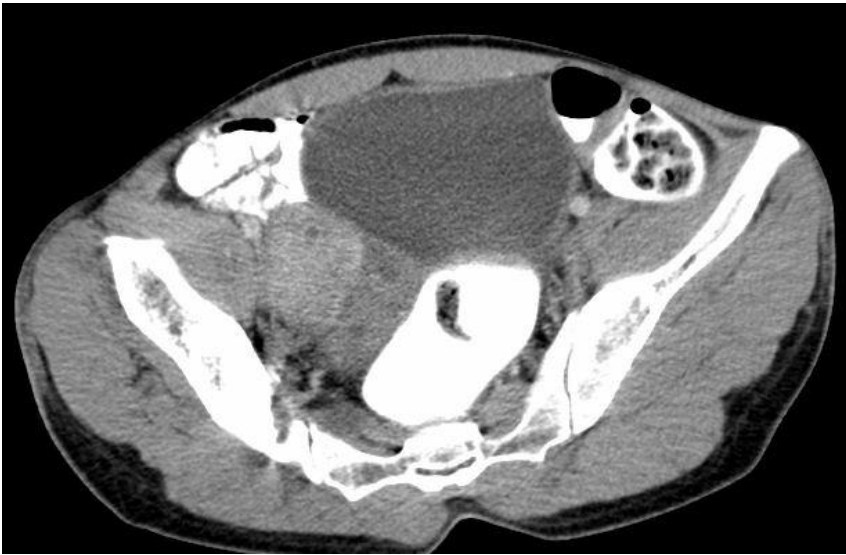


Fig 3



Fig 4.



Fig 5



Fig 6

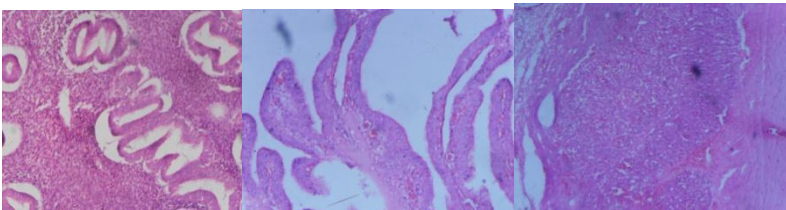


Fig 7



Fig 8



Fig 9

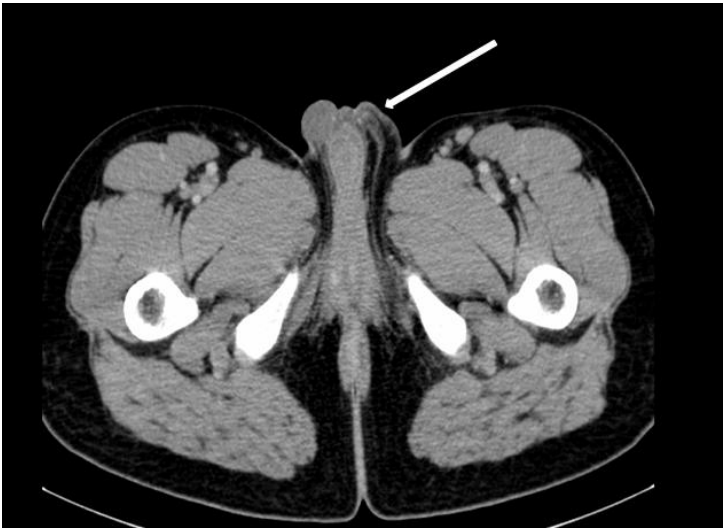


Fig 10

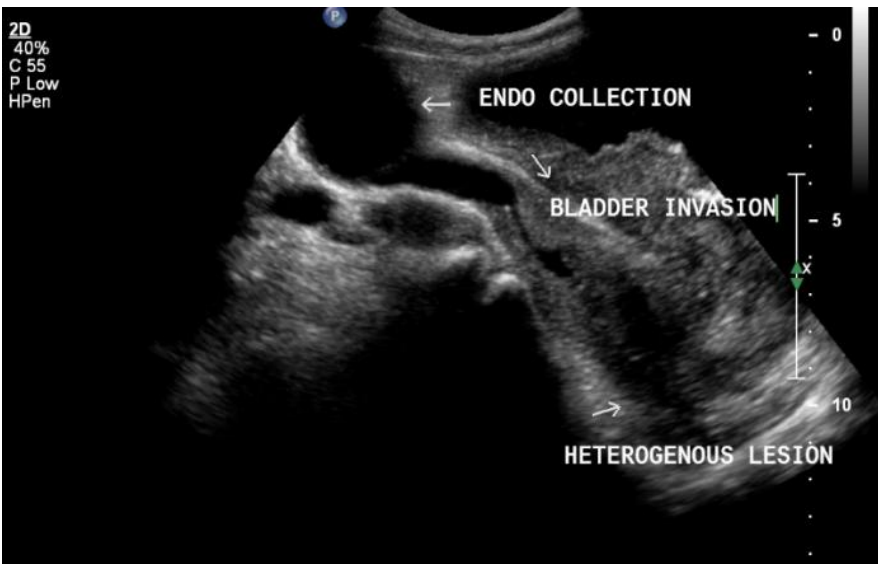


Fig 11.

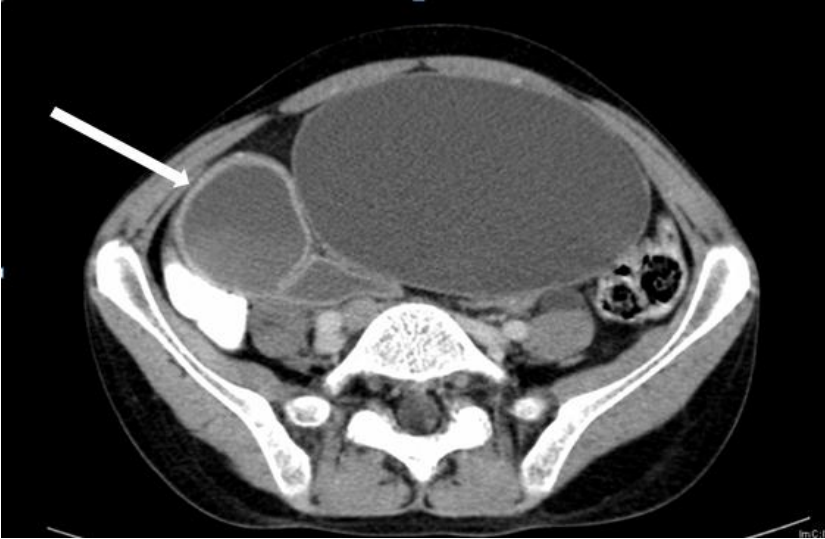


Fig12



Fig 13

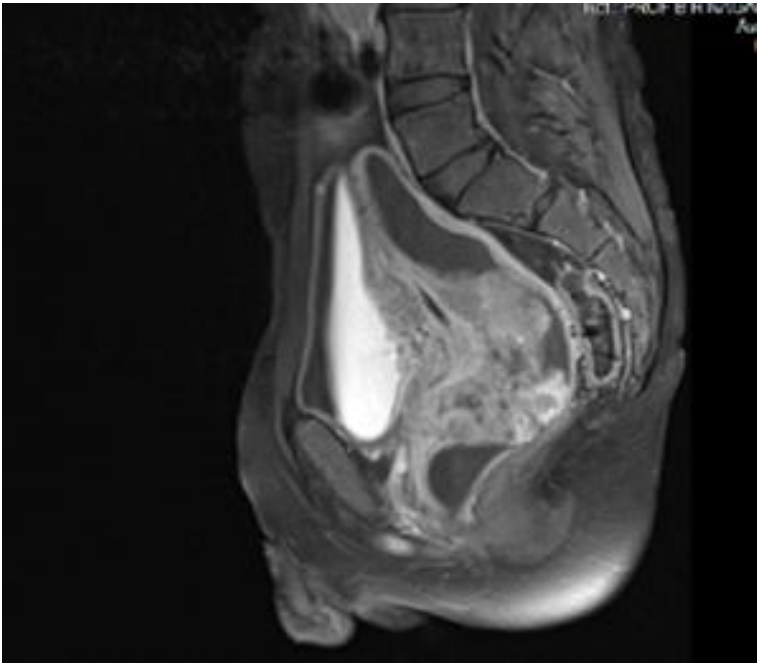


Fig14

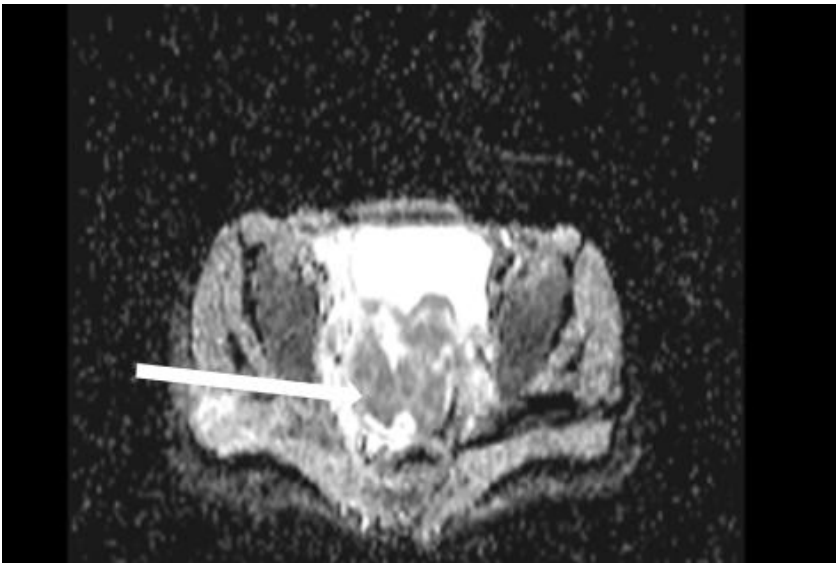


Fig 15

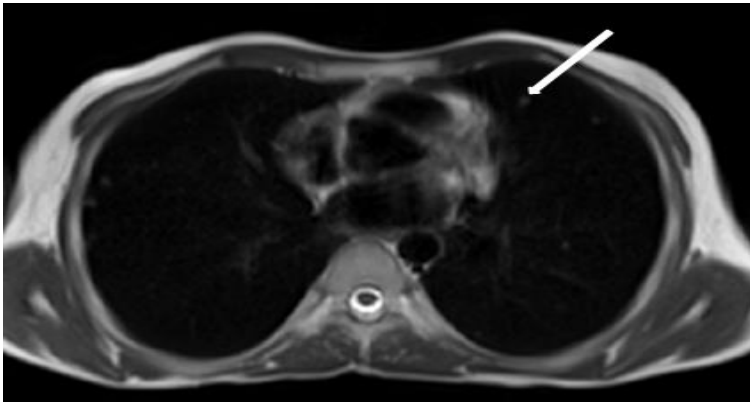


Fig 16

Figures: fig 1. USG showing tubular thick walled anechoic structure posterior to bladder, fig 2, USG showing thick walled oval to round cystic lesion to the right of above said tubular lesion in fig 1, the lesion showed low level echogenic contents. Fig 4 , CECT showing a heterogeneously enhancing lesion with soft tissue attenuation posterior and to the right of bladder , fig 5 pear shaped structure with heterogeneously enhancing lesion in lower one third located posterior to bladder. Fig 6 showing gross specimen of removed uterus and left ovary with fallopian tube. Uterus shows subserosal fibroids. Fig 7 Histopathological slide showing ovarian . endometrial and fallopian epithelium respectively . fig 8 . CECT showing Heterogeneously enhancing mass in left inguinal canal at the level of superficial ring (arrow)which proved to be seminoma in left undescended testis fig 9 CECT showing thick walled cystic lesion speck of calcification showing peripheral enhancement seen in left para vesicle space(arrow) proved to be simple ovarian cyst on histopathology, fig 10 depicting empty left hemi scrotum. Fig 11 USG showing tubular thick walled structure with heterogenous solid lesion with increased colour upatke on doppler with extension into bladder base and into lumen notd in lower one third of the tubular lesion. Fig 12 & 13 , thick walled cystic lesion to the right of bladder showing heterogeneously enhancing soft tissue attenuating lesion invading bladder lumen (fig 13) . Fig 14 contrast MRI T1 W image showing heterogeneously enhancing lesion in above said tubular structure invading into bladder , depicting malignant nature of the lesion with low ADC values (fig 15) . fig 16 MRI. T1 W image showing Multiple iso intense lesions in both the lungs which showed restriction on DWI- suggesting metastasis

DISCUSSION

When the external genitalia do not have the typical anatomic appearance of normal male or female genitalia, the condition is known as ambiguous genitalia. This condition can be caused by various disorders of sexual differentiation or intersex disorders. Not all disorders of sexual differentiation result in ambiguous external genitalia; some disorders can have normal external genitalia (eg, Turner syndrome [45,XO] with female phenotype, Klinefelter syndrome [47,XXY] with male phenotype) (1).

DSDs can be classified on a pathophysiologic basis as disorders of chromosomal, gonadal, or phenotypic sex origin. On the basis of gonadal histologic features, these disorders were originally classified into four broad groups: female pseudohermaphroditism, male pseudohermaphroditism, true hermaphroditism, and gonadal dysgenesis (1).

DSDs have been defined as “congenital conditions in which development of chromosomal, gonadal, or anatomic sex is atypical” (2). Female pseudohermaphrodites (46,XX DSD) have a female genotype and two ovaries for gonads, but their external genitalia show a variable degree of virilization. Male pseudohermaphrodites (46,XY DSD) have a male genotype and two testes for gonads, but their external genitalia show a variable degree of feminization.

True hermaphrodites (ovotesticular DSD) have both testicular and ovarian tissues in the gonads (1).

Ovotesticular DSD (True Hermaphroditism).—The characteristic imaging feature of true hermaphroditism is the presence of an ovotestis or of one testis and one ovary in the same patient. An ovotestis may be seen as a structure with a combination of testicular echo-texture and follicles.

T1- and T2-weighted MR imaging sequences, with their multiplanar capability and superior tissue characterization, can provide detailed anatomic information .

MR imaging is more sensitive than US in the evaluation of the gonads (3) but is still not completely reliable for excluding intraabdominal gonads. Ectopic gonads, testes, and noncystic immature ovaries have intermediate signal intensity on T1-weighted MR images and high signal intensity with an intermediate-signal-intensity outer rim on T2-weighted images (4). Streak gonads are difficult to detect and can be seen as low-signal-intensity stripes on T2-weighted images (5). High-signal-intensity foci in streak gonads could represent neoplastic change (4). Clitoral hypertrophy in XX DSDs can be differentiated from the penis at MR imaging on the basis of absent or poorly developed supporting penile structures such as the bulbospongiosus muscle and posteriorly located transverse perinei muscles (6).

Because 20%–30% of children with XY PGD and 15%–20% with MGD develop a gonadal neoplasm within the 1st or 2nd decade of life, streak gonads should be removed (7). The presence of a well-defined part of the Y chromosome GBY [gonadoblastoma locus on the Y chromosome] is implicated in the development of malignant neoplasms in dysgenetic gonads (8).Gonadoblastoma is the most common tumor, usually arising from dysgeneticintraabdominal gonads (1), and is considered to be a precursor to the development of type II germ cell tumors seen in these patients. Type II germ cell tumors include (a)seminomatoustumors such as seminoma and dysgerminoma, and (b)nonseminomatoustumors such as embryonal carcinoma and choriocarcinoma. The presence of an echogenic focus at US associated with the pelvic organs or found in ectopic gonadal tissue within the inguinal canals or labioscrotal folds should be regarded with suspicion, since gonadoblastomas often calcify. There is increased risk of developing Wilmstumor, particularly when XY gonadal dysgenesis is associated with glomerulopathy in Drash syndrome. Screening for Wilmstumor with renal US every 6 months to 1 year up to school age has been recommended in children with dysgenetic gonads(9).

CONCLUSION:

A child with ambiguous genitalia should be evaluated by a multidisciplinary team using a coordinated approach to arrive at a timely diagnosis so that proper gender assignment can be made early in life. Imaging plays an important role in demonstrating the anatomy and potential effects on other organs. US is the preferred noninvasive modality for initial evaluation. MR imaging can be used when US fails to localise gonads in ectopic sites with better soft tissue resolution. Ectopic gonads are prone for malignant changes more than normal gonad. So early diagnosis of such tumors will increase the life span of patient. A multidisciplinary approach must be established for the patient and family while incorporating the psychosocial aspects also.

Abbreviations: CAH = congenital adrenal hyperplasia; CAI = complete androgen insensitivity; DSD = disorder of sex development; MGD = mixed gonadal dysgenesis; MIS = müllerian inhibiting substance; PGD = pure gonadal dysgenesis
CECT- contrast enhanced computed tomography, NECT- non enhanced computed tomography, FSH – follicular stimulating hormone, LH- luteinizing hormone, ADC – apparent diffusion coefficient, USG – ultrasonography.

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