



Case Report

Incidental inguinal tubercular lymphadenitis in a female of androgen insensitivity syndrome- A rare presentation

Paridhi¹, Shalini Bahadur¹, Madhuvan Gupta¹, Shalini Shukla¹, Shivani Kalhan¹, Deepak Goel¹, Deeksha Singh¹, Vivek Gupta¹

¹Department of Pathology, GIMS, Greater Noida, India

Keywords:

Androgen insensitivity syndrome, Tubercular lymphadenitis, Inguinal tuberculosis, testicular feminization, a disorder of sex development, Ambiguous genitalia

ABSTRACT

Androgen insensitivity syndrome is a rare X-linked recessive disorder occurring in phenotypic women with a male genotype (46, XY) resulting due to mutation in the X chromosome. On the other hand, tuberculosis is a chronic granulomatous infection caused by *Mycobacterium tuberculosis*, an acid-fast bacillus. We report a case of a 22-year-old unmarried female presenting with bilateral inguinal pain and primary amenorrhea, which, on a comprehensive evaluation, revealed complete female external genitalia and intra-abdominal testes. The karyotype was 46 XY, hence a diagnosis of complete Androgen insensitivity syndrome was made. One of the 'probable testes' removed surgically was an inguinal lymph node with tuberculous lymphadenitis. Isolated inguinal tuberculous lymphadenopathy, by itself, is rare. The co-occurrence of complete Androgen insensitivity syndrome and inguinal tuberculous lymphadenopathy is a highly unusual and rare association that has not been documented in the literature reviewed.

Correspondence:

Dr. Madhuvan Gupta, MD

Department of Pathology

Government Institute of Medical Sciences, Greater Noida

ORCID ID: 0000-0002-7896-7823

Email: drmadhuvangupta@gmail.com

Received : January 14, 2023; Accepted : March 22, 2023

Citation: Paridhi, Bahadur S, Gupta M, et al. Incidental inguinal tubercular lymphadenitis in a female of androgen insensitivity syndrome- A rare presentation. J Pathol Nep. 2023; 13(1):2022-5. DOI: 10.3126/jpn.v13i1.51477

Copyright: This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



INTRODUCTION

Androgen insensitivity syndrome (AIS), alternatively known as testicular feminization (TF) is a rare condition with an incidence of 1 in 20,000-64,000 male births. It is associated with a mutation on Xq11-12 for the human androgen receptor, leading to insensitivity of the receptor to testosterone, due to the failure of androgen to bind to its receptor. Patients are usually phenotypic women or young girls with testes.^{1,2} The term TF was earlier coined for this entity, which is a misnomer. The terms TF and AIS are interchangeably used. AIS can be partial (PAIS) or complete (CAIS). Partial AIS (PAIS) patients show a variable degree

DOI : 10.3126/jpn.v13i1.51477

of masculinization phenotypically with partial androgen response. CAIS patients, on the other hand, have normal development of breast and external genitalia with sparse to absent axillary and pubic hair, presence of vagina, and absence of uterus because of normal anti-müllerian hormone action.³ In these cases, an integrated approach with detailed history and clinical examination supplemented by imaging, hormonal assays, karyotyping, and gonadal biopsy is necessary to arrive at a conclusive diagnosis.⁴

Tuberculosis (TB) continues to be rampant in the Indian subcontinent despite concerted efforts under National Tuberculosis Elimination Programme. Infection by *Mycobacterium tuberculosis* leads to chronic granulomatous infection in the lungs and extra-pulmonary organs.⁵ Among the extra-pulmonary organs infected by *Mycobacterium tuberculosis*, lymph nodes are the most common. Further, the cervical group of lymph nodes is the most commonly infected lymph node. Tuberculous lymphadenitis is, however, rarely seen in inguinal lymph nodes.⁶ Also, when involved, they are associated with scrofuloderma or lupus vulgaris. Primary, isolated inguinal lymphadenopathy with no association with scrofuloderma or lupus vulgaris is an extremely rare presentation of tuberculous lymphadenitis.⁷

CASE REPORT

A 22-year-old unmarried woman presented in the surgery clinic with complaints of recurrent bilateral inguinal pain and primary amenorrhea. She had no significant past history.

There was no family history of any major illness including tuberculosis. On examination, the patient had well-developed breasts with sparse axillary and pubic hair. Local examination showed normal appearing external genitalia, urinary meatus, and hypoplastic labia. A 3 to 4-centimeter-long vagina with normal rugae was identified on per speculum examination. The cervix, however, could not be visualized. A per rectal examination, as well as ultrasonography (USG), failed to detect the uterus and adnexa (fig 1a). A preliminary diagnosis of ambiguous genitalia was arrived at. Routine blood investigations including Complete Blood Count, Liver Function Test, and Kidney Function test were within normal limits, except for mildly raised ESR. The patient was advised Magnetic Resonance Imaging (MRI) along with Luteinising hormone (LH) and follicle-stimulating hormone (FSH) levels.

MRI confirmed the absence of a uterus and adnexa. Ovoid hyperintense lesions of approximately 40 x 25 mm in size were identified in bilateral inguinal regions on T2 weighted imaging. These were reported as undescended testes. LH and FSH levels were 27.10mIU/ml (1.9 - 12.5mIU/ml) and 8.4mIU/ml (2.5 - 10.2mIU/ml) respectively. Karyotyping was performed thereafter, revealing a normal 46 XY karyotype and confirming the clinical suspicion of complete androgen insensitivity syndrome. The patient, who had been raised a female, was counseled along with her parents, and the removal of bilateral testes was recommended. A bilateral orchidectomy was performed and surgical specimens were submitted for histopathology.

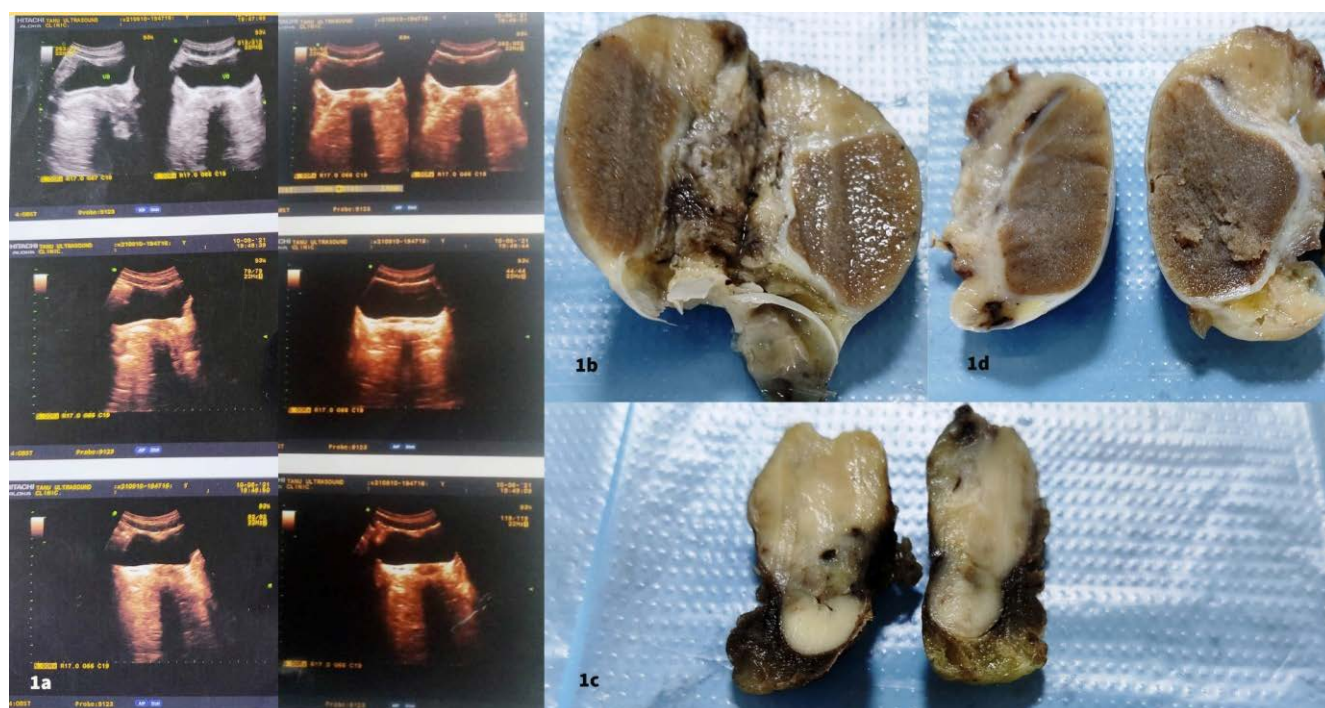


Figure 1a: USG of the patient showing absent uterus and adnexae. **1b:** Gross specimen of left testis showing normal appearing testicular tissue on the cut surface. **1c:** Tissue submitted as right testis with homogenous grey-white cut surface. **1d:** Gross specimen of right testis and showing normal appearing testicular tissue on the cut surface.

The gross specimen of the left testis received was greyish white to brown, measuring 4.5 X 3 X 2 cm, and showed normal appearing testicular tissue on the cut surface (fig 1b). Histologically, atrophic seminiferous tubules with thickened basement membranes showing few germ cells in varying stages of maturation were identified. There was interstitial fibrosis and Leydig cell hyperplasia (fig. 2c). The tissue submitted as the right testis measured 3 X 1.5 X 1.2 cm, & had a homogenous grey-white cut surface (fig. 1c). Micro-sections displayed lymph nodes with effaced architecture and caseating granulomas with Langhan's giant

cells. Ziehl-Neelsen stain confirmed the presence of acid-fast bacilli (fig 2a, 2b). Since the second testis was not found on histopathological examination, a second exploratory laparotomy was performed subsequently and the right intra-abdominal testis was removed (fig. 1d). This, on histopathological examination, revealed atrophic testis with similar morphology as previously excised testis (fig. 2d). A diagnosis of atrophic bilateral testes with right inguinal tuberculous lymphadenitis was rendered in this patient of complete androgen insensitivity syndrome.

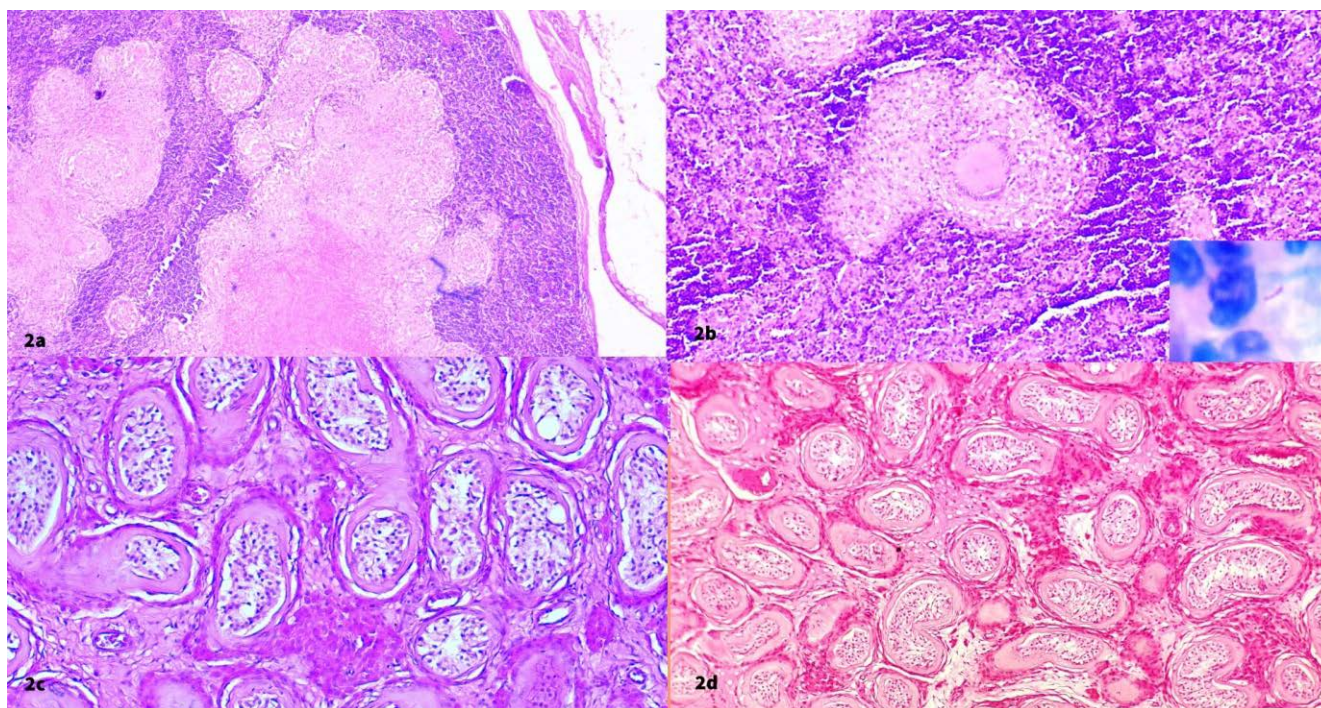


Figure 2: **2a:** HPE of lymph node showing effaced architecture and caseous necrosis (HE stain, 100X). **2b:** HPE of lymph node showing caseating epithelioid cell granulomas (400x, H&E). Inset showing acid-fast bacteria (HE stain, 1000X). **2c:** HPE of left testis showing atrophic seminiferous tubules with thickened basement membrane and Leydig cell hyperplasia (HE stain, 400X). and **2d:** HPE of right testis showing similar morphology as left testis (HE stain, 400X)

DISCUSSION

Significant progress in the understanding of AIS has been made since the 1950s, beginning with the work of Lawson Wilkins.⁸ This disorder has been linked to mutations in the gene for the human androgen receptor, located at Xq11-12, leading to the insensitivity of the receptor to testosterone.² The patient presents with a wide spectrum of phenotypic appearances/ clinical manifestations ranging from well-developed external genitalia with female phenotype in CAIS to ambiguous genitalia with variable phenotype in PAIS.⁹

The patient under discussion had primary amenorrhea till 22 years of age. Primary amenorrhea is the failure to attain menarche by 16 years of age, in the presence of normal growth and secondary sexual characteristics. The relative prevalence of causes of primary amenorrhea is hypogonadotropic-hypogonadism (48.5% of cases),

hypogonadotropic-hypogonadism (27.8%), and eugonadal (pubertal delay with normal gonadotropins; 23.7%). Androgen insensitivity is a rare etiological factor leading to primary amenorrhea (1.5% of cases).²

In cases of undescended testes, bilateral orchidectomy is done to remove the intra-abdominal testes, to ameliorate the risk of malignant transformation.¹⁰ The malignant tumors commonly associated with this syndrome are seminomas and gonadoblastomas, although other histological types such as teratomas, choriocarcinomas, yolk sac tumors, and embryonal carcinomas may also be present. On the other hand, benign tumors such as Leydig cell, and/or Sertoli cell tumors and Sertoli- Leydig cell hamartomas may also be associated with undescended testes.^{11,12} Literature documents that half of the patients not undergoing orchidectomy subsequently develop invasive tumor within five years of diagnosis.¹²

Successful management of patients with CAIS necessitates a comprehensive approach including counseling, gonadectomy, and estrogen replacement. Gonadectomy is best delayed until after puberty as pubertal development proceeds smoothly in response to endogenous hormonal production. Once the testes have been removed, estrogen needs to be supplemented in order to maintain femininity.² In the present case, gonadectomy was performed in early adulthood following incidental diagnosis, and estrogen replacement therapy was started subsequently.

Inguinal lymphadenopathy necessitates investigation for underlying pathology if the diameter exceeds one cm. Infections are the most common cause of localized lymphadenopathy and, in the inguinal region, it commonly occurs because of sexually transmitted diseases (herpes simplex virus, gonococcal infection, syphilis, chancroid, granuloma inguinale, and lymphogranuloma venereum). TB is a rare cause of inguinal lymphadenopathy. Malignancies like Hodgkin's disease, non-Hodgkin's lymphoma, melanoma, and squamous cell carcinoma of the penis, vulva, and anus can also cause inguinal lymphadenopathy, albeit less commonly.¹³

Tuberculous lymphadenitis is the most common extrapulmonary manifestation of TB; comprising 30–50% of all the cases of tuberculosis. Out of these, 57 % of cases involve cervical, 26 % supraclavicular, 12 % axillary, and 3% submandibular lymph nodes. Isolated inguinal tuberculous lymphadenitis is rare, accounting for 4-8 % of tuberculous lymph nodes.^{6,14} Further, tuberculous infection of the inguinal lymph node is usually associated with cutaneous TB (scrofuloderma or lupus vulgaris). Primary or isolated inguinal lymphadenopathy without such association is an extremely rare presentation.¹⁵

CONCLUSIONS

Among the spectrum of disorders causing ambiguous genitalia, CAIS is a rare etiology. It requires a concerted, multi-disciplinary approach not only in diagnosis but also in its management. The co-occurrence of isolated inguinal tuberculous lymphadenitis in the present case of CAIS is an extremely rare association and no similar case was found in the literature even after extensive search.

REFERENCES

1. Souhail R, Amine S, Nadia A, Tarik K, Khalid EK, Abdellatif K, Ahmed A. Complete androgen insensitivity syndrome or testicular feminization: review of literature based on a case report. *Pan Afr Med J*. 2016;25:199. [Crossref](#)

2. Rajput, Rajesj & Jain, Deepak & Yadav, Laxminarayan & Yadav, Tekchand. Primary amenorrhoea in a young female- complete androgen insensitivity syndrome: a rare cause. *Indian Journal of Clinical Practice* 2016; 27. 445-47. [Website](#)
3. Lanciotti L, Cofini M, Leonardi A, Bertozzi M, Penta L, Esposito S. Different Clinical Presentations and Management in Complete Androgen Insensitivity Syndrome (CAIS). *Int J Environ Res Public Health*. 2019;16(7):1268. [Crossref](#)
4. Khanna K, Sharma S, Gupta DK. A Clinical Approach to Diagnosis of Ambiguous Genitalia. *J Indian Assoc Pediatr Surg*. 2019;24(3):162-169. [Crossref](#)
5. Bhardwaj AK. Tuberculosis control programme from NTCP to RNTCP to NTEP. *Indian J Comm Health*. 2020;32(3):469-70. [Website](#)
6. Vagholkar, Ketan et al. Isolated tuberculous inguinal lymphadenopathy: a diagnostic challenge. *International Journal of Research in Medical Sciences* 2014;4(1):1251-[Crossref](#)
7. Khan AS, Bakhshi G, Ellur S, Bhosikar N, Jagtap J, Kaura T. Primary kochs inguinal lymphadenopathy presenting as a mass. *Bombay Hospital Journal*. 2009. [Website](#)
8. Hughes IA, Deeb A. Androgen resistance. *Best Pract Res Clin Endocrinol Metab*, 2006, 20(4):577-98. [Crossref](#)
9. Balducci R, Ghirri P, Brown TR, Bradford S, Boldrini A, Boscherini B, Sciarra F, Toscano V. A clinician looks at androgen resistance. *Steroids*. 1996;61(4): 205-11. [Crossref](#)
10. Gîngu C, Dick A, Pătrășcoiu S, Domnișor L, Mihai M, Hârza M, Sinescu I. Testicular feminization: complete androgen insensitivity syndrome. Discussions based on a case report. *Rom J Morphol Embryol*. 2014;55(1):177-81. [Website](#)
11. Kravarusic D, Segulier-Lipszyc E, Feigin E, Nimri R, Nagelberg N, Freud E. Androgen insensitivity syndrome: risk of malignancy and timing of surgery in a paediatric and adolescent population. *Afr J Paediatr Surg*. 2011;8(2):194-8. [Crossref](#)
12. de Souza RF, Pereira da Silva J, Vieira Balla B, Neves Ferreira R, ChambôFilho A. Bilateral Sertoli Cell Tumors in a Patient with Androgen Insensitivity Syndrome. *Case Reports in Obstetrics and Gynecology*. 2017, 8357235. [Crossref](#)
13. Mohseni S, Shojaiefard A, Khorgami Z, Alinejad S, Ghorbani A, Ghafouri A. Peripheral lymphadenopathy: approach and diagnostic tools. *Iran J Med Sci*. 2014 ;39(2 Suppl):158-70. [Website](#)
14. Ramirez I. Isolated, Unilateral Inguinal Tuberculous Lymphadenitis. *Am J Trop Med Hyg*. 2019;100(4):770-771. [Crossref](#)
15. A Dayal, S Pai, K Shenoy, P Kansakar, A Kannan, Y Sharma, G Rodrigues, S Khan. Isolated Primary Tuberculosis Of Inguinal Lymph Nodes: An Acute Presentation. *The Internet Journal of Surgery*. 2007;14(1). [Website](#)