CASE REPORT

Leydig cell hyperplasia in the setting of Klinefelter syndrome

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SUMMARY

A man in his 20's with Klinefelter syndrome presented to the urology clinic with a recent history of left-sided orchalgia. Ultrasound evaluation demonstrated multiple small hypoechoic lesions bilaterally, with the largest lesion measured at 5 mm×6 mm×8 mm. Testis cancer tumour markers, chest radiographs and abdominal CT imaging were negative. A partial orchiectomy was performed on the largest lesion, demonstrating the presence of Leydig cell hyperplasia.

BACKGROUND

Klinefelter syndrome is the most frequent sex chromosome disorder in males. It results from the presence of an extra X chromosome (47, XXY). Previous case reports and case series have demonstrated extragonadal germ cell tumours, testicular germ cell tumors and Leydig cell hyperplasia.^{1–3} Few such reports, however, have described the radiographical findings seen in Leydig cell hyperplasia.

CASE PRESENTATION

A man in his 20's presented to the urology clinic with a history of left-sided orchalgia. Physical examination demonstrated bilaterally small testes. With the differential diagnosis including Klinefelter syndrome, a karyotype was assessed, confirming the diagnosis. A testis ultrasound demonstrated multiple, hypoechoic lesions with internal flow. The largest lesions measured 5 mm×6 mm×8 mm (figure 1). An MRI of the scrotum was also performed, confirming the presence of these lesions (figure 2). Serum tumour markers for testis cancer (β-human chorionic gonadotropin, α-fetoprotein, lactate dehydrogenase) were assessed and were negative. Luteinising hormone and testosterone were obtained and were within normal limits.

After counselling the patient on his options, he elected for a partial orchiectomy, understanding that without tissue confirmation, a malignant process could not be ruled out definitively. Intraoperative ultrasound was utilised to identify the dominant lesion as it was non-palpable. Frozen section demonstrated Leydig cell hyperplasia. This was subsequently confirmed on permanent section. Based on the frozen section findings, the decision to perform a partial, rather than radical, orchiectomy was made given the benign nature of this condition.

INVESTIGATIONS

In this case, the key investigations were the testis ultrasound, the serum tumour markers and the intraoperative frozen section. The ultrasound

demonstrated multiple bilateral lesions, which in the setting of Klinefelter syndrome, may lead one to consider Leydig cell hyperplasia more likely than a malignancy. This is further confirmed by the absence of tumour marker elevation. In this patient's case, an MRI was ordered on the recommendation of the radiology service, but in retrospect, did not play a crucial role in decision-making.

DIFFERENTIAL DIAGNOSIS

The evaluation of hypoechoic testis lesions demonstrated on ultrasound should always consider germ cell tumours and stromal tumours such as Leydig cell tumours. Leydig cell hyperplasia can also be considered, particularly in the setting of Klinefelter syndrome. In addition to negative serum tumour markers, the presence of multiple small lesions, particularly if bilateral, should direct one to consider Leydig cell hyperplasia. Negative serum tumour markers do not rule out malignancy, so the overall clinical picture must be considered. A chest radiograph and CT scan of the abdomen and pelvis are appropriate to rule out metastatic disease. The distinction between Leydig cell tumours and Leydig cell hyperplasia can be made histologically. Depending on the patient's age and history, lymphoma and granulomatous disease should also be considered.

TREATMENT

If the patient is amenable to observation, a patient with Klinefelter syndrome and multiple bilateral testis lesions does not require tissue confirmation

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Figure 1 Axial T2 MRI of left testicle.

Figure 2 Testicular ultrasound showing testicle with multiple hypoechoic lesions.

provided tumour markers are negative and there is no other evidence of malignancy. If the patient or clinician is not comfortable with observation, tissue diagnosis should be obtained via a partial orchiectomy with frozen section. If malignancy is identified on frozen section, completion radical orchiectomy should be performed at that time.

OUTCOME AND FOLLOW-UP

The patient did well postoperatively and his orchalgia has resolved. He will undergo periodic physical examination and ultrasound surveillance of his testes.

DISCUSSION

The testicular histology in Klinefelter syndrome has been noted to be fairly normal through childhood, with histology becoming

increasingly abnormal with age.¹ Adults have been described as having very large areas of Leydig cell hyperplasia.¹ The ultrasonographic appearance of Leydig cell hyperplasia has been described as multiple small hypoechoic, hypervascular lesions.² In addition to malignant germ cell tumours, malignant Leydig cell tumours should be included in the differential diagnosis.³

Learning points

- Leydig cell hyperplasia should be considered in Klinefelter syndrome patients with multiple small testis lesions on ultrasound.
- Malignant germ cell tumour and malignant Leydig cell tumour should be considered in the differential diagnosis.
- Partial orchiectomy with frozen section can allow for testis-sparing surgery.

Competing interests None declared.

Patient consent Obtained.

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