CASE REPORT

One lump or two? Concomitant Leydig cell tumour and paratesticular leiomyoma in an adult man

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SUMMARY

We present the first reported case of a concomitant Leydig cell tumour (LCT) and paratesticular leiomyoma in an adult man with a history of bilateral cryptorchidism. An 80-year-old man presented with a 2-month history of a left testicular lump associated with mild discomfort and a gradual increase in size on a background of bilateral cryptorchidism requiring multiple orchidopexy procedures as a child. Ultrasound confirmed a lesion suspicious for malignancy and he proceeded to a left radical orchidectomy. Histopathological assessment of the left testis revealed a concomitant testicular LCT with rare malignant features and paratesticular leiomyoma.

BACKGROUND

Genetic studies have identified potential mutations that could potentially cause Leydig cell tumours (LCTs) but there are no known associations between concomitant LCTs and paratesticular tumours. The presence of cryptorchidism in adults with LCTs and paratesticular neoplasms individually has been previously reported and it appears intuitive that cryptorchidism is likely to be associated with this concomitant presentation.

This report represents the first documented case in the literature of a unilateral concomitant LCT and paratesticular leiomyoma on a background of bilateral cryptorchidism.

CASE PRESENTATION

An 80-year-old man presented with a 2-month history of a left testicular lump associated with mild discomfort and a gradual increase in size. He had a history of bilateral cryptorchidism requiring multiple orchidopexy procedures culminating in fixing the left testis to the inner thigh which was subsequently released.

On physical examination, he had a firm mass felt in the left testis and atrophy of the right testicle. His tumour markers were negative for malignancy.

A left radical orchidectomy was subsequently performed. The histopathology of the left testis revealed concomitant unilateral testicular LCT and paratesticular leiomyoma.

INVESTIGATIONS

Ultrasound examination noted the left testis to be larger than the right and containing several solid masses, the largest measuring 14 mm in diameter. There was associated increased vascularity in the left testis as well as large septated epididymal cysts, but no increased vascularity in the epididymis. The

right testis had a heterogeneous echotexture with no increased blood flow.

Histology reported a testis measuring 50×45×45 mm showing a nodular protuberance that extended from its posterior aspect measuring 25×25×20 mm. On gross examination there was a diffusely haemorrhagic testicular parenchyma and a separate, well-defined, paratesticular nodule. The separate nodule had a firm, cream-coloured cut surface with a whorled appearance with no evidence of necrosis or haemorrhage.

Histologically the paratesticular nodule was unencapsulated and composed of thick bundles and sweeping fascicles of cytologically bland spindle cells. The individual tumour cells showed evidence of smooth muscle differentiation, with abundant eosinophilic cytoplasm, poorly defined cell borders and plump cigar-shaped nuclei. There was no necrosis or cytological atypia and no mitotic activity was observed. The features were classical of a leiomyoma.

The remaining testis showed a well-vascularised tumour comprising nests of eosinophilic tumour cells with well-defined cell borders. The tumour measured 50 mm in maximal dimension demonstrating extracapsular extension and lymphovascular invasion. The cells had round, centrally placed nuclei and prominent nucleoli, suggesting Leydig cell origin but did also demonstrate mitotic figures. Immunohistochemistry showed strong positive staining with inhibin and a complete lack of staining for CD-117 confirming a diagnosis of an LCT with potential malignant behaviour.

OUTCOME AND FOLLOW-UP

A left radical orchidectomy was performed. The histopathology of the left testis revealed concomitant unilateral testicular LCT and paratesticular leiomyoma.

DISCUSSION

LCTs are the most common pure testicular sex cord-stromal tumours, accounting for up to 3% of all testicular tumours.¹ They can occur at almost any age, but are noted to have a bi-modal distribution, with a peak incidence at 6–10 and 20–50 years of age.²

Clinical presentation can be quite varied but testicular swelling is noted in about 40% of patients.³ In children, LCTs are often hormonally active resulting in isosexual precocious puberty and its associated symptoms of deepening of the voice and advanced bone age. Less common presentations include feminising or virilising syndromes as a result of increased production of oestrogens and/or androgens.^{4 5}

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Paratesticular tumours are uncommon and their reported prevalence varies between 3% and 16%.⁶ They occur in a complex anatomical area which includes the contents of the spermatic cord, testicular tunics, epididymis and vestigial remnants.⁷ Up to 90% of paratesticular tumours are believed to originate from the spermatic cord, although it is often difficult to definitively ascertain the exact site of origin.⁸ Although any type of soft-tissue neoplasm can be found in the paratesticular region, the most common benign tumours are lipomas, adenomatoid tumours and leiomyomas.⁹

Clinically, paratesticular tumours are nearly always indistinguishable from testicular tumours, and can present as a painful or painless mass or swelling that is sometimes associated with a hydrocele.

Currently, the majority of testicular and paratesticular tumours are diagnosed by ultrasonography but increasingly MRI is being used. MRI can detect small non-palpable LCTs otherwise not visible on ultrasonography.¹⁰ On ultrasonography, LCTs usually appear as a non-homogeneous hypoechoic testicular nodule with peripheral hypervascularity and minimal internal colour Doppler flow.¹¹ On MRI, LCTs are best observed on T₂-weighted images. On T₁-weighted precontrast images, the tumours have a signal similar to the rest of the testicular parenchyma but can still show significant homogeneous enhancement that permits observation of the morphology, size and location of the tumour. On T₂-weighted images, the tumours exhibit low signal intensity and are partially surrounded by a line of high signal intensity, which allows much clearer visualisation from the surrounding structures.¹²

The imaging modality of choice for the diagnosis of paratesticular tumours is high-resolution scrotal ultrasonography. Benign tumours are hyperechoic and homogeneous while malignant neoplasms can appear either homogeneously hypoechoic or have a heterogenous pattern involving hypoechoic and hyperechoic areas. Similar to LCTs, MRI has the potential to provide greater detail in terms of better defining the exact location of the neoplasm and how it relates to the different paratesticular structures, which might not be routinely possible with ultrasonography.^{11 12}

LCTs are usually unilateral and solitary, with only about 3% of LCTs found to be bilateral. While cryptorchidism is a well-established epidemiological risk factor for testicular germ cell tumours, LCTs usually arise in normally descended testes.^{1 2 13} Testicular tumour markers including serum α -fetoprotein, β -human chorionic gonadotropin and lactate dehydrogenase are invariably within normal limits.

LCTs in adults are infrequently associated with cryptorchidism. Of the 480 LCTs reported in the literature only 20 are reported to be associated with either unilateral or bilateral cryptorchidism.¹⁴ One case of bilateral LCT with unilateral cryptorchidism and a further case of unilateral LCT with contralateral cryptorchidism has been documented in the literature.^{15 16}

Carmignani *et al*'s¹³ report of 24 patients found that 41.7% of LCTs in adults were diagnosed incidentally on ultrasonography, 29.2% were palpated on clinical examination, 16.6% presented symptomatically with testicular pain, 12.5% with gynecomastia and less commonly with impotence and loss of libido. Overall, endocrinopathy was present in about 30% of cases with assays demonstrating varying levels of steroid secretion, elevated serum oestradiol and/or testosterone levels especially when feminisation was present. Urine and serum endocrinological tests including urine ketosteroids, plasma cortisol or the dexamethasone suppression test may help differentiate LCTs from other adrenocortical disorders.^{9 17-19}

Generally, LCTs present as a well-circumscribed mass that does not show significant necrosis or cytological atypia. The edge of the lesion is typically non-infiltrative but in rare cases extratesticular extension can occur in an otherwise benign lesion. Mitotic figures are, at most, infrequent.^{20 21}

The vast majority of LCTs pursue a benign clinical course. However, these tumours do hold the potential for malignant clinical behaviour. Of these, 90% of LCTs are regarded as benign, with only 10% classified as malignant.¹⁵ Case reports have suggested that an LCT with malignant features on histology has a 20% chance of presenting already with metastases and a 40% chance of developing secondary foci within 2 years.¹ The only definite criterion for a diagnosis of malignant LCT is the presence of clinicopathologically proven metastatic spread.^{20 21} Furthermore, malignant spread has only ever been documented as occurring in the adult population.²

Despite the lack of firm criteria for a diagnosis of malignancy in LCT, routine histological examination may reveal features that indicate the potential for these tumours to behave in a malignant fashion. Specifically, tumours of large size (50 mm or more in greatest dimension) and those showing cytological atypia, necrosis, frequent mitotic activity, infiltrative margins and vascular invasion should be regarded with high clinical suspicion.^{20 21} Typically, clinically proven malignant LCTs show at least three of these features.²¹ In the case of our patient, the large size of the tumour, its infiltrative margins and areas of extratesticular spread were accompanied by frequent mitotic figures and focal lymphovascular invasion. Thus, at least four features suggesting the potential for malignant clinical behaviour were observed. This patient therefore remains under ongoing surveillance.

The majority of paratesticular pathologies are usually benign cystic lesions of the epididymis, scrotal fluid collections and inflammatory lesions or hernias. Paratesticular tumours are uncommon with the most common paratesticular neoplasm being benign lipoma of the spermatic cord. In the epididymis, adenomatoid tumours are most commonly seen and usually involve the lower pole.

Although paratesticular tumours are uncommon up to 30% of these may be malignant. The most commonly reported lesions are sarcomas with leiomyosarcoma (32%), rhabdomyosarcoma (24%) and liposarcoma (20%) representing the histological subtypes most frequently seen.^{20 21}

Leiomyoma is the second most common tumour of the epididymis and can be solid or cystic in nature. It is a distinct, mass forming lesion and must be distinguished from a non-neoplastic proliferation of smooth muscle, which can also occur in the paratesticular soft tissues.²² Furthermore, it must be distinguished from its malignant counterpart, leiomyosarcoma. Leiomyosarcoma is the second most common sarcoma of the paratesticular region.²³

The distinction between leiomyoma and leiomyosarcoma chiefly relies on the presence or absence of mitotic activity and nuclear atypia.²³ Rare mitoses, amounting to less than 1 mitotic figure per 50 high-power fields, are acceptable in a leiomyoma of the paratesticular region. The presence of more frequent mitoses should prompt a careful search for nuclear atypia.²⁴ Cytological atypia is typically readily identified within a leiomyosarcoma but areas of subtle or focal atypia may still indicate malignancy.²⁴ In summary, the distinction between the two lesions can be difficult and requires extensive sampling of the lesion and careful histological assessment.

This report represents the first documented case in the literature of a unilateral concomitant LCT and paratesticular

leiomyoma on a background of bilateral cryptorchidism. Genetic studies have identified potential mutations that could potentially cause LCTs but there are no known associations between concomitant LCTs and paratesticular tumours.²⁵ The presence of cryptorchidism in adults with LCTs and paratesticular neoplasms individually has been previously reported and it appears intuitive that cryptorchidism is likely to be associated with concomitant presentation in this case report.

Patient's feedback

This patient was extremely grateful for the clean resection of his tumour, which resulted from early detection by his local doctor, rapid triage and review by the urology department and subsequent uncomplicated surgery. The patient is undergoing regular follow-up and has been very satisfied with the care he has received.

Learning points

- ▶ Despite an increasing role for advanced imaging of testicular masses, the current recommended management remains radical orchidectomy.
- ▶ Cryptorchidism increases risk of testicular cancer even after orchidopexy.
- ▶ Leydig cell tumours (LCTs) can rarely be malignant or exhibit malignant traits requiring close follow-up, such as in this patient.
- ▶ Genetic studies have identified potential mutations that could potentially cause LCTs but there are no known associations between concomitant LCTs and paratesticular tumours.

Contributors All the authors contributed significantly to this article, in research of the background and literature review, review of the case history, pathology research and write-up and to overall editing.

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