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CASE REPORT

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# Testicular leukaemic infiltration in relapsed acute lymphoblastic leukaemia: a case report

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## Abstract

**Background** Although paediatric patients with acute lymphoblastic leukaemia (ALL) have improved survival following modern chemotherapy treatment, disease relapses still occur in 20–25% of them. Our case had relapsed ALL with testicular leukaemic infiltration, which is rare, with less than 2% incidence.

**Case presentation** We describe a case of an 11-year-old boy with a background history of ALL presenting with painless unilateral scrotal swelling. An initial ultrasound of the testes showed heterogeneity throughout with hypervascularity on colour-flow imaging on the affected testis. Some areas are hypoechoic with dilated tubules. The histopathology of the follow-up testicular biopsy revealed malignant cells and leukaemic infiltration. Patient subsequently received chemotherapy treatment at another centre.

**Conclusions** Testicular relapse of ALL is relatively rare with the use of improved contemporary frontline treatment with better outcomes. With its non-specific symptoms, radiological imaging can significantly facilitate timely diagnosis and contribute to appropriate further management and improved prognosis.

**Keywords** Testis leukaemic infiltration, Acute lymphoblastic leukaemia, Case report

## Background

Acute lymphoblastic leukaemia (ALL) accounts for approximately 25% of all childhood cancers and 80% of childhood leukaemia, with a maximal incidence rate between 1 and 6 years [1]. Despite current aggressive frontline treatments, 20–25% of them experience relapses in the form of bone marrow relapse, extramedullary relapse (EMR) and combined relapse (bone marrow and extramedullary) [2]. Possible sites of EMR include central nervous system and testis.

Testicular involvement of ALL usually presents with painless enlargement of the testis. At the time of diagnosis, it occurs in less than 1% of boys [3]. Modern treatment regimens have reduced the incidence of ALL testicular relapse from 6 to 12% in the 1970s to less than 2% since 2000 [3, 4].

Here, we report a rare case of relapsed ALL with biopsy-proven testicular involvement. This case report aims to increase the awareness of potential testicular leukaemic infiltration in patients presenting with acute testicular symptoms with a history of ALL. It also highlights the role of initial radiological imaging and follow-up biopsy in the timely diagnosis of relapsed ALL.

## Case presentation

An 11-year 11-month boy presented to our paediatric urology clinic with painless left scrotal swelling for two weeks. The patient experienced no pain, no fever, no urinary tract infection symptoms, no shortness of breath and had no penile discharge, no history of trauma and no family history of leukaemia or malignancy. The swelling

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was soft to firm in consistency. He had been diagnosed with ALL 6 years earlier in another tertiary hospital. He received chemotherapy treatment based on UKALL protocol and was in remission. The protocol includes systemic administration of cyclophosphamide, cytarabine, steroid, vincristine, mercaptopurine, asparaginase, anthracyclines and intrathecal methotrexate. Prior to presentation, he received a full course of antibiotic from another clinic to treat presumed orchitis.

On physical examination, his left testis appeared to be enlarged and firm, non-tender and no skin discolouration. His right testicle was palpably normal. His lungs were clear to auscultation bilaterally with no crepitations. Chest radiograph was clear. On palpation, his abdomen was symmetric and non-tender without distension. No mass, hepatomegaly or splenomegaly was noted on ultrasound. The patient's routine urinalysis results were normal, and urine culture was negative. Scrotal ultrasound showed that the left testicle was significantly larger than the right, measuring 5.7 cm in length by 1.2 cm anterior–posterior by 2.2 cm transversely. The left testis also showed heterogeneity throughout with hypervascularity on colour-flow imaging. Some areas are hypoechoic with dilated tubules. The epididymis was not swollen. The pampiniform plexus was normal in calibre. The scrotal sac was not thickened. Minimal hydrocele was noted. No septation or sediment in the fluid was seen (Figs. 1, 2 and 3).

Right testis was normal in size, measuring 1.5×1.8×3.0 cm. It was homogenous in appearance with no focal lesions and normal vascularity. The epididymis and pampiniform plexus were normal (Figs. 4, 5). There were no enlarged inguinal nodes bilaterally (Figs. 6, 7). Differential of subacute or chronic torsion was less likely

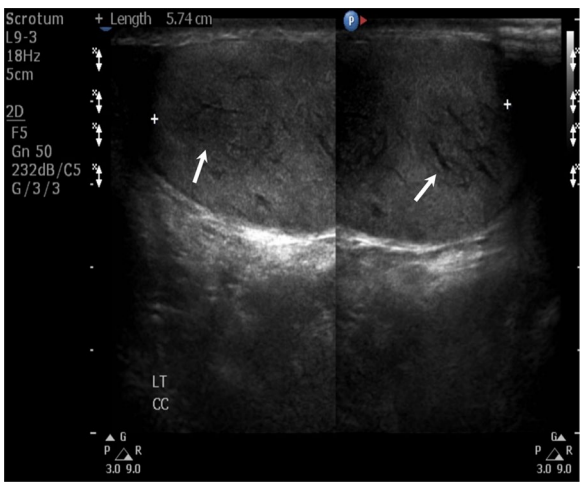


**Fig. 1** Ultrasound (longitudinal view) shows heterogeneous (arrow) and enlarged left testis

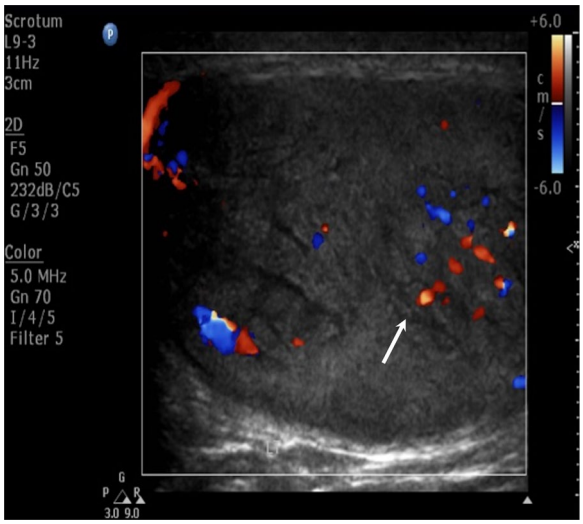


**Fig. 2** Ultrasound of the left testis shows heterogeneity throughout with hypervascularity on colour-flow imaging (arrow)

in view of the absence of pain. With the background history of ALL, leukaemic infiltration was suspected based on the preliminary imaging result.

Excisional testicular biopsy was subsequently performed to confirm testicular leukaemic infiltration. Left testicular lesion macroscopic specimen was labelled as left testicular lesion. Three strips of whitish tissue measuring 10 mm in aggregate length were obtained. Microscopic section shows 3 cores of tissue diffusely infiltrated by small blasts with condense

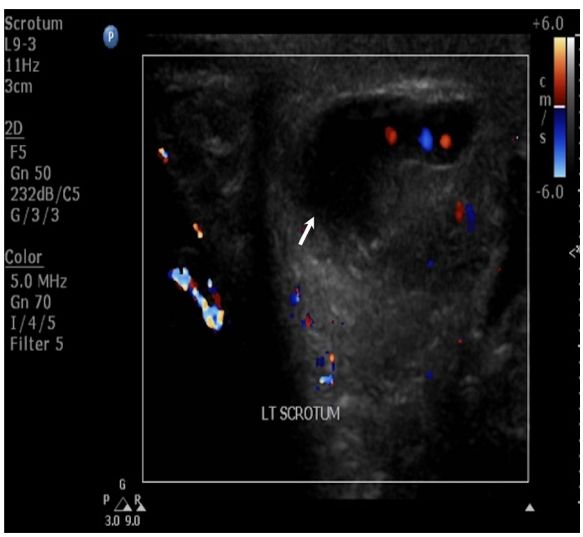


**Fig. 3** Ultrasound of the left scrotum (transverse view) shows minimal hydrocele (arrow). No septation or sediment in the fluid is seen

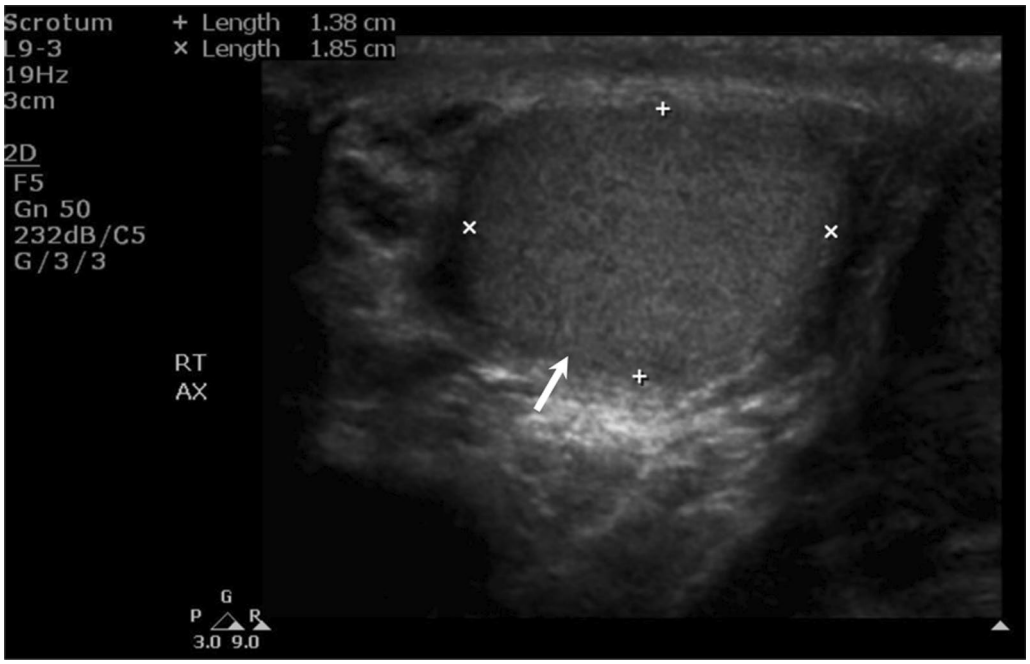


**Fig. 4** Ultrasound (transverse view) of the right testis shows that it is normal in size and homogenous in appearance

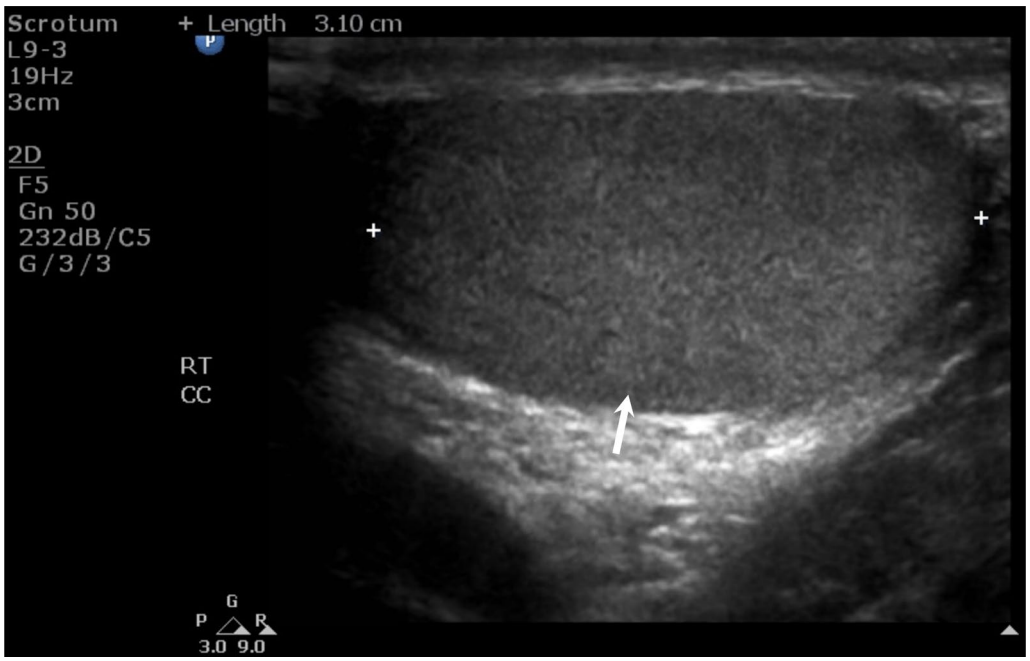


**Fig. 5** Ultrasound (longitudinal view) of the right testis shows that it is normal in size and homogenous in appearance

nuclear chromatin, indistinct nucleoli and scanty cytoplasm, and mitosis is hardly seen. No area of necrosis is observed. Some entrapped seminiferous tubules are present. Immunohistochemically, the blasts are positive for TdT, CD79a and PAX5. They are negative for CD3. The complete blood count upon presentation and the subsequent bone marrow aspirate and trephine biopsy showed no excess blasts or abnormal lymphoid cells. Hence, immunophenotyping by flow cytometry was not carried out for both peripheral blood and bone marrow

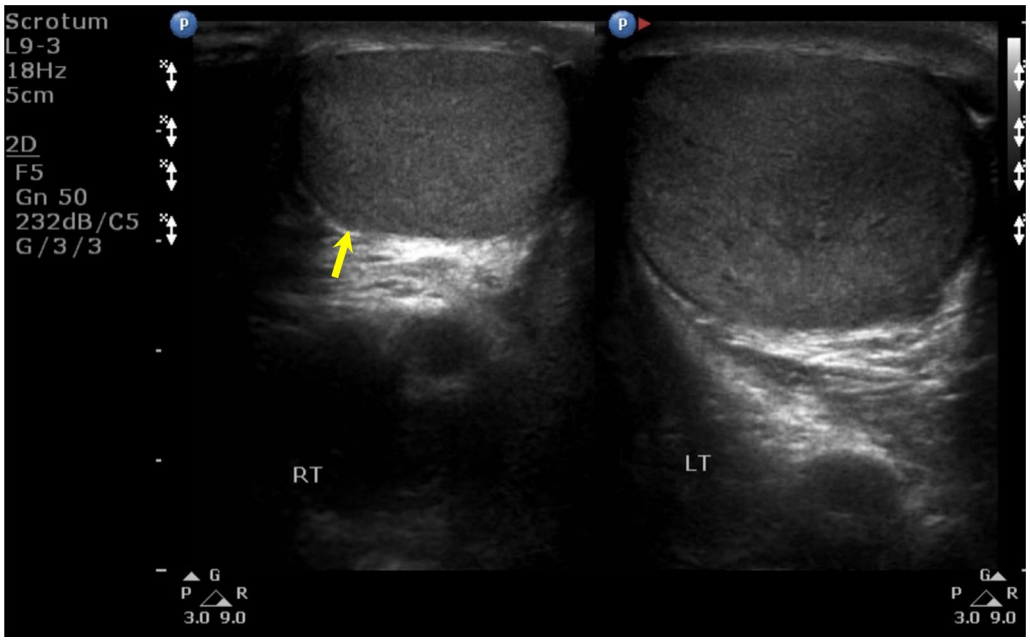


**Fig. 6** Ultrasound (transverse view): Right testis is normal in size and homogenous in appearance (arrow), while left testis is enlarged and heterogeneous

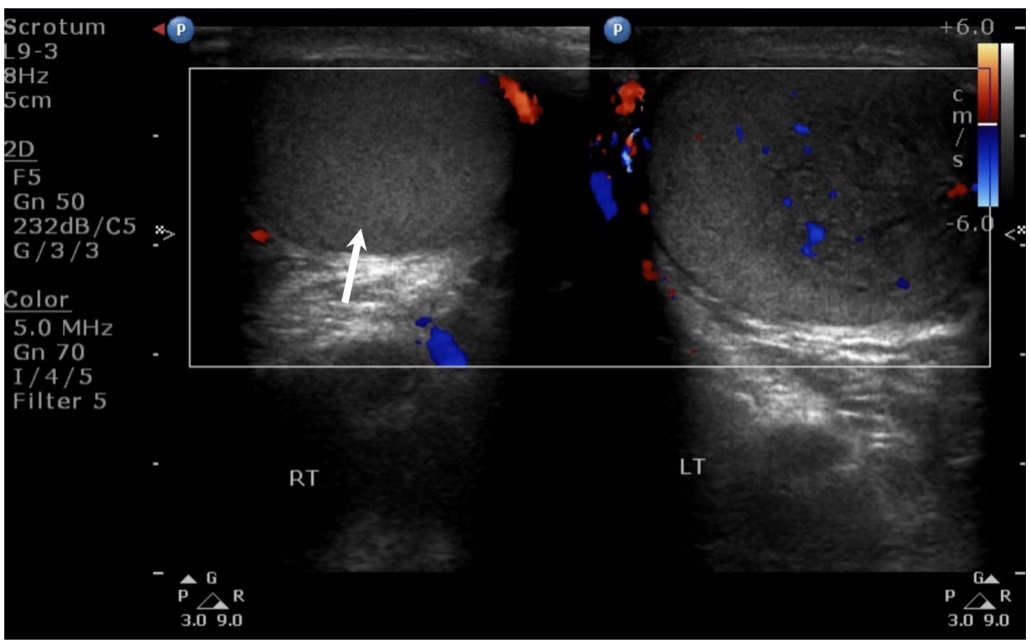


**Fig. 7** Ultrasound shows that the right testis is normal in size, homogenous in appearance and without focal lesions. No abnormal vascularity is seen within (arrow)

samples. There was no evidence of disease relapse at other sites apart from the testis. The final diagnosis was isolated testicular relapse of ALL. Patient returned to his home state for further chemotherapy treatment.

## Discussion

Chemotherapy has limited efficacy on the testicles as certain drugs penetrate the blood-testicular barrier insufficiently. The use of intermediate and high-dose

**Table 1** Differential diagnosis of leukaemic infiltration, subacute/chronic torsion and acute orchitis

| Ultrasound | Leukaemic infiltration | Subacute/chronic torsion | Acute orchitis |
|---|---|---|---|
| Grayscale | Homogenous/heterogeneous | Heterogeneous | Heterogeneous |
| Doppler signal | Increased | Decreased/absent | Increased |
| Scrotal skin swelling | No | No | Yes |
| Hydrocele | Yes | Yes | Yes |

methotrexate within ALL treatment protocols since the 1980s significantly reduced the incidences of testicular relapse [5]. Nevertheless, an EMR may herald a bone marrow relapse within one to twelve months. Therefore, a prompt EMR diagnosis is of paramount importance to improve treatment outcome and prognosis [6].

Based on a study by Mazzu et al., in most of the cases with testes leukaemic infiltration, grayscale sonograms shows either homogeneously hypoechoic testes in patients with diffuse round-cell infiltration or multifocal hypoechoic lesions of various sizes. Colour Doppler sonography revealed increased intralesional flow in all areas of leukaemic involvement irrespective of lesion size [7]. In our case, ultrasound findings were heterogeneous with no focal lesion seen in the enlarged left testis. Hypervascularity was seen on colour-flow imaging.

Although colour Doppler sonography may provide useful information, differentiating infiltration from inflammatory processes of the testes remains difficult. The differential diagnosis for left testicular swelling includes acute orchitis, subacute/chronic torsion and neoplastic disorders as stated in (Table 1). Although 18F FDG PET/CT has shown some usefulness in detecting extramedullary acute leukaemia [8], there is no study to date which investigates its role in detecting testicular leukaemic infiltration.

In our case, symptoms persisted despite an appropriate course of antibiotics, therefore orchitis could be ruled out. The testicular lesion is hence highly suspicious of testis leukaemic infiltration in view of a background of ALL, no improvement after antibiotic treatment and presence of enlarged testis. As such, a testicular biopsy was carried out to confirm the diagnosis of leukaemic infiltrations of testis.

Currently, routine testicular biopsy for ALL monitoring has become obsolete with the emergence of modern chemotherapy regimen. In selected high-risk patients, frequent and detailed testicular examination including the evaluation of their size and hardness are still warranted to detect disease relapse. Risk factors for EMR in ALL include male sex, age < 1 year or 10 years at diagnosis, cytogenic abnormalities such as t(9; 22), WBC count of > 50,000/L and T-cell lineage [6]. Identification of testicular involvement with or without concurrent bone marrow relapse can alter management in terms of choice and intensity of chemotherapy regimens, the addition of testicular radiotherapy or orchiectomy and the employment of immunotherapy [9, 10].

This case report highlights the combined role of clinical, radiological and histopathological findings in clinical suspicion of testicular involvement in male patients with a history of ALL. Testicular biopsy following abnormal ultrasonographic findings helps to confirm the rare leukaemic testicular involvement. Even though the definitive treatment plan and outcome for this patient was not obtained as patient did not proceed with treatment at our centre, this case report emphasizes the role of prompt radiological investigation in guiding timely diagnosis and definitive treatment.

## Conclusions

Despite decreased incidence of testicular relapse of ALL with contemporary treatment, a high index of suspicion must be maintained in patients with a history of ALL presenting with testicular symptoms or complaints. The most frequent sonographic appearance of leukaemic infiltration is diffuse heterogeneous enlargement with hypoechogenicity. Hypervascularity is typical. Testicular biopsy confirms the diagnosis and guides further management.

### Abbreviations

ALL Acute lymphoblastic leukaemia
EMR Extramedullary relapse

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Not applicable.

### Author contributions

AQQ was involved in conceptualization and original draft preparation. JA and SWYT reviewed and edited the manuscript. HAH supervised the study. All authors contributed to the article and approved the submitted version.

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### Availability of data and materials

All data generated or analysed during this study are included in this published article.

## Declarations

**Ethics approval and consent to participate**
Ethics approval was waived by the hospital's ethics committee for single patient case report. Written informed consent for publication was obtained from the patient. Only anonymized data and images were used.

**Consent for publication**
Written informed consent was obtained from the patient for the publication, and only anonymized data and images were used.

**Competing interests**
The authors declare that they have no competing interests.

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## Publisher's Note