A case of Acute Lymphoblastic Leukemia presenting with Macroorchidism in a fourteen-year-old boy: A rare presentation

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Citation

Abstract
Macroorchidism refers to having abnormally large testes (usually greater than 95th percentile for age) commonly attributed with Fragile X syndrome. Here is discussed a case of a fourteen year old boy who came to us with complaints of mildly painful testicular swelling whose investigations revealed something very surprising.

FINANCIAL DISCLOSURE
The cost of all investigations done for the patient was borne by the West Bengal State Government as a scheme to supply free healthcare to the financially less privileged.

INTRODUCTION
The differential diagnoses of a patient with bilaterally symmetrically enlarged testes are:

- Lymphomas,
- Relapse of Acute Lymphoblastic Leukemia (ALL),
- Familial Gonadotrophin independent isosexual precocity (testotoxicosis) which is self-limited autosomal recessive disorder1. It occurs due to gain of function mutation of Leutinising Hormone (LH) receptor of testis .
- Tumors secreting Human Chorionic Gonadotropin, as in hepatomas, hepatoblastomas, teratomas.
- McCune Albright syndrome. It is characterized by sexual precocity, café au lait spots and fibrous dysplasia. It occurs due to gain of function mutation of Gsβ (G protein stimulatory subunit β).
- Inadequately treated congenital adrenal hyperplasia (CAH) due to 11-hydroxylase or 21-hydroxylase deficiency.

Here is illustrated a case of Bilateral enlargement of testis fitting with a diagnosis of macroorchidism.

CASE REPORT
A fourteen-year-old boy who came to us with the following complaints:

Fatigue for four months.
Gradually progressive mildly painful swelling of both testes.
Swelling of both breasts for three months.
He also had a history of three units of blood transfusion four months back.
Investigations done at that time were unrevealing as to the cause of anemia.
He also noted a small lump on his neck about three months back that has also grown in size.
There is no history of lump anywhere else, fever, weight loss, anorexia, skin rash, joint pain, sore throat, bone pain, recurrent infections, bleeding per rectum or any other site of the body, previous history of blood transfusion, drug abuse, chronic drug use for any other problem, unsafe sexual practices.
He has nocturnal penile erections and masturbates regularly.
No other family members have similar history. He is the only child of his parents.
A case of Acute Lymphoblastic Leukemia presenting with Macroorchidism in a fourteen-year-old boy: A rare presentation

ON EXAMINATION

He was 56 inches tall, of average build with no obvious abnormality than those given below. He had bilateral testicular enlargement about 30ml in volume each (mean for boy of fourteen years is 8ml and 95th percentile corresponds to 15 ml). The testis were firm to hard in consistency, mildly tender, warm and one could get above the testicular swellings.

Transillumination test was negative and the scrotal skin was normal.

His sexual maturity was Tanner's stage 3, with mild gynaecomastia.

His Stretched Penile Length was approximately 10 cms.

He had a firm left submandibular gland swelling which was free, non-tender with free overlying skin.

There was mild pallor, temperature was normal and other parts of the examination were normal. He had mild sternal tenderness. His Intelligence quotient was tested by Stanford-Binet scale and found to be average.

INVESTIGATIONS

Routine investigation & Hormonal assessment:
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Figure 3

<table>
<thead>
<tr>
<th>Hormones and Testosterone levels</th>
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<tr>
<td>Follicle stimulating Hormone (FSH) - 8.01mIU/ml</td>
</tr>
<tr>
<td>Luteinising Hormone (LH) - 7.0mIU/ml</td>
</tr>
<tr>
<td>Serum Free Testosterone - 4.74ng/ml (normal adult levels)</td>
</tr>
</tbody>
</table>

FNAC report showed-hypercellular marrow with suppressed granulopoiesis and lymphopoiesis, few megakaryocytes and plasma cells.

More than 90% of the marrow consisted of nonerythroid lymphoblastsoplasmablasts.

Trephine biopsy revealed markedly hypercellular marrow due to diffuse infiltration by immature mononuclear cells having fine nuclear chromatins, prominent nucleoli and irregular nuclear membrane; all three hematopoietic elements are suppressed.

Figure 4

Figure 3: This is a peripheral blood smear showing a lymphoblast at 10 o clock positions and a normal lymphocyte at 4 o clock position.

Figure 5

Figure 4: Bone marrow smear showing infiltration by immature pleomorphic lymphoblast.
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**Figure 6**
Figure 5: A typical Lymphoblast

FNAC from the testicular swelling as well as the submandibular swelling showed cytomorphology suggestive of Lymphomatous/Leukemic infiltration.

Ultrasonography of both testes and breasts were done.

It showed normal breasts without malignant infiltrations and complete destruction of both testicular sonographic signature.

Ultrasonography of the abdomen was normal.

**Figure 7**
Figure 6: Ultrasonography of Lt Testis showing loss of normal architecture.

**DISCUSSION**
Acute Lymphoblastic leukemia (ALL) presenting with bilateral testicular swelling is quite a rare scenario. A study showed microscopic testicular involvement in newly diagnosed Acute Lymphoblastic leukemia to be 21%.

Since the clinical incidence of testicular relapse varies widely from 1 to 40%, and since microscopic infiltrates in autopsies have been reported to be 64 to 92% in boys, it is suggested that testicular infiltration escapes clinical detection until the organ is several times its normal size.

Testicular infiltration was evaluated by testicular ultrasonography (USG) and biopsy and the correlation analyses between these methods were carried out in a group of boys with Acute Lymphoblastic leukemia followed up at Dr. Behçet Uz Children's Hospital.

Testicular ultrasonography and biopsy findings were evaluated in 8 cases with painless testicular enlargement. Three cases showed no evidence of infiltration at the biopsy.

Five had microscopic evidence of testicular disease.

Thus, testicular biopsy may be a more valuable method if it is performed whenever involvement is suspected clinically. Frequent and detailed testicular examination, evaluation of their size and hardness should be preferred to routine biopsies.
According to these results, it can be concluded that if there is clinical suspicion of testicular involvement, it is appropriate to perform testicular biopsy directly without an ultrasonographic examination 4.

So even though most studies 5, 6, 7 have focused on testicular involvement in Acute Lymphoblastic leukemia only as a part of relapse, probably greater percentage of patients have clinical or subclinical involvement at the time of initial presentation.

A study that was done to find out the testicular involvement in Acute Lymphoblastic Leukemia by only Fine Needle Aspiration Biopsy showed significant (34/106) number of cases had testicular involvement by leukemic cells. Those tissues had shown leukemic cells without any Sertoli cells in the aspirate as is seen in this case 8.

Another study showed that positive testicular biopsy results early in remission identified patients at a slightly higher risk of subsequent adverse events but did not influence survival. However, because negative biopsy results (94.5%) did not alter the prescribed treatment, the small number of positive biopsy results did not warrant undertaking the procedure in most male patients with Acute Lymphoblastic Leukemia, and this procedure was abandoned 9.

This case report presents a very rare scenario where testicular enlargement has been the presenting complaint of a patient with Acute Lymphoblastic Leukemia.

Subsequent to the diagnosis, it was decided to start him on a four drug induction regimen with Vincristine, Prednisolone, L-asparaginase and Adriamycin. After four weeks of treatment a bone marrow study was done which did not reveal any abnormality.

Testicular irradiation was given with a dose of 12 Gy.

He went through the regimen without any problems. He was discharged and is currently on Vincristine, Dexamethasone and L- Asparginase as consolidation therapy. He is under regular follow up at the Department of Hematology, Calcutta Medical College and Hospital.

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References

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