CASE REPORT

An Unusual Site of Acute Lymphoblastic Leukaemia Relapse: Challenge for Gynaecologists

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Introduction

Secondary involvement of female genitourinary system [1, 2] is more common in lymphoma than leukaemia [3, 4]. In leukaemia, acute myeloid leukaemia (AML) is known to have extra medullary involvement (chloroma, granulocytic sarcoma, etc.) [5, 6]. In case of acute lymphoblastic leukaemia (ALL), except for CNS and testis other extra medullary sites are rarely involved [7, 8]. Amongst genitourinary organs, testis is the most common site of involvement in ALL [8]. Cases of ovarian and cervix involvement in ALL are limited to case reports only [9–13].

Case Report

A 47-year-old female, known case of precursor B cell ALL treated in the year 2010 with modified BFM protocol, again presented with complaints of vague sensation of lump in right lower abdomen for 2 months. The general physical examination was unremarkable. A lump of approximately 5 × 5 cm

Fig. 1 a, b Baseline CECT pelvis showed heterogeneously enhancing solid mass lesion in the right adnexa of with $8.3 \times 5.8 \times 8.2$ cm in maximum dimensions (marked in arrow)

Fig. 2 Fine needle aspirate from right inguinal lymph node shows many lymphoid blasts. **a** Giemsa ($\times 10$). **b** H&E ($\times 20$)

was palpable in right iliac fossa on abdominal examination. Colposcopic examination showed unhealthy and friable cervical mucosa. Haemogram and other laboratory parameters were within normal limits. CECT pelvis showed heterogeneously enhancing solid mass lesion in the right adnexa of $8.3 \times 5.8 \times 8.2$ cm in maximum dimensions (Fig. 1a, b). Differential diagnosis of either metachronous ovarian carcinoma or isolated relapse of ALL was kept.

Colposcopic biopsy of cervix showed diffuse infiltration by atypical cells (Fig. 2a, b). On Immunohistochemistry (IHC), these malignant cells were positive for LCA, TdT and CD10, and other markers like CD20, CD3, CD56, CK, vimentin, synaptophysin, ER and PR were negative (Fig. 3a, b, c, d). FNAC from adnexal mass also confirmed leukaemic infiltration of right ovary (Fig. 4a, b). Bone marrow biopsy confirmed systemic relapse (Fig. 5a, b, c, d). She was started on ALL-REZ BFM 2002 protocol and also given involved-field radiotherapy (24 gray in 12 fractions). On day + 30, a repeat CECT pelvis was done which showed complete resolution of adnexal masses (Fig. 6a, b). She is currently on chemotherapy with subsequent plan for allogeneic HSCT from one of his matched siblings.

Discussion

Ovaries and cervix are fairly uncommon sites to be involved in acute lymphoblastic leukaemia. Hence even in previously known cases of ALL, ovarian masses are taken

Fig. 3 **a** Biopsy from adnexal mass shows diffuse infiltration by tumour cells ($\times 10$). **b** The tumour is predominantly composed of

lymphoid blasts which are positive for LCA—leucocyte common antigen on IHC (**c**) and TdT (**d**) and CD 10 (not shown)

Fig. 4 Fine needle aspirate from the adnexal mass shows numerous lymphoid blasts. **a** Giemsa ($\times 10$). **b** H&E ($\times 10$)

Fig. 5 Bone marrow Bx. **a** Aspirate showing blast cells with 2–3 times the size of mature lymphocyte with open-up chromatin and prominent nucleolus. **b** Hypercellular marrow spaces for the age of patient with erythroid preponderance. Megakaryocytes were mildly

increased with a few immature forms. **c** IHC showed an increase in the number of CD79a positive B cells; **d** CD34 stain highlights endothelial cells in proliferating vessels and blast cells

as an epithelial malignancy if the patient is middle aged or more (like our patient) or a germ cell malignancy if the patient is younger. Hence, a high index of suspicion should be kept while evaluating these symptoms in cases with suspected or known ALL.

Extramedullary relapse (EMR) is more common in AML with lymph nodes and skin as the frequent site of involvement [14]. Rare sites like pancreas, mediastinum, pleura, spinal cord are also reported in medical literature [15–17]. In case of ALL, most common site of EMR is central nervous system.

Gonadal infiltration is more commonly an autopsy finding in cases of acute leukaemia [4, 18]. Testis is more common site of extra medullary involvement than ovary [19]. Isolated clinical relapse with ovary and cervix as the primary site of involvement is uncommon [11, 13, 20]. Abdominal symptoms can be vague and nonspecific. In such cases, patients may present to either a surgeon or gynaecologist. Many a time diagnosis is made after receiving the final report of biopsied/resected specimens [21, 22].

Largest case review of ovarian involvement in ALL is done by Pais et al. (23 cases) and Kim et al. (31 cases) [9, 23]. In the review study by Kim et al., the average duration of ovarian relapse from initial diagnosis of ALL was 53.7 months. No association was found between the kind of chemotherapy regimen used and the risk of development of ovarian relapse [9].

Routinely, ALL patients after completion of maintenance phase are followed at 3–4 month interval with detailed physical examination and haemogram. In our case, routine examination could detect an ovarian mass only when it was large enough to be palpated per abdomen. By that time, this patient also showed evidence of disease recurrence in the bone marrow. This case and significantly large series of similar cases published by Pars and Kim et al. suggest that at least biannual gynaecological pelvic examination should be included in regular follow-up of adult females after completion of their therapy to detect EMR in limited stage [9, 23].

Treatment of such cases is a big challenge. However, often it is noted that extra medullary relapse of leukaemia

Fig. 6 a, b Follow-up CECT pelvis after chemotherapy showed complete resolution of heterogeneously enhancing solid mass lesion

is harbinger of imminent or subsequent systemic relapse. Therefore, all isolated relapses like ovarian relapse should be treated with systemic chemotherapy combined with local radiotherapy.

Conclusion

The aim of reporting this case is to notify about unusual yet relevant presentation of EMR of ALL. Commonly, ALL patients will present to haematologists with usual bone marrow failure symptoms. However, there is a need to sensitise people working in specialised areas like gynaecology about possibility of acute leukaemia presenting in form of tubo-ovarian mass. At times, early detection of a malignancy is all that counts!!

Compliance with Ethical Standards

Conflict of interest On the behalf of all the co-authors, I hereby state that there is no conflict of interest involved in this study which requires specification.

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