Case Report

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Case Report

A Case of B-Cell Lymphoblastic Lymphoma Presenting with an Isolated Epidural Mass Treated Successfully with Radiotherapy Followed by UKALL Chemotherapy Protocol

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Abstract: B-cell lymphoblastic lymphoma (B-LBL) is an aggressive type of non-Hodgkin lymphoma that usually involves lymph nodes, skin and soft tissue. Bone marrow and peripheral blood are normally spared from involvement by the disease. B-LBL typically forms sold masses that have similar pathologic and immunophenotypic features of the liquid counterpart, B-cell acute lymphoblastic leukemia (B-ALL). Presentation of B-LBL with a solitary epidural mass at the cervical spine is very rare and the optimal treatment of such cases is unknown. Most of the literature on management of B-LBL comes from small case series, pediatric patients, or as part of retrospective data that combine B-LBL with B-ALL cases. The case presented herein, showed a unique presentation that was then treated with three modalities, namely, surgical resection, radiotherapy, and consolidation with systemic chemotherapy adopted from United Kingdom acute lymphoblastic leukemia (UKALL) protocol. The patient attained a complete response following the planned treatment and is still in remission five years from the time of his initial diagnosis.

Keywords: lymphoblastic lymphoma; UKALL; LBL; B-LBL; epidural

Introduction:

B-lymphoblastic leukemia (B-ALL)/lymphoma (B-LBL) is recognized in the 5th edition of the World Health Organization (WHO) classification of haematolymphoid tumours as one of the precursor B-cell neoplasms.(1) When the disease presents primarily with nodal or extranodal involvement, the term lymphoma (B-LBL) is used, however, if there is an extensive bone marrow and peripheral blood involvement, the proper term used is leukemia (B-ALL). Lymphoblastic lymphoma (LBL) of a T-cell origin (T-LBL) is more common than B-LBL which only constitutes about 10% of all LBLs.(2) The usual presentation of B-LBL includes involvement of lymph nodes, skin, soft tissue, bone and rarely the mediastinum.(2, 3) Solitary epidural involvement is rare. Histologically and immunophenotypically, these two entities, namely B-ALL and B-LBL, are essentially identical. Typically, the neoplastic cells are composed of small to medium-size immature blast cells with scant cytoplasm and moderately condensed chromatin. Immunophenotype studies such as flowcytometry and or immunohistochemistry of B-LBL will confirm B-cell origin by positivity of B-cell markers such as CD19, cCD79a, and cCD22 in addition to expression of the immature marker, TdT. Since B-LBL cases are rare, they are typically treated similar to B-ALL. The prognosis of B-LBL in adults is not entirely clear but it is largely extrapolated from B-ALL or the pediatric literature. It is believed that the prognosis of B-LBL is relatively favourable and becomes less favourable as patients get older in age.(4, 5) The optimal treatment of patients with B-LBL who present with solitary lesions specially those presenting as epidural mass, is unclear.

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Whether surgical removal or localized radiation is sufficient remains unclear It is usually preferred to treat these cases with systemic chemotherapy with the idea to kill any possible microscopic disease that could potentially disseminate to other tissues if left untreated.

Here a report of a unique and rare presentation of a B-LBL case is presented in details. The case was treated surgically after which, radiation and systemic treatment were initiated with an intensive chemotherapy protocol adopted from UKALL study.(6) The patient attained a complete remission (CR) and is alive in a stable condition for more than four years.

Case Description:

The patient is a 30-year-old Saudi gentleman who presented in December 2019 with a three-month history of neck pain and stiffness associated with changes in hand writing, upper limbs numbness, and difficulty to do fine motor skills. He presented to another local hospital and his investigations showed a complete blood count (CBC) that revealed a hemoglobin of 151 gm/L, mean corpuscular volume of 94.5 fL, platelets of 342.0 x10^9/L, total white blood cell count (WBC) of 8.1 x10^9/L and absolute neutrophil count (ANC) of 0.0 x10^9/L. Coagulation profile showed normal international normalized ratio (INR) of 0.96, prothrombin time (PT) of 13.5 seconds, and a mildly elevated partial thromboplastin time (PTT) of 36 (normal: 25-35) seconds. Peripheral blood film confirmed the absence of abnormal cells or blasts. A magnetic resonance imaging (MRI) was done that showed an enhancing soft tissue mass within the anterior epidural space at the level of cervical vertebral body (C) C3-C4 with possibility of impingement of the adjacent nerve root on the left side. See Figure 1.

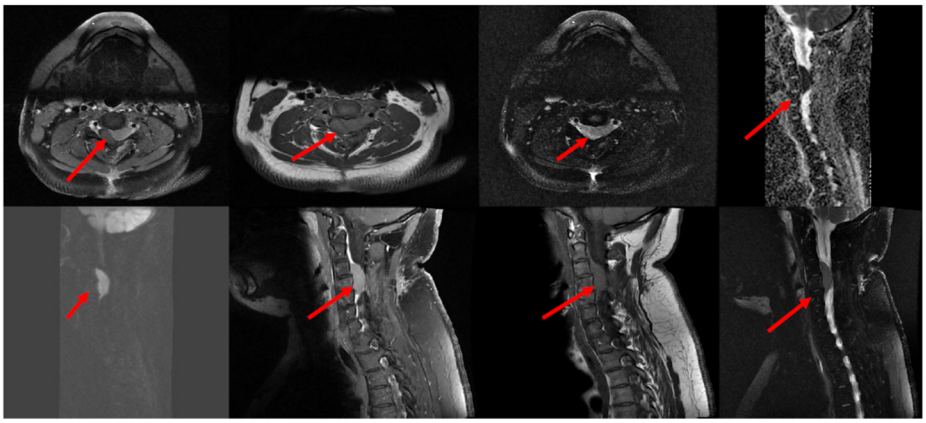

Figure 1: MRI of the cervical spine showed that there is an intraspinal epidural mass (arrows) measuring 1.2 x 1.8 x 3.2 mm (AP, TV and CC diameters) in the ventrolateral aspect at the level of C3-C4 extending to the left neural foramen, impinging the adjacent nerve root and compressing the spinal cord with cervical myelopathy. The mass demonstrates avid homogeneous enhancement in postcontrast study and DWI restriction.
Abbreviation: Magnetic resonance imaging (MRI), anteroposterior (AP), transverse (TV), and craniocaudal (CC) planes.

At the beginning of February 2020, the patient underwent anterior decompression and lesion resection at C3-4 and C5 laminectomy. A large panel of immunohistochemical stains were done on the pathologic sample and it showed that the tumor cells are strongly positive for TdT, CD99, CD79A, PAX5, CD43 and CD10, CD45, FLI1, CD20, CD3 and CD34. The stains for synaptophysin, NSE, WT1, myogenin, MPO, CD2, CD5, CD8 and CD1A are all negative. The proliferation marker Ki67 was positive in 70% of tumor cells, while PAS stain is negative. See Figure 2.

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Fig. 2 A-2377-HE-600

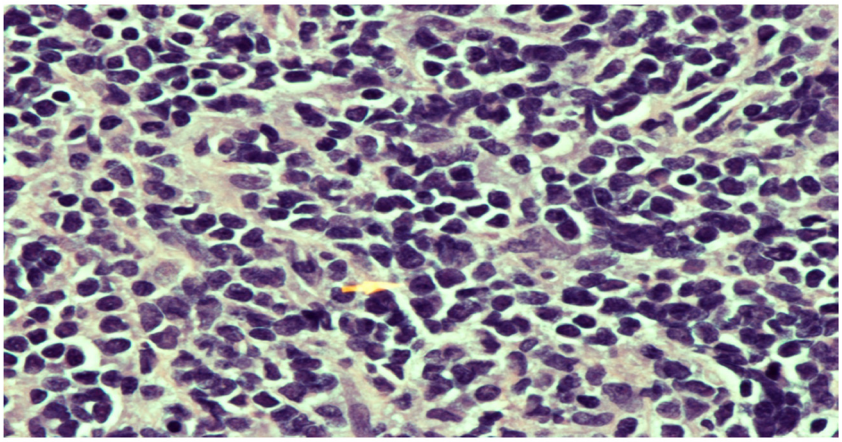

Fig. 2A High power microscopic view of lymphoblastic lymphoma. Note the presence of numerous monotonous lymphoid cells showing irregular Nuclei, fine nuclear chromatin and conspicuous nucleoli in some cells.
(H/E stain x 600)

Fig. 2B-2377-TdT IHC stain-600

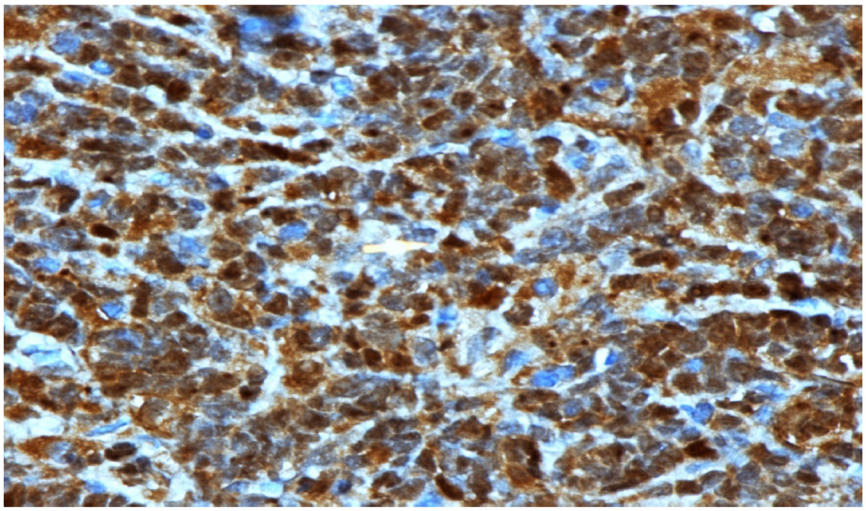

Fig. 2B: TdT Immumohistochemical stain. Note the strong positive nuclear staining. Mag. X 600.

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Fig. 2C-2377-CD79A-600

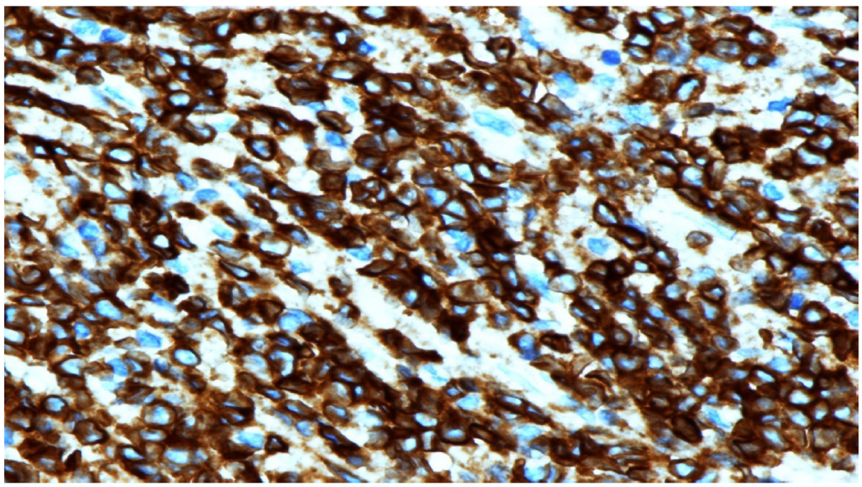

Fig. 2C Strong positive membranous staining of the lymphoma cells with CD79A confirming the B cell linage of these cells. Mag x 600.

Fig. 2D-2377-CD99-600

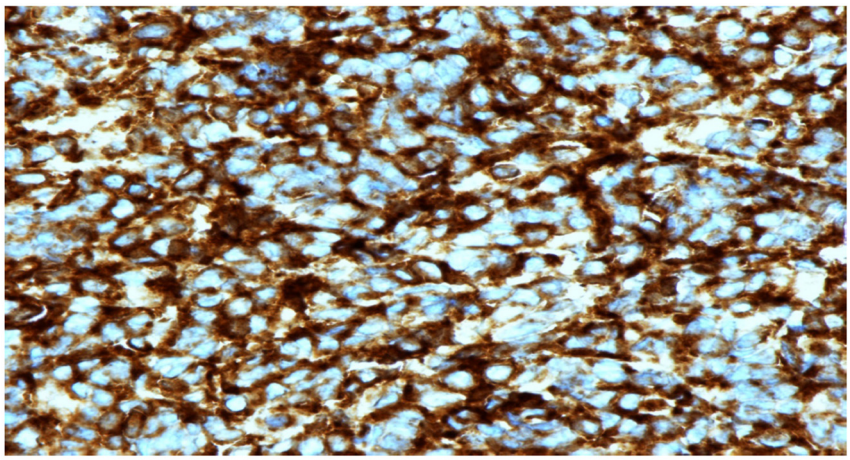

Fig. 2D Strong positive cytoplasmatic and membranous attaining with CD99 stain. This stain, although not specific, is commonly positive in cases of lymphoblastic lymphoma. Mag x 600.

Bone marrow aspiration and biopsy was also done and showed a normocellular marrow with active trilineage hematopoiesis with no morphological or immunophenotypical evidence of increase in blasts.

In addition to the aforementioned MRI, a computed tomography scan (CT) of the neck/chest/abdomen and pelvis was done and showed no evidence of disease elsewhere and absence of any significant lymphadenopathy. A positron emission tomography (PET) was also done and showed no other areas of any suspicious uptake.

After his surgery, the patient was referred for radiotherapy and was prescribed 2500 centi-gray (cGy) in 5 fractions to the C spine.

The patient was then commenced on United Kingdom acute lymphoblastic leukemia 14 protocol (UKALL14) on June 2020. On July 8th, 2020 a follow up MRI of the cervical spine was done after completion of induction chemotherapy and showed a significant improvement and resolution of anterior intraspinal epidural mass at the level of C3 and C4 vertebral bodies.

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After completion of his chemotherapy protocol, a repeat MRI was done on 15 May 2023 and showed persistent complete resolution of the C3-C4 anterior epidural mass without evidence of recurrence. See Figure 3.

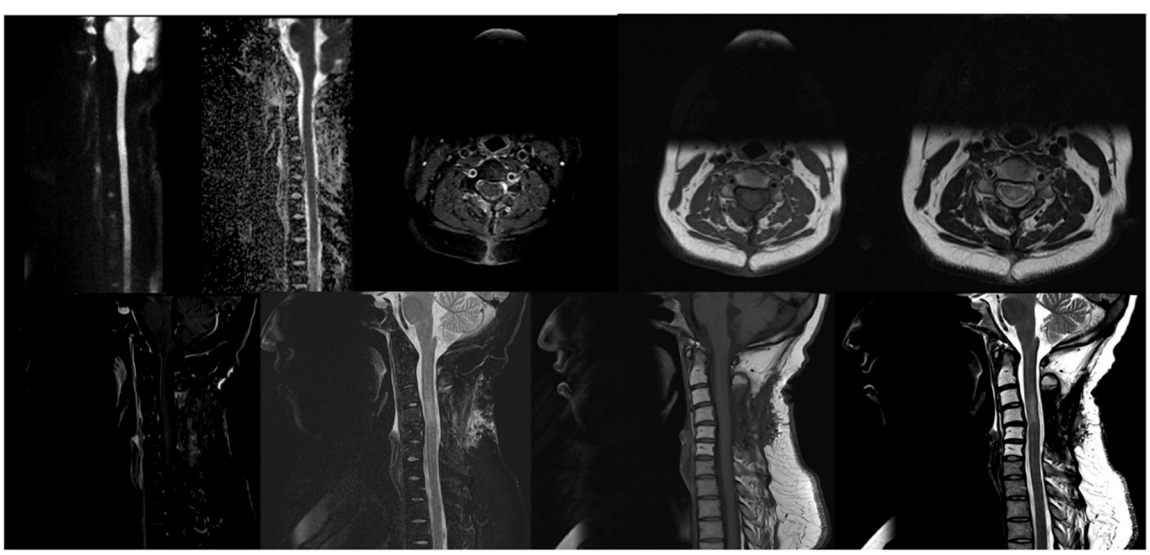

Figure 2: follow up MRI Showed that there has been interval laminectomy at C3-C5 levels, resolution of the large intraspinal anterior epidural mass on the ventrolateral aspect of the canal at the level of C3-C4, improvement of the signal alteration within spinal cord due to cord myelopathy, no significant diffusion restriction, stable faint mild enhancement of C4 vertebra and new alteration on T1 and T2-weighted images at C2 to C6 vertebrae related to radiotherapy.

Discussion:

B-LBL is a very aggressive type of B-cell lymphomas, which typically presents rapidly and involve the lymph nodes, skin and or other soft tissues. Other possible albeit rare sites of involvement are liver, renal, testicular, rectal or small bowel.(7-11)

Epidural involvement as a primary site of the disease is vanishingly rare. There are no enough cases reported in the literature with such a presentation. In one of the rare studies found in the literature, Nambier et al. reported a case that developed paraparesis secondary to a spinal lesion that was later diagnosed as B-LBL, however the treatment of that case was different from ours.(12) In that study the patient was treated with combination chemotherapy with cyclophosphamide, vincristine, adriamycin, and dexamethasone (hyper-CVAD) protocol.

Unfortunately, the natural history, prognosis and optimal treatment of B-LBL in adults is unknown and largely derived from case reports and retrospective series or extrapolated from the pediatric literature of B-ALL/LBL.(13) Nevertheless, multi-agent chemotherapy regimens are usually used in a similar fashion to B-ALL.(14) One important difference however lies in the inability to measure MRD accurately in B-LBL which makes transplantation decision difficult. Documentation of complete remission through different means such as imaging modalities such as MRI in our case will be of paramount importance.(15) Presumably, positron emission tomography (PET) scan can be used as well to assess treatment response although no enough evidence to support such practice.(16, 17)

Also unknown is whether surgery and or radiation alone is enough in truly localized disease. It is assumed that systemic treatment is still needed to clear microscopic disease similar to treatment of other limited stage aggressive B-cell lymphomas such as Burkitt or diffuse large B-cell lymphoma. The use of UKALL protocol has been shown to be effective in B-ALL. We have opted to treat our patient with this protocol, which at the time, was our standard ALL protocol.

The patient tolerated treatment reasonably well. He achieved complete remission and remained stable and he is likely cured from the disease. His last follow up was more than 4 years after diagnosis.

Conclusion:

Epidural presentation of B-LBL is rare. Treatment should include a multidisplinary team that includes neurosurgery, radiation oncology and hematology. Surgical decompression with or without

radiation is frequently needed to rapidly reverse compression symptoms followed by systemic multi-agent chemotherapy to cure the underlying microscopic disease.

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