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Case Report

Bilateral Optic Nerve Infiltration as an Initial Site of Relapse of Acute Lymphoblastic Leukemia in Remission

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Abstract

An 18 year old male patient diagnosed as Acute Lymphoblastic Leukemia (ALL) two years back was treated by the MCP 841 protocol. The patient attained remission and was being on the maintenance phase of the protocol. The patient while being investigated for diminution of vision was diagnosed as isolated CNS relapse in the form of bilateral optic nerve leukemic infiltration. The patient was treated with chemotherapy systemic and intra-thecal along with radiotherapy. The treatment resulted in regaining of vision in one eye while the other stayed refractory to the treatment.

Keywords: Optic nerve; CNS relapse; ALL

Introduction

Central Nervous System (CNS) relapse in Acute Lymphoblastic Leukemia (ALL) is in a phase where the incidence is expected to decrease due to advent of better systemic chemotherapy [1,2], CNS prophylaxis *via* both chemo and radiotherapy, but the fact that the life span of patients have significantly increased compared to yester years contributes to increased incidence [3]. Cases after complete systemic remission presenting with isolated bilateral optic nerve relapse is rarely reported [4,5].

Case Presentation

An 18 year old male, presented with fever 15 days, with swelling in neck both sides. Clinical examination showed multiple, palpable bilateral neck nodes, just palpable hepatomegaly. The hemogram showed elevated total count 18250, with 20% lymphoblasts. The bone marrow examination and flow cytometry confirmed a B-cell ALL. CSF cytology was negative at baseline. The patient was started on MCP 841 protocol, was in remission after induction. There were few episodes of febrile neutropenia during the course of treatment, but was uneventful. In the second Maintenance phase (M2), the patient presented to the OPD with c/o progressive dimness of vision since 1 week. There was no history of loss of consciousness, seizures, disorientation, headache, trauma to eye, diplopia or pain in the eyes. On examination the patient was conscious and oriented, vitals stable. The CNS examination was normal except the optic nerve [6]. The ophthalmic examination is as follows: Left eye: Optic disc atrophy present, generalized oedema, Vascular sheath thickening and tortuosity, superficial flame shaped haemorrhage. Right eye: Vascular sheathing present, generalized oedema present, foveal reflexes dull, vitreous, macula and retinal vessels- normal.

The patients MRI brain revealed abnormal diffuse enlargement and homogenous enhancement of intra-orbital, intra-cranial/ cisternal segments of bilateral optic nerve (Figure 1). The features favoured the diagnosis of leukemic infiltration. The CSF study revealed 5% leukemic cells. The haematological examination, peripheral blood film and bone marrow examination was normal. The working diagnosis of ALL CNS relapses.

The patient was immediately started on radiotherapy doubting the effectiveness of systemic chemotherapy on optic nerve. A total dose 20Gy/10 fraction was delivered. (Patient had received the same dose as prophylactic cranial irradiation during the second phase induction of his MCP 841 protocol). He was simultaneously started on ALL relapse protocol of alternating HYPER CVAD with MTX/ARA-C with biweekly triple intrathecal therapy consisting of cytarabine, methotrexate and dexamethasone. Patient tolerated the treatment well. Psychologic assistance in the form of counselling was also provided as the patient found it hard to cope with the loss of vision mentally. After a period of 1month of completion of local therapy, his best corrected visual acuity in right eye improved to 6/12 with normal colour vision. Unfortunately Left eye stayed refractory to treatment with best corrected visual acuity being 6/60. Unfortunately the patient finally succumbed to the disease in 5 months after initiation of therapy.

Discussion

ALL is a systemic disease, affecting the progenitor stem cells and the lymphoblast. Therapy is mainly intensified chemotherapy with or without Hematopoetic Stem Cell Transplant (HSCT). However, relapses are common during treatment or after attaining remission.

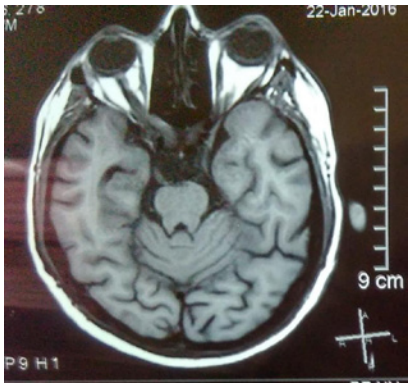

Figure 1: Abnormal diffuse enlargement and homogenous enhancement of intra-orbital, intra-cranial/cisternal segments of bilateral optic nerve.

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Table 1: Risk factors associated with the development of ALL CNS involvement.

Serial No	Risk Factors
1	Higher incidence in younger adults [3]
2	Mature B-cell/T-cell subtypes increased [4,5]
3	The Philadelphia (Ph) chromosome positivity [6]
4	Lymph node enlargement, mediastinal mass, extra-medullary localizations [7]
5	Lactate Dehydrogenase (LDH) level [8]
6	White Blood Cell (WBC) count and proliferative index [8]
7	Serum β2-microgobulin [8]

The commonest forms of relapses are bone marrow, testes and mediastinum. CNS relapse with bone marrow involvement are also seen, but isolated CNS relapse are rare. Prophylactic intrathecal methotrexate and cranial radiotherapy has reduced the relapse rates significantly to about 9% and the associated bone marrow relapse to about 4% of the patients [1,2]. In our case an 18 year old case of ALL in maintenance phase developed B/L progressive loss of vision, in the absence of the bone marrow involvement. CSF showed 5% leukemic cells. The patient had received intra-thecal methotrexate and prophylactic cranial radiotherapy as part of the treatment protocol and was under remission in the second phase of remission when he was diagnosed with CNS relapse. The MRI imaging confirmed bilateral involvement of the optic nerve.

Several risk factors have been associated with the development of ALL CNS involvement (Table 1). LDH, proliferative index and serum β2-microgobulin are considered significant. If the patient has one risk factor, the probability of developing CNS disease at 1 year is 13%, the probability is >20% if >2 risk factors are present [7,8]. But ultimately the presence of leukemic cells in the Cerebrospinal Fluid (CSF) is considered the most crucial feature of risk. In our case the risk factors were, patient was 18 year old young adult with palpable bilateral palpable cervical lymph nodes, total count at presentation-18250/mm^3, blasts-20% in the marrow and flow cytometry- B-cell ALL, CSF fluid at relapse positive for leukemic cells.

In relapsed ALL, therapy is usually salvage systemic chemotherapy with CNS directed therapy. The patient in our case was re-irradiated, cranial radiotherapy of 20Gy/10fractions was given. Also the patient was given biweekly triple intrathecal injection of cytarabine, methotrexate and dexamethasone. Systemic directed salvage chemotherapy in the form of alternating HYPER CVAD with MTX/ARA-C was also started after the completion of local therapy. After a period of 1 month of completion of local therapy, his best corrected visual acuity in right eye improved to 6/12 with normal colour vision. Unfortunately Left eye stayed refractory to treatment with best corrected visual acuity being 6/60.

The prognosis of adult patients who experience CNS relapse is very poor with a median OS of six months and a projected 5-year OS of zero. In our case the patient finally succumbed to the disease in 5 months after initiation of therapy.

Conclusion

The newer therapies have gradually increased the survival rates in ALL, but have presented a new challenge to physician with relapses. CNS relapses are rare but the incidence is increasing. CNS relapses are difficult to treat because of the poor penetration of systemic chemotherapy it becomes even more challenging to treat an optic nerve relapse. Early detection along with tailored radiotherapy could brighten up the day of optic nerve relapse cases.

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