Case report

Encephalomyelopathy in a child with acute lymphoblastic leukemia who had received radiotherapy and intrathecal chemotherapy

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Summary

Encephalomyelopathy is a rare complication of chemotherapy and radiotherapy , and it is a serious cause of morbidity and mortality in the children with Acute Lymphoblastic Leukemia (ALL).

A fifteen years old girl, who was diagnosed with ALL 3 years ago, developed CNS relapse 2 years after diagnosis and undertook CNS relapse protocol (2400 cGy cranial + 1500 cGy spinal radiotherapy, meanwhile intrathecal chemotherapy with MTX + ARA-C + Prednisone 5 times). Eight months later from radiotherapy, firstly right hemiparesy consequently quadriplegia and quadriparestesia developed, stool and urine incontinence occured, respiration problems started and progressively increased, so she exitus due to respiration deficiency.

Key Words: Leukemia, Encephalopmyelopathy, Radiation Myelitis.

Introduction

Acute leukemia is the most common pediatric malignancy[1,2]. Significant improvements in treatment protocols for childhood leukemia have led to a marked increase in cure rates. However, treatment-related complications and side effects of drugs is a significant problem. Both radiation therapy and intrathecal chemotherapy with extensive systemic chemotherapy are used to treat ALL with central nervous system (CNS) relapse[1], but both may cause neurologic damage. We reported a child with ALL who developed encephalomyelopathy, following the administration of chemotherapy and radiotherapy.

Case Report

A 15 years old girl who was diagnosed with ALL for 3 years, received high-dose systemic methotrexate (HDMTX) ($2g/m^2$) according to the protocol of St. Jude ALL T-XIII-I/H, she relapced in CNS two years after diagnosis and received 2400 cGy cranial + 1500 cGy spinal radiotherapy and intrathecal chemotherapy with MTX + ARA-C + Prednisone.

At the 94th week of treatment, she complained about the pain in her neck and weakness in the right foot and hand. In the physical examination , muscle strength was 2/5 in the right lower extremity, 3/5 in the right upper extremity, 4/5 in the left lower extremity, 5/5 in the left upper extremity, Deep tendon reflexes were hypoactive in the upper extremities, whereas the reflexes couldn't have been taken in the lower extremities. Moreover, she had bilateral babinski response, abdominal skin reflex couldn't have been

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taken. Cerebrospinal fluid examination was normal.

Craniospinal magnetic resonance imaging (MRI) was performed. There were common nodular signal change in the right middle cerebellar pedincul level and medium pons level. Nodular signal change was observed in joining tendency of centrum semiovale and bilateral periventricular and in subcortical white matter areas. In cervical MRI, from medulla oblangata to the level of the corpus of C3 vertebra , there was significant expansion and signal change. In post-contrast T1 weighted series, there was a hypointens lesion about 4x1 cm. diameters with intensive contrast on its periphery in the localization of the upper cervical spinal cord (Figure 1). There was signal change with fatty degeneration especially in the level of the corpus of C2 vertebra. All of this pathological findings suggest that these defined lesions are occured this zone secondarily after radiotherapy.

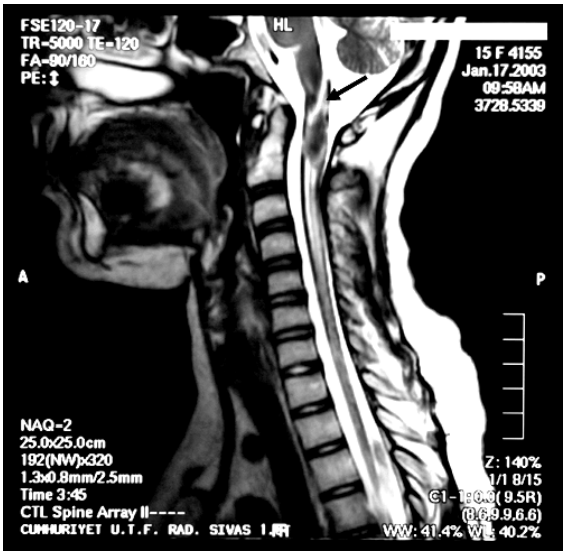

Figure 1: Craniocervical MRI:Sagittal post-contrast T1-weighted image of a 15 years old girl shows a hypointens lesion about 4x1 cm. diameters with intensive contrast on its periphery in the localization of the upper cervical spinal cord

The patient received dexametazon therapy against brain edema and carbamazepine for central neuropathy. Her neurological deficiency progressively increased, so she was dead after the 8-mounth of radioterapy.

Discussion

The leukemias are the most common malignant neoplasms in childhood, accounting for about 41% of all malignancies that occur in children younger than 15 yr of age. Acute Lymphoblastic Leukemia (ALL) accounts for about 77% of cases in childhood leukemias[1].

The CNS and testes are the two most common sites of extramedullary relapse[2]. Sistemic chemotherapy does not penetrate to these tissues as well as it penetrates other organs. CNS relapse occurs among 5 to 10 % of patients[2]. The treatment protocol in CNS relapse includes intrathecal medication and craniospinal irradiation. Systemic chemotherapy must also be used because these patients are at high risk for subsequent bone marrow relapse[1].

These chilren are at increased risk for neuropsychological problems, because of more aggresive CNS therapies are needed for the relapses[2]. Development of Encephalopmyelopathy, depending on intratechal chemoterapy and irradiation, is rather rare complication especially in children[1-3]. Numerous reports have described diagnostic imaging abnormalities in the CNS in children with ALL; the frequency of these changes ranges from 0 % to 79 %[2].

Symptoms, in our case, started 8 months after the radiotherapy process. The range may be from as early as 3 months to as late as 19 years. The more delay in the starting of symptoms, the worse the prognosis is[2,4].

The severity of cranial radiation effects varies among individual patients and depends on the dose schedule, the size and

location of the radiation field, the amount of time elapsed after treatment, the childs age when the radiation was administered, and childs gender. Girls may be more susceptible than boys to CNS toxicity[2,4], MTX application before, during and after radiotherapy process potentializes some changes depending on radiotherapy. However MTX may be less neurotoxic if given before rather than after radiotherapy[2,5].

Pacco and colleagues[6], in their study on the children with ALL who received only chemotherapy or chemoterapy with radiotherapy, couldn't find any significant difference between these two groups in the view of MRI changes of the white matter. MRI is more sensitive than computed tomography in the early diagnosis and management of leukoencephalopathy[6]. Among the cases reported in the literature, complete or partial recovery of neurologic deficits was observed, while the patients died from the initial oncologic disease or neurotoxicity progression[2,7].

Unfortunatelly, an effective treatment protocol for this complication is not defined yet[7].
Today, approximately 80% of children treated for ALL, in developed contries will enjoy long-term disease free survival and, in most instances, will be cured[1,2]. Despite this prognosis, however, patients may be death depending on the complications in the treatment secondarily or the infections during the illness rather than primarily of the disease itself.

Ephalomyeloenpathy is a rare complication depending on the radiotherapy and chemotherapy, and it is a serious reason of morbidity and mortality.

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