A RARE CASE OF CNS LYMPHOMA IN A CHILD

Carina O. Agilar, MD

ABSTRACT

B cell Lymphoblastic Lymphoma, a type of Non-Hodgkin Lymphoma, accounts for only 1% of all hematological malignancies in children. Osteolytic bone lesions and skin or subcutaneous lesions are the common sites of predilection, with only 6% of cases presenting with central nervous system involvement at the time of diagnosis. Here we present a case of a child presenting with sensorimotor deficits of the lower extremity. Patient was initially assessed to have an infectious process but upon histologic examination, a diagnosis of B cell Lymphoblastic Lymphoma was confirmed. Patient subsequently underwent chemotherapy with noted significant clinical improvement thereafter.

Keywords: Non Hodgkin's Lymphoma, B cell Lymphoblastic lymphoma, CNS lymphoma, paraplegia, spinal cord compression, Pott's Disease

INTRODUCTION

Non-Hodgkin lymphoma (NHL) is the fifth most common diagnosis of pediatric malignancy in children below 15 years of age, accounting for approximately 7% of childhood cancers in the developed world. Lymphoblastic leukemias are a type of NHL, majority of which are of B-cell type. B-lymphoblastic lymphoma displays a predilection for lymph nodes, bone and skin, accounting for 75% of cases, with rest occurring in miscellaneous sites such as head and neck (parotid gland and Waldeyer's ring), retroperitonium, breast, ovary, brain and soft tissues.

Primary central nervous system lymphoma (PCNSL) is an aggressive form of non-Hodgkin's lymphoma that is confined to brain, leptomeninges, eyes, or spinal cord. This can affect all age groups with a median age in the sixth decade. However, PCNSL is an extremely rare tumor in the pediatric population. Histologically, the most common subtype is diffuse large B-cell lymphoma (DLBCL). [1]

This paper presents a case of a child diagnosed with B cell Lymphoblastic Lymphoma initially presenting with back pain and weakness of lower extremities, eventually leading to paraplegia.

CASE PRESENTATION

An 11-year-old female presented with a three-month history of intermittent low back pain and weakness of bilateral lower extremities. There was no history of trauma, fever, weight loss, night sweats. MRI done upon consult showed cord compression and edema most marked at T2-T3 levels, which may represent an infectious process. Patient was initially assessed to have Tuberculous spondylitis (Pott's Disease) and was started on anti-Koch's therapy. However, patient had progression of weakness, now associated with numbness of abdominal area and bilateral lower extremities, bowel and bladder incontinence, and eventually, inability to walk. Secondary opinion sought hence patient was brought to our institution.

On physical examination, patient had stable vital signs, afebrile, no palpable lymph nodes, no hepatomegaly or splenomegaly, Glasgow coma scale 15, intact cranial nerves, with sensory deficit from T4 level down, manual muscle test 0/5 on bilateral lower extremities, with bilateral ankle clonus and Babinski.

Diagnostic workup showed normal CBC result with elevated ESR at 130 mm/hr. Chest Xray showed biapical pleural thickening more on the right, with opacities extending towards both paravertebral/paratracheal regions also more on the right, down to the level of T4. Cervicothoracic MRI showed enhancing paravertebral mass with neuroforaminal, subligamentous and epidural spread, abnormal marrow signals at T2 and to a lesser degree T1 with compression deformity at T2 vertebra resulting into cervicothoracic kyphosis, and cord compression with edema, most severe at T2-T3. Thoracic CT scan showed paravertebral soft tissue mass at C7 to T4 and bone involvement at T2, which could be from a chronic infectious/inflammatory process, such as tuberculous spondylitis. Initial assessment was Pott's Disease C7-T4 with T2 pathologic burst fracture, to consider spinal abscess, rule out malignancy.

Patient subsequently underwent posterior

decompression via wide laminectomy T1-T3, posterior instrumentation C7-T4, deep bone biopsy. Intraoperatively, there was no direct abscess but with noted soft tissue epidural mass/tissue enveloping the entire dura from T1 to T4 which was sent for histologic examination. TB culture, AFB smear, Gene Xpert MTB/RIF of the said mass turned out negative. Immunohistochemistry showed positive TdT and CD79a, consistent with B Cell Lymphoblastic Lymphoma. Patient was subsequently referred to Pediatric Oncology service.

Positron Emission Tomography (PET) scan revealed the following findings: Hypermetabolic soft tissue density mass in the paravertebral regions of C7 to T4 effacing the spinal canal and widening the neural canals, relating to the biopsy proven lymphoma. Hypermetabolic lytic lesions in the T1 and T2 vertebral bodies, left acetabulum, left ilium as well as the left superior and inferior pubic ramus with thickening of the obturator internus and externus muscles suggestive of **osseous metastasis**. Multiple hypermetabolic right scapular and rib lesions. Compression fracture of the T2 vertebral body, likely pathologic. Interval demonstration of orthopedic rods and pedicular screws transfixing the C7, T1, T3 and T4 vertebral levels. Hypermetabolic **internal mammary nodes and paraesophageal node may be metastatic**. No evidence of enlarged cervical, mediastinal and abdominopelvic lymph nodes (Fig. 1).

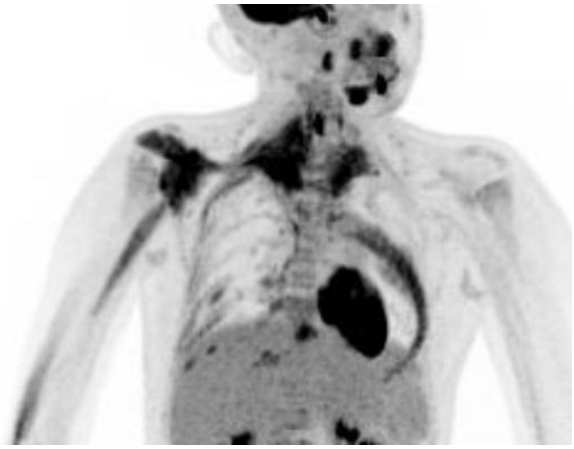


Fig. 1. PET scan showing metastatic process

Patient was subsequently started on a chemotherapeutic regimen with Cyclophosphamide and Vincristine. Intrathecal methotrexate was initiated during the same admission which patient tolerated well with no untoward reactions. Patient was started on Prednisone.

Physical therapy initiated with noted improvement in pain control. Motor deficit improved after a few days postoperatively and patient was eventually able to mobilize in bed and sit with feets dangling in bed. Sphincteric disturbance was relieved with noted good bowel and bladder control. Physical examination showed spastic lower extremities, with involuntary movements. Sensory on lower extremities reportedly around 50-60%.

Patient was subsequently discharged and opted to transfer to hospital of choice for subsequent chemotherapy sessions.

Currently, patient already had five cycles of chemotherapy with noted significant improvement in motor function of lower extremities. Patient is now reportedly able to lift both feet and stand with support. Manual muscle test 5/5 on all extremities with no sensory deficit and with good bowel and bladder control. Patient has been undergoing regular physical therapy three times a week and is scheduled for repeat PET scan.

DISCUSSION

Non-Hodgkin lymphomas (NHL) are malignant neoplasms of lymphoid cells, the predominant cells of the immune system. Lymphoblastic lymphoma, a form of non-Hodgkin lymphoma, primarily affects precursor derived from B cell progenitors, T cell progenitors, mature B cells, or mature T cells. This condition arises from immature T cells in more than 80% of cases and immature B cells in the remainder of cases.

Clinical Manifestation

The clinical presentation of pediatric NHL varies depending upon the type of lymphoma and the areas of involvement. Symptoms develop quickly, usually over one to three weeks. Symptoms can include fatigue, infections, or easy/spontaneous bruising or bleeding. Bone pain or arthralgias may be prominent complaints, and constitutional symptoms (eg, fever, night sweats, unintentional weight loss) are often present, but are generally mild. Hepatomegaly, splenomegaly, and/or lymphadenopathy are present in up to half of adults. Central nervous system (CNS) involvement may be manifest as cranial

neuropathies or meningeal symptoms. [5]

Central nervous system (CNS) involvement occurs in 6% of pediatric NHL with rates ranging from 8.8% in Burkitt lymphoma to less than 3% in diffuse large B cell lymphoma. A significant minority of patients will have systemic complaints of fever, weight loss, or night sweats (ie, B symptoms). While certain clinical presentations are suggestive of specific NHL histologies, a definitive diagnosis requires a biopsy of involved tissue.

According to the World Health Organization definition, primary central nervous system lymphoma refers to those cases confined to the CNS parenchyma, dura, leptomeninges, cranial nerves, and spinal cord or the intraocular compartment in immunocompetent patients. On the other hand, secondary CNS lymphoma refers to systemic non-Hodgkin's lymphoma that has disseminated to the CNS. [6]

Four different modalities of spinal localization have been reported [7, 8]: (1) involvement of paravertebral lymph nodes with adjacent vertebral invasion and epidural extension through neural foramina, (2) malignant vertebral infiltration with or without intra- and para-spinal involvement, (3) isolated involvement of epidural space, and (4) intramedullary involvement. In most cases spinal cord compression occurs in the thoracic region, less frequently in the lumbar region, while cervical involvement is quite rare. This could be justified by the thoracic cavity's size and the vertebral lymphatic drainage [6]. In most cases the clinical presentation includes 2 stages: (1) the prodromal stage, observed days to months before the diagnosis, consists of back and radicular pain or limbs numbness and tingling; (2) cord compression stage, with motor and sensory deficit and sphincteric loss, is often delayed, but sometimes can be present from the outset.

Differential Diagnosis

The presenting symptoms and signs of NHL in children and adolescents may be caused by a variety of diseases and the differential diagnosis includes other malignant, infectious, and inflammatory diseases.

In the case of the patient, neither anterior mediastinal mass nor lymphadenopathy were present, the two most presenting form of lymphoblastic lymphoma. Lymphoma of the spine has a variable clinical presentation, closely mimicking Pott's spine when they do, and patients present late in the course of the disease. Lymphomas of the spine, although rare, cause considerable differential diagnostic difficulty from tuberculous spondylitis which is common in our country. The ultimate answer to the diagnostic dilemma lies in histopathological examination. [9]

Diagnostic workup

Most patients with lymphoblastic lymphoma have findings associated with anemia, neutropenia, and/or thrombocytopenia due to bone marrow involvement. The white blood cell count may be decreased, normal, or markedly elevated.

Initial imaging studies (eg, ultrasound, radiographs, computed tomography) are often performed as part of the evaluation of presenting symptoms (eg, abdominal pain). These may demonstrate masses and/or lymphadenopathy in the neck, chest, or abdomen. Pediatric NHL, unlike Hodgkin lymphoma, may involve non-contiguous areas.

In addition, routine staging of pediatric NHL should include contrast enhanced computerized tomographic (CT) imaging of the neck, chest, abdomen, and pelvis. This CT both serves to help determine disease stage at diagnosis and to provide a baseline study for comparison to determine response to treatment. Integrated positron emissions tomography (PET)/CT scanning is more sensitive and specific than CT in certain histologic subtypes of NHL, including the most common subtypes seen in children

Imaging of the bones with plain films, CT, and/or magnetic resonance imaging (MRI) is not routinely performed in NHL, but is indicated in the presence of bone pain and/or suspicion of a pathologic fracture. Bone lesions in NHL are mostly osteolytic on plain films, in contrast to those in patients with Hodgkin lymphoma, which are predominantly osteoblastic. If there is suspicion of spinal cord compression, urgent MRI of the entire spinal column is indicated, since multiple sites may be involved. MRI (with and without gadolinium) of the head is also indicated for patients with neurologic symptoms or signs.

[11]

Management

Management of CNS lymphoma will almost always include emergency decompressive surgery, with or without resection, in the acute phase followed by radiotherapy and chemotherapy. Lymphoblastic lymphomas are treated similar to acute lymphoblastic leukemia with combination chemotherapy protocols consisting of intensive remission-induction chemotherapy, central nervous system prophylaxis, consolidation chemotherapy, and subsequent maintenance therapy for 18 months.

The preferred treatment modality for pediatric lymphoblastic lymphoma is combination chemotherapy based on regimens used for acute lymphoblastic leukemia (ALL). With this approach, children with early stage (I or II) or advanced stage (III or IV) lymphoblastic lymphoma achieve survival rates of >90 and >80 percent, respectively. The role of surgery is limited to surgical biopsy of a peripheral lymph node, a bone marrow aspiration, or aspiration of pleural fluid to establish the diagnosis. There is no role for surgical debulking of disease due to the high sensitivity of the tumor to chemotherapy. Likewise, there is no routine need for radiation therapy. Radiation is generally reserved for patients with pathologically proven involvement of the central nervous system (CNS) at the time of diagnosis. Testicular involvement at diagnosis does not require testicular radiation. [10]

Prognosis

There have been inadequate studies regarding the overall survival rate of B cell lymphoblastic lymphoma presenting with CNS involvement in the pediatric population. However, primary spinal epidural lymphoma generally in adults has a 3-year overall survival rate of 81.1%, and disease-free survival rate was 46.3%. [13]

Prognosis in B cell ALL/LBL is associated with age, clinical features, and cytogenetic/genetic features. Clinical features that are associated with unfavorable prognosis include: Age (≤1 year or ≥10 years old). Many infants have translocations involving the KMT2A (MLL) at 11q23, which is associated with a poor prognosis at any age.Older children more often have hyperdiploidy and t(12;21), which confer a better prognosis. Adult B cell ALL/LBL is more often associated with t(9;22) or poor risk t(v;11q23.3) abnormalities, and survival is poorer than in childhood cases. Leukocyte count ≥50,000/microL. Race (Hispanic or Black) due to genomic variations and socioeconomic factors.

CONCLUSION

The initial manifestation of lymphoma presenting with a spinal lesion is rare; it is even rarer when encountered as an isolated disease focus. Hence, physicians should consider the possibility of a lymphoproliferative disorder in the differential diagnosis of compressive myelopathy. The clinical, radiological, and histological features of this disease can mimic other medical conditions causing compressive myelopathy, including pathological compression fractures, infectious lesions, or carcinomatous deposits. This makes the diagnosis difficult and often leads to significant delays in initiation of effective treatment. [12]

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