

NEUROLOGIC MANIFESTATIONS IN HEMATOLOGICAL MALIGNANCIES – A CASE SERIES

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Abstract

Background: Leukemias and lymphomas represent a heterogenous group of hematological malignancies that affect both the central and peripheral nervous systems. It could be the direct manifestation of the disease per se or due to drugs used in the treatment of the diseases. Neurological manifestations may develop in a known case or it could be the unmasking factor of underlying hematological malignancy. We present a case series with 9 patients with the neurological manifestations due to hematological malignancies. Our observations confirm that there are numerous neurological complications from leukemias and lymphomas. Through a difficult process of differential diagnosis and appropriate therapy, only a multidisciplinary approach enables timely recognition of these complications.

INTRODUCTION

Leukemia and lymphoma are systemic diseases that affect many end-organs, together with the nervous system. These malignancies may produce intraparenchymal or extra-axial mass lesions or meningeal infiltration, which can directly impact the central or peripheral nervous systems and leads to many neurological complications.^[1,2]

Neurological manifestations in hematological malignancies may be due to (1) Direct leukemic infiltration over meninges as neoplastic meningitis, parenchyma as mass lesions, and cranial nerves as palsies (2) Coagulopathy and leukostasis causing ischemic, hemorrhagic stroke and posterior reversible encephalopathy syndrome (3) Immune compromise leading to CNS infections either by disease per se, or following splenectomy or antileukemic treatment (4) Paraneoplastic like sensory, autonomic neuropathy. These may be the initial manifestations or they may occur during the disease.^[1]

Many chemotherapeutic agents used for the treatment of hematological malignancies will have many detrimental neurological side effects and produce many neurological signs and symptoms (2). Thus, we have reviewed these neurological manifestations of lymphoma and leukemia.

Case 1

A 48-year-old male patient presented with acute onset dysphagia for liquids and numbness over the left face. On examination, the patient had left 9th and

10th cranial nerve palsies along with left-sided numb chin syndrome, no limb deficit, and the fundus was normal. On investigation, he was found to have plasma cell leukemia and his MRI brain was normal.

Case 2

A 76-year-old male presented with fever, headache, and altered sensorium for 5 days. On admission, he was drowsy, obeying commands, and had neck stiffness. Routine investigations showed raised total WBC count of 42200, found to have chronic lymphocytic leukemia. CSF examination showed raised protein and polymorphs with culture suggestive of pneumococcal infections. The old record of the patient revealed a recent recovery from pneumococcal meningitis 3 months back.

Case 3

A 50-year-old female who was under chemotherapy with cytarabine, for acute myeloid leukemia-M2 presented with subacute onset of weakness in all 4 limbs. On examination, she had a limb power of 3/5 on the upper and 2/5 on the lower limbs and deep tendon reflexes were absent suggestive of polyradiculoneuropathy, which was confirmed by a nerve conduction study. MRI spine showed diffuse multifocal bone marrow infiltration over the dorsal and lumbar spine with rim enhancement (FIG 1). CSF analysis was normal with negative for viral markers. The patient improved with steroids and physiotherapy.

Case 4

A 19-year-old male presented with a sudden onset of weakness in both lower limbs. Examination revealed a lower limb power of 3/5 with sensory level at D6 and bladder involvement. MRI spine was suggestive of an intradural extramedullary tumor from the D3-D9 level (FIG 2). The patient underwent posterior laminectomy and a biopsy of the tumour was suggestive of myeloid sarcoma. A bone marrow biopsy was done, which revealed acute myeloid leukemia M2.

Case 5

A 33-year-old female, with a known case of acute myeloid leukemia-M3, developed a headache for the last 3 days with vomiting. The patient was conscious, and oriented, with no meningeal signs or limb deficit. Fundus examination showed papilloedema. MRI brain was suggestive of left temporal venous hemorrhagic infarct with left transverse and sigmoid sinus thrombosis (FIG 3 & 4). She was started on injection heparin and anticoagulants improved.

Case 6

A 32-year-old male, on chemotherapy for acute myeloid leukemia-M2 with cytarabine, presented with sudden onset of facial deviation to the right with weakness of eye closure of the left side and numbness over the right face. Examination showed patient has got left LMN facial nerve palsy with right numb chin syndrome. CT brain didn't reveal any abnormality.

Case 7

A 19-year-old female presented in an unconscious state in ICU. On examination, the patient was unresponsive, her pupils were dilated, and had a sluggish response to light. Her fundus examination showed bilateral retinal hemorrhages. CT brain revealed multiple intracerebral bleeds (FIG 5). On investigations, she was diagnosed with acute myeloid leukemia. She succumbed even with aggressive management.

Case 8

A 34-year-old female presented with acute onset of left-sided horizontal diplopia with facial deviation to the right side. On examination, she was found to have left 6th and 7th cranial nerve palsies, on the investigation, she was HIV positive and diagnosed as non-Hodgkin lymphoma-diffuse large cell B-cell type. CT brain with contrast didn't reveal any abnormality.

Case 9

A 30-year-old female, known as acute myeloid leukemia-M5 on chemotherapy with cyclophosphamide and daunorubicin, presented with a burning sensation in both the foot and palms over the last 1 month. On examination, she had glove and stocking type of sensory loss over both lower limbs to knees with absent bilateral ankle reflexes. Romberg's sign was positive, which is suggestive of

peripheral neuropathy. The nerve conduction study showed the axonal form of sensorimotor polyneuropathy. Her B12 level was normal.

Here, in our case series, 2 out of 9 patients developed neurological complications in the form of multiple cranial nerve palsies. Also, in 1 patient, an unconscious state with multiple intracerebral bleeds was reported. Recurrent pneumococcal meningitis, polyradiculopathy, spinal cord tumour with paraplegia, cerebral venous thrombosis and peripheral neuropathy were observed in patients 2, 3, 4, 5, and 9 respectively.

Moreover, out of 9 patients, 3 patients were diagnosed as acute myeloid leukemia-M2, 1 patient was diagnosed as acute myeloid leukemia-M3, 1 patient with acute myeloid leukemia-M5, and 1 patient with acute myeloid leukemia. Moreover, 1 patient was diagnosed as plasma cell leukemia, and 1 diagnosed with chronic lymphocytic leukemia. Also, 1 patient was reported as HIV positive with non-Hodgkin lymphoma-diffuse large cell B-cell type.

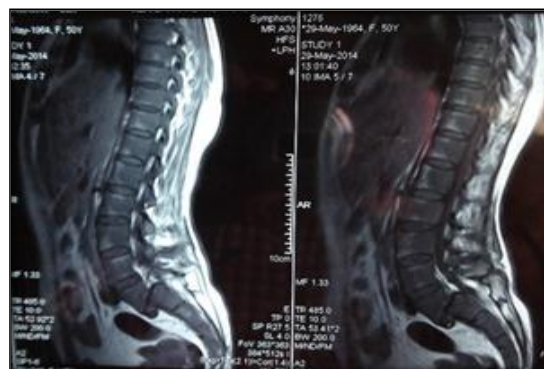


Figure 1: MRI spine showing diffuse multifocal bone marrow infiltration over dorsal and lumbar spine



Figure 2: MRI spine showing intradural extramedullary space occupying lesion from D3 to D9 level

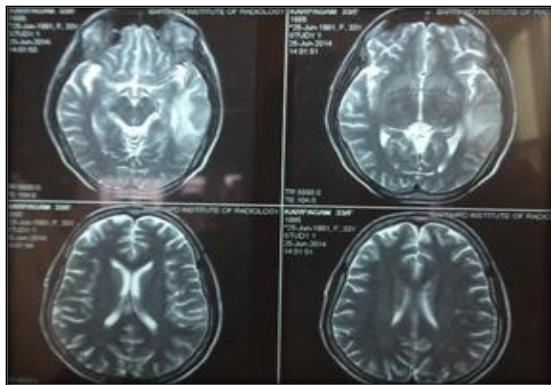


Figure 3: MRI brain showing left temporal lobe hemorrhagic infarct



Figure 4: MRI cerebral venogram showing filling defect in left transverse and sigmoid sinus suggestive of thrombosis

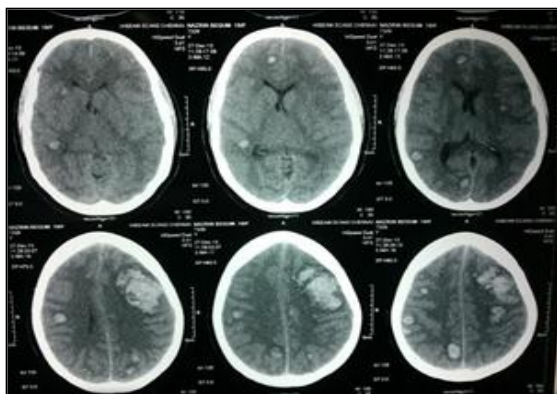


Figure 5: CT brain showing multiple intracerebral bleeds

DISCUSSION

According to our observations, neurological complications from leukemias and lymphomas can be multifold in patients with hematological malignancies. In such patients, final diagnosis and quick therapies are advised to stop the spread of

cancer or to avoid further development of neurological complications. Thus, to rule out hidden haematological malignancy in neurological circumstances, a strong index of suspicion should be underlined.^[1,2]

Overall, in our series of hematological patients, 22% of patients were reported with cranial nerve palsy, while facial nerve palsy was reported in one patient (11%). Also, we have seen an unconscious state with multiple intracerebral bleeds in 1 patient. In addition, we have noticed recurrent pneumococcal meningitis, polyradiculopathy, spinal cord tumour with paraplegia, cerebral venous thrombosis and peripheral neuropathy in other patients.

Hematologic malignancies are known to have various predispositions for nervous system pathology. Infection, inflammatory disease, iatrogenic effect, mechanical effect, and vascular disease are some of the possible causes of cranial nerve-related disorders. The neurologic side effects of cancer may influence both the central and peripheral nervous systems. These issues could show up as metastases in several organs, including the brain, leptomeninges, plexus, and the base of the skull. They typically impact 25% of individuals with metastatic cancer and have a significant morbidity and death rate.^[3,4]

Our case series and analysis has limitations including the small number of patients, which reflects the rarity of neurological problems in patients with haematological malignancies, and the short follow-up period.

CONCLUSION

Neurological complications of Leukemias and Lymphomas are multifold. A high index of suspicion should be emphasized in neurological emergencies to rule out hidden hematological malignancy.

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