Cranial nerve multineuritis as clinical onset of extramedullary relapse of acute myeloid leukemia

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INTRODUCTION

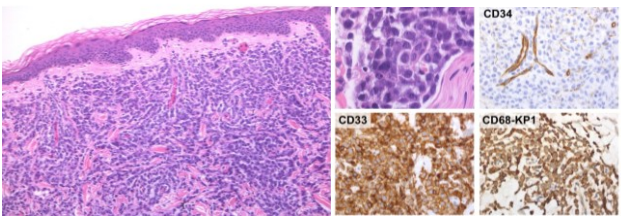
Acute Myeloid Leukemia (AML) is a hematologic malignancy characterized by the clonal expansion of myeloid progenitors. While it primarily affects the bone marrow, extramedullary relapse occurs in 3–5% of cases, and it is linked to poor prognosis. Central nervous system (CNS) involvement presents diagnostic challenges due to nonspecific symptoms.
CNS manifestations include leptomeningeal dissemination, nerve infiltration, parenchymal lesions, and myeloid sarcoma, occurring at any disease stage and frequently asymptomatic.

MATERIALS AND METHODS

A 62-year-old man with a recent history of AML in remission presented with diplopia and aching paresthesias in the left periorbital region spreading to the left frontal area.
The diagnostic workup included neurological and hematological evaluation, lumbar puncture, brain CT, brain magnetic resonance imaging (MRI) with contrast, and dermatological evaluation with skin biopsy due to the appearance of nodular skin lesions on the abdomen and thorax.

RESULTS

Neurological evaluation showed hypoesthesia in the left mandibular region, consistent with left trigeminal nerve involvement, extending to the periorbital and frontal areas, and impaired adduction of the left eye with divergent strabismus in the primary position due to left oculomotor nerve palsy. Brain MRI showed an equivocal thickening of the left oculomotor nerve without enhancement. Cerebrospinal fluid (CSF) analysis initially showed elevated protein (47 mg/dL) with negative cytology; a repeat lumbar puncture one week later detected leukemic cells. Skin biopsy revealed cutaneous AML localization. A diagnosis of AML relapse with CNS and cutaneous localization was made. Salvage therapy with FLAG-IDA-VEN (fludarabine, cytarabine, idarubicin, venetoclax) and intrathecal methotrexate, cytarabine, and dexamethasone was started. Subsequent lumbar punctures were negative for leukemic cells. Due to high-risk status and extramedullary disease, the patient underwent allogeneic hematopoietic stem cell transplantation. Post-transplant aplasia was complicated by septic shock; the patient succumbed to an invasive fungal infection.



Histological examination of the skin lesion disclosed a diffuse dermal infiltrate of myeloid blasts with slightly irregular nuclear contours, finely disperse chromatin, and small nucleoli (upper panel and mid left panel). The neoplastic cells were negative for CD34, CD117, and MPO, with diffuse positivity for CD33 and CD68-KP1. The overall histological features were consistent with skin involvement of AML with monoblastic differentiation. (H&E and peroxidase stain; original magnification ×10, ×40 and ×63). FISH analysis on the skin lesion was not performed.

CONCLUSION

This case illustrates the diagnostic complexity and poor prognosis of extramedullary AML relapse involving the CNS.
Early recognition of neurological signs, including cranial nerve dysfunction, is crucial for timely diagnosis and management.
Although initial investigations were negative, further analyses—including repeated CSF examinations and skin biopsy—led to the identification of leukemic involvement. Although neuroleukemiosis cannot be confirmed without nerve biopsy, the combination of clinical presentation, neuroimaging, and CSF data strongly supports the diagnosis of extramedullary relapse of AML.
Multidisciplinary evaluation remains essential for detecting extramedullary relapse.
Despite treatment achieving CSF clearance, the prognosis remains unfavorable, underscoring the need for vigilant clinical suspicion in hematologic patients presenting with neurological symptoms.

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