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Strabismus and diplopia in a patient with acute myeloid leukemia

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Data Interpretation D
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Conflict of interest: None declared

Patient: Male, 64
Final Diagnosis: Acute myeloid leukemia (AML)
Symptoms: —
Medication: —
Clinical Procedure: —
Specialty: —

Objective: Unusual clinical course

Background: Central nervous system (CNS) involvement is a sporadic presenting finding in patients with acute myeloid leukemia (AML) both at diagnosis and at relapse. Moreover patients with CNS localization are often asymptomatic, while sometimes show meningeal signs and symptoms or, extremely rarely, signs of cranial nerve impairment.

Case Report: Here we report on a patient with refractory AML who suddenly developed strabismus and diplopia. Both neurological and ophtalmologic examinations were suggestive of a bilateral VI cranial nerve palsy. Noteworthy, both a cranial CT and MRI were substantially normal, while a rachicentesis was performed and cerebrospinal fluid examination was clearly suggestive of a meningeal involvement by AML.

Conclusions: This is to our knowledge the first reported case in which the clinical picture of meningeal localization in an AML patient was dominated by an isolated abducens cranial nerve impairment. Moreover it highlights as unexplained strabismus and diplopia can be considered as a potential sign of CNS involvement, even if conventional imaging is negative.

MeSH Keywords: Cranial Nerve Diseases • Diplopia • Leukemia, Myeloid, Acute – cerebrospinal fluid

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/890526

Background

Central nervous system (CNS) involvement is an uncommon presenting finding in patients with acute myeloid leukemia (AML), as 5–7% of patients show neoplastic cells in their cerebrospinal fluid [1]. This occurrence is more frequent in acute lymphoid leukemia (ALL) patients, up to 15% of which can present CNS involvement at diagnosis [2]. Importantly, even in a cohort of 458 relapsed AML patients, the risk of meningeal localization was extremely low, with an overall 5-year cumulative incidence of 1.3% [3]. From the clinical point of view, patients with leukemic involvement of the CNS are often asymptomatic, but some show meningeal signs and symptoms or, extremely rarely, signs of cranial nerve impairment. Here we report on a patient with refractory AML who suddenly developed unexplained strabismus and diplopia.

Case Report

Our patient was a 64-year-old man who came to our attention in August 2011 because of anemia and leukocytosis. Peripheral blood counts showed: Hb 9.7 g/dL; WBC 67.0×10^6/mm^3 and platelets 369×10^6/mm^3. Peripheral blood and bone marrow smears were clearly suggestive of an AML, M4 subtype according to the FAB classification. Both cytogenetic and molecular analyses results were negative. After an initial cytoreduction with hydroxyurea, he underwent a classical 3+7 induction regimen with Cytarabine and Daunorubicin. A first disease re-evaluation showed a reduction of the blast count below 5% in the bone marrow, a marked dysplasia involving the white cell lineage, and an incomplete blood counts recovery. However, a further bone marrow examination performed 2 months after starting induction showed an increase of blast percentage up to 25%. He was then started on Azacitidine, receiving 6 cycles from November 2011 to May 2012 with no response. He was then admitted to our ward because of sudden convergent strabismus and diplopia. Peripheral blood values were: Hb 10.4 g/dL; WBC 12.1×10^6/mm^3 and platelets 8×10^6/mm^3 and he was still having cytoreduction with Hydroxyurea, as well as regular transfusional support with packed red blood cells and pools of platelets. At that time both neurological and ophthalmologic examinations were suggestive of a bilateral VI cranial nerve palsy, but no other neurological abnormalities could be detected. Interestingly, both a cranial CT and MRI were substantially normal. In the next few days neither strabismus nor diplopia improved and the patient developed an intense cervicalgia and thereafter dizziness, nausea, and vomiting. Therefore, a rachicentesis was performed and cerebrospinal fluid examination was clearly suggestive of a meningeal involvement by AML (Figure 1). The patient was immediately started on a chemotherapeutic program based on Fludarabine and Cytarabine, but he unfortunately died after an acute cholecystitis a few days later.

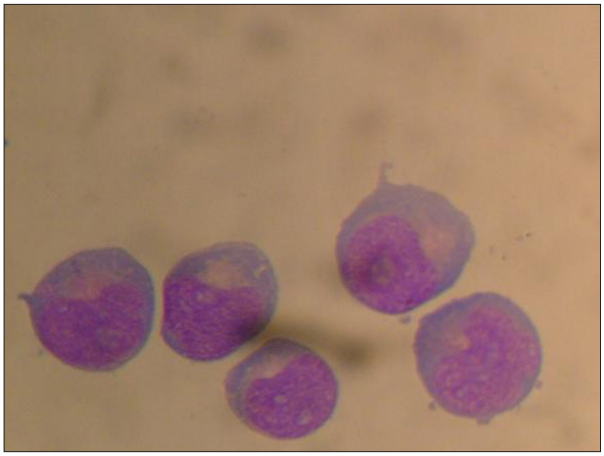

Figure 1. Cerebrospinal fluid morphological examination showed several monocytoid blasts, clearly suggestive of a meningeal involvement by AML.

Discussion

CNS involvement is an extremely rare complication in patients affected by AML. Factors associated with an increased risk at diagnosis are high white blood cell counts, elevated lactate dehydrogenase, younger age, and extramedullary disease, as well as specific FAB subtypes such as M4, M5, and the AML variant with abnormal bone marrow eosinophils and inv [4–7]. In a large cohort of relapsed AML patients, the only factor predisposing to CNS relapse identified on multivariate analysis was the use of old- rather than new-generation therapeutic induction regimens [2]. CNS relapse was demonstrated to be an extremely unlikely event after bone marrow transplantation for acute leukemia in first remission [8].

Most patients with leukemic CNS localization are asymptomatic, but some of them display clear signs of meningeal involvement. On the other hand, cranial nerve palsies secondary to leukemic infiltration are extremely rare in patients with AML. In more detail, 5 AML patients with cranial nerve impairment secondary to leukemia have been reported since 1980. The involved nerves were primarily facial [9] and trigeminal [10] in 1 patient each, and oculomotor in 3 cases [10–12]. A granulocytic sarcoma was demonstrated in 2 cases [9,10]. In most cases, MRI results were the determinant for the diagnosis of CNS involvement [10–13]. Three patients presented this complication at different time points after stem cell transplantation [10,11,13].

Conclusions

Our case deserves some additional remarks. Firstly, the possibility of this rare complication of the AML clinical course is further highlighted. As shown by the literature review, very few cases of cranial nerve impairment have been reported

in AML patients. However, this eventuality should be always taken into account, not only in ALL, but also in AML patients.

Moreover, the present case suggests that unexplained strabismus and diplopia can be considered as a potential sign of CNS involvement, even if conventional CNS imaging is negative, therefore suggesting that a cerebrospinal fluid evaluation should always be performed in this clinical scenario.

Lastly, this is to our knowledge the first reported case in which the clinical picture of meningeal localization in an AML patient was dominated by isolated abducens cranial nerve impairment, further demonstrating how signs and symptoms of CNS involvement in patients with hematologic disorders can sometimes be puzzling and difficult to interpret.

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