



Intracranial hypertension associated with treatment of acute promyelocytic leukemia with all-trans retinoic acid (ATRA): a case report

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Case presentation

Female, 18 years-old, without relevant family history, referred to Neurology by Hematology for headache. Three years ago, she was diagnosed with Acute Promyelocytic Leukemia (APL) currently on maintenance therapy with All-Trans Retinoic Acid (ATRA). The patient reports that in all previous cycles presented headache with the following characters: one-side temporal location, pulsating quality, moderate intensity, with nausea and vomiting, photophobia and phonophobia, uncertain duration, with simple analgesics response. In the current cycle, she relates continuous pain, severe intensity and unresponsive to medication. On examination, there were no focal neurological findings and on funduscopic examination there was no papilledema. MRI and laboratorial tests were normal. Cerebrospinal fluid (CSF) opening pressure was 35 cmH₂O, no other alterations. 15 milliliters of CSF were removed, with a closing pressure of 25 cmH₂O. A hypothesis of Intracranial Hypertension associated with use of ATRA was made. Afterwards, there was important improvement of the headache, with residual pain of mild intensity. Therefore, acetazolamide was started at a dose of 250 milligrams every 12 hours with complete resolution of symptoms.

Discussion

Acute myeloid leukemia (AML) comprises a heterogeneous group of aggressive blood cell cancers that arise from clonal expansion of malignant hematopoietic precursor cells in the bone marrow. Acute promyelocytic leukemia (APL) is a biologically and clinically distinct variant of AML. APL is classified as acute promyelocytic leukemia with PML-RARA. The cytogenetic hallmark of APL is a translocation involving RARA, the retinoic acid receptor alpha locus on chromosome 17. Without treatment, APL is the most malignant form of AML, with a median survival of less than one month. A key component of this therapy is the use of all-trans retinoic acid (ATRA), which promotes the terminal differentiation of malignant promyelocytes to mature neutrophils. The use of ATRA can cause intracranial hypertension (IH), more common in children and adolescents, and low doses reduces the risk of this complication. The diagnosis of IH is suspected in patients with headache, papilledema, and/or vision loss. Evaluation includes a physical examination, evaluation of the optic nerve, lumbar puncture, and cerebral imaging studies. The diagnosis is confirmed in patients with increased intracranial pressure, normal CSF and negative cerebral imaging studies. Papilledema is common, but not necessary for the diagnosis. Some patients may require serial lumbar puncture or intracranial pressure monitoring to document sustained elevated pressures. On occasion, the symptoms improve after the initial diagnostic lumbar puncture. If this occurs, no further medical treatment is necessary. If symptoms persist, therapeutic options include the temporary discontinuation or dose reduction of ATRA, analgesics, and/or the administration of steroids and acetazolamide.

Final Comments

The use of ATRA may cause intracranial hypertension. Lumbar puncture and brain imaging studies are useful to confirm the diagnosis of IH and institute the appropriate treatment. In the case of APL, the patient needs to receive ATRA because of high efficacy of medication in reduces mortality, and then acetazolamide may help to control headache.

Keywords: Acute promyelocytic leukaemia, All-trans retinoic acid, Idiopathic intracranial hypertension.