letter to the editor
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OCCURENCE OF CEREBELLAR THROMBOHEMORRHAGE DURING ALL-TRANS RETINOIC ACID (ATRA) THERAPY IN A CASE OF ACUTE PROMYELOCYTIC LEUKEMIA

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Sir,

acute promyelocytic leukemia (APL) is a well defined subset of acute myeloblastic leukemia, type M3 and M3v of the FAB classification, which present peculiar biological and clinical features. These features include the frequent association at diagnosis of a life threatening coagulopathy characterized by thrombohemorrhagic complications, the presence of a specific cytogenetic abnormality [the t(15-17) translocation] and the response to differentiating agents such as all-trans retinoic acid (ATRA).[1]

In fact, most recent clinical trials including ATRA induced a clinical morphological remission in APL patients.[1-3] But many authors reported the adverse effects of ATRA therapy in patients affected from acute promyelocytic leukemia (APL).[1-4] During ATRA treatment an increase in the number of white blood cells (leukocytosis) was observed, sometimes associated with embolism, thrombosis and cerebral infarction.[3,5] Fujivara[6] reported a case of an APL patient who developed a cerebellar thrombotic occurrence four weeks after ATRA therapy without leukocytosis.

Recently, we observed a 33-year-old man, affected by APL, who developed a cerebellar hemorrhage on the 12th day of ATRA therapy.

At the onset of the disease the patient was pancitopenic (WBC count was 1200/μL, platelet count was 27×10^9/L and hemoglobin was 8.4 g/dL); clinical and laboratory data demonstrated abnormalities of hemostasis such as elevated D-dimer (>1000 g/L) and low fibrinogen, confirming the presence of a disseminated intravascular coagulation (DIC).

The patient was put on a treatment schedule which comprised ATRA (45 mg/m^2/day) until achievement of complete remission and idarubicin (10 mg/m^2) on the 2nd, 4th, 6th, and 8th days.

During the first seven days we observed a normalisation of coagulopathy (DIC) and complete disappearance of hemorrhagic diathesis. On the 11th day from the beginning of ATRA therapy the patient suddenly presented clinical symptoms of cerebellar disturbance (headache, ataxia, diplopia). WBC count was 700/μL, PLT count was 50×10^9/L and coagulation profile was completely normal. Head CT scanning revealed the presence of a intraparenchimal cerebellar hemorrhage with compression on fourth ventricular region. A ventricular device was positioned to decrease the endocranial hypertension and substainal hemorrhagic liquor was detected. The patient was immediately treated with dexamethasone (12 mg/iv/day) and glycerol solution.

During the first 48 hours the clinical picture seemed to be slightly improved, but after 10 days, in the presence of continuos leukopenia (ANC < 500/mL) without any presence of blast cells, the patient underwent to pulmonary infection complicated by acute distress respiratory syndrome and died.

Our observation, similar to others reported[6] seems to suggest a potential role of ATRA therapy to induce a late adverse effect such as thrombohemorrhagic occurrences.

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