Acetazolamide-Induced Agranulocytosis in a Patient with Pseudotumor Cerebri

Sir,

Pseudotumor cerebri (PTC), otherwise known as idiopathic intracranial hypertension, is a syndrome defined by elevated intracranial pressure without evidence of a structural lesion or hydrocephalus on neuroimaging and a normal cerebrospinal fluid (CSF) composition. The classic symptoms of PTC are headache, nausea, tinnitus, blurring of vision, and diplopia.[1]

Acetazolamide was the drug of choice for the initial treatment. Common adverse effects of acetazolamide include paresthesia, fatigue, metallic taste, gastrointestinal upset, loss of appetite, hyperchloremic acidosis, and crystalluria.[2] Also, there have been a few reports of hematologic disorders in association with acetazolamide in literature.[3-5] We report a case of agranulocytosis in a patient with PTC due to acetazolamide therapy.

A 9-year-old boy, who was previously healthy, was admitted to our hospital with a complaint of headaches, vomiting, and blurred vision for 2 weeks. His medical history was unremarkable. On examination, the vital signs, including the blood pressure, were normal. He was conscious and had no meningeal signs. The neurological examination was normal except for a right eye abduction deficit. The ophthalmologic examination revealed bilateral papilledema. The results of laboratory examinations (complete blood cell count, liver enzymes, kidney function parameters, serum electrolytes, C-reactive protein, erythrocyte sedimentation rate) were normal. Magnetic resonance imaging of the brain was normal. We performed lumbar puncture. The CSF showed no pleocytosis and normal protein and glucose concentrations. CSF openning pressure was 55 cm/H_2O. We considered a diagnosis of PTC and started acetozolamide treatment at a dosage of 10 mg/kg.

Three weeks after treatment, agranulocytosis was detected on routine blood count and the patient was hospitalized. Before acetazolamide treatment, laboratory data included a hemoglobin (Hb) 13.6 g/dL, white blood cell (WBC) 7.90 cells/mm^3 with 60.7 neutrophils, and platelet 256 × 10^3/μL. At the time of hospitalization, the following results were

observed: Hb 10.3 g/dL, WBC 4.0 cells/mm^3 with 40.6% neutrophils, platelet 223 × 10^3/μL, total bilirubin 3.8 mg/dL, direct bilirubin 0.8 mg/dL, and indirect bilirubin 2.88 mg/dL. Agranulocytosis was progressive [Table 1]. Hemoglobin and platelet levels were normal during acetazolamide therapy. During the follow-up of the patient, serum serum sodium, potassium, creatinine, and urea levels were normal. Serology for infection was negative. Bone marrow examination showed normality of the precursors of the three series. The cause of agranulocytosis was thought to be acetazolamide and his acetazolamide therapy was discontinued (36th day of treatment). The WBC count was 5900 and 6100 cells/mm^3, respectively, after 7 and 10 days after acetoloazamide was discontinued.

Table 1: Leukocyte count evolution

Cells/mm^3	Before acetazolamide	After acetazolamide (treatment)				
		Day 23	Day 25	Day 28	Day 30	Day 35
Leucocytes	7900	4000	3100	2700	2300	2100
Neutrophils	4740	1600	1085	690	460	420

Acetazolamide is the most commonly prescribed carbonic anhydrase inhibitor for the medical management of PTC.[1] There have been reports that adverse effects associated with acetazolamide include paresthesias, dysgeusia, fatigue, nausea, diarrhea, hypokalemia, metabolic acidosis, renal stones, drowsiness, depression, or dizziness.[2,6] Also, acetazolamide-associated hematopoietic adverse events were previously described in the literature.[3-5] Maclean *et al*.[3] reported a case of severe pancytopenia with dysplastic characteristics in the bone marrow induced by acetazolamide. Kodjikian *et al*.[4] described acetazolamide-induced pure thrombocytopenia in a 67-year-old man. In another study, Keisu *et al*.[5] reported the records of 11 patients with aplastic anemia attributed to acetazolamide. Agranulocytosis by acetazolamide has been previously reported.[7] Hoffman *et al*.[1] reported agranulocytosis associated with the administration of acetazolamide in a 68-year-old man. We reported a case with agranulocytosis due to acetazolamide therapy. To our knowledge, this is the first case of acetazolamide-induced agranulocytosis in children. Agranulocytosis or severe neutropenia is defined by an absolute neutrophil count <500/mm^3.[8] Drug-induced neutropenia or agranulocytosis is mediated by immunoallergic and toxic mechanisms.[9] Drug-induced agranulocytosis is a serious entity that implies an increased risk of infections. Carbonic anhydrase inhibitor may increase the frequency of agranulocytosis by either accumulation and toxicity or elevating the probability of immunoallergic reaction, or both.

In conclusion, because acetazolamide is the most commonly used drug for PTC, children treated with acetazolamide should be warned against these potential adverse effects, to facilitate early withdrawal of drug.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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