was seen by slitlamp microscopy. Not only did diffuse loss mean deviation appear, but abnormal areas appeared with high intraocular pressure in the present patient. If corneal edema affected visual field, only diffuse loss would occur. Refractive error was corrected at examination of FDT. Good visual acuity was maintained under high intraocular pressure. In conclusion, FDT perimetry may show intraocular pressure-dependent, reversible changes.

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Acetazolamide-Induced Thrombocytopenia

Acetazolamide (Diamox; Duramed Pharmaceuticals Inc, Cincinnati, Ohio) is a carbonic anhydrase inhibitor commonly used in ophthalmology to reduce intraocular pressure and to treat some forms of macular edema. Acetazolamide-associated thrombocytopenia was previously described as part of aplastic anemia or other organ involvement; however, evidence that the drug may also cause accelerated platelet destruction has never been provided.1,3 Herein we report an acetazolamide-induced pure thrombocytopenia with the highest level of evidence for a causal relationship of the drug to thrombocytopenia.

Report of a Case. A 67-year-old man who had been receiving metformin for 20 years because of type 2 diabetes mellitus was admitted to our department for cataract surgery. The day after the surgery, intraocular pressure was elevated and 2 daily 250-mg tablets of acetazolamide were prescribed. As the intraocular pressure normalized on day 3, acetazolamide was stopped. A routine blood cell count with examination of the blood smear disclosed an unexpected and isolated thrombocytopenia (platelet count, 31 × 10^3/µL) (Figure 1). In the bone marrow, quantitatively and morphologically normal megakaryocytes, including some immature forms, were observed, indicating normal platelet production. Recovery from thrombocytopenia was shown later by ambulatory tests. Drug-induced thrombocytopenia was not suspected.

Eleven months later, acetazolamide (375 mg/d) was prescribed again, this time for macular edema. Two weeks later, the patient developed extensive purpura and was seen in our department a week later. He was hospitalized and found to have a platelet count of 3 × 10^3/µL (Figure 2). Acetazolamide, but not metformin, treatment was immediately discontinued. The platelet count rose spontaneously to 20 × 10^3/µL the next day, 73 × 10^3/µL 3 days later, and 246 × 10^3/µL after 10 days. Thrombocytopenia did not recur.

Comment. To our knowledge, acetazolamide-induced thrombocytopenia has been previously reported in only 4 cases.1,3 Moreover, in no case was the causality level high enough to ascertain that the drug was responsible.

As recommended by the American Society of Hematology,4 diagnosis of isolated thrombocytopenia in elderly patients requires bone marrow aspiration to exclude myelodysplasia. In our patient, no bone marrow disorder was found to explain the thrombocytopenia.

Diagnosis of acetazolamide-induced thrombocytopenia was based on positive data including challenge and in vivo rechallenge tests highly suggestive of causation: (1) Thrombocytopenia occurred within a few hours or days after ingestion of the drug. (2) Spontaneous recovery from thrombocytopenia was complete and sustained after the drug was discontinued, this pattern being seen on 2 occasions. (3) Reexposure to acetazolamide resulted in recurrent thrombocytopenia.

However, no specific laboratory test was performed to identify circulating drug-dependent antiplatelet antibodies and to confirm

![Figure 1. Timeline of platelet count after first introduction of acetazolamide. Vertical lines indicate period of acetazolamide administration.](http://archophht.jamanetwork.com/pdfaccess.ashx?url=/data/journals/ophth/9930/ on 04/02/2017)
the diagnosis. Indeed, there are no standard assays for such antibodies, no standardized criteria for distinguishing positive from negative results, and no data on sensitivity and specificity of these assays based on clinical criteria for a causal relationship.1,3

Although causality assessment methods in pharmacology remain a matter of debate, in our patient acetazolamide caused pure and severe thrombocytopenia with “certain” evidence according to the World Health Organization system of causation of a drug reaction6 with “very likely” evidence according to the French standardized methodology7 and with the highest level of evidence (“definite”) according to standardized criteria recently developed by Rizvi et al2 (database available at http://moon.ouhsc.edu /jgeorge). Such high levels of evidence for the causal relationship of acetazolamide to thrombocytopenia have never been reported until now, to our knowledge.

Discovery of isolated thrombocytopenia in a patient who is taking several medications also presents a challenging clinical problem. The principal interest of the level of evidence is to help clinical decision making about which drugs may more likely be implicated as a cause of thrombocytopenia and therefore should be discontinued as quickly as possible.

Acetazolamide should be considered a definite thrombocytopenia-inducing agent. Potential consequences of thrombocytopenia seem to be limited when the drug is prescribed for a few days, whereas it appears different with much longer treatment. In that case, regular complete blood cell count, especially in the presence of bleeding, should be recommended.5

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