Case report

Thrombocytopenic purpura associated with ingestion of acetaminophen (Tylenol)

Joseph D. Skokan, M.D.
James S. Hewlett, M.D.

Department of Hematology and Medical Oncology

George C. Hoffman, M.B., B. Chir., M.R.C. Path.

Department of Laboratory Hematology

Acetaminophen (Tylenol, N-Acetyl p-aminophenol) is a relatively safe nonsalicylate analgesic with few reported adverse effects or reactions. Its increasing use prompts our report of a case of thrombocytopenic purpura associated with the administration of acetaminophen. This complication, thrombocytopenia without depression of the leukocyte count, although speculated on, has not been documented.[1]

Case report

A 61-year-old man was examined March 4, 1968, 18 months after he had undergone a modified Vineberg mammary artery implant procedure. He had aching and stiffness in the left shoulder, for which acetaminophen, two tablets four times a day, was prescribed. On March 10, 1968, he was awakened by a sensation of fullness in the lower part of the abdomen, and subsequently passed a grossly bloody bowel movement. Later that day he noted petechiae on his extremities and scalp; he also bled from numerous razor nicks. There was no history of gastrointestinal bleeding, nor of any type of abnormal hemorrhage. The only other prescribed medication was erythrityl tetranitrate (Cardilate), four to six tablets a day, which he had been taking since October 30, 1967. There was no history of toxic exposure.

Examinations on March 11, 1968, revealed multiple petechial lesions over the entire body, including the face and scalp. There was no lymphadenopathy or hepatosplenomegaly. The blood hemoglobin level was 13.6 g/100 ml, hematocrit reading was 41%, the white cell count was 4,900/cu mm, with a normal differential count, and the platelet count was 10,000/cu mm. A stool specimen was strongly positive for occult blood. Acetaminophen therapy was discontinued, and the patient was then given prednisone, 40 mg a day orally. Clinical improvement was rapid, and there was no further rectal bleeding. By March 14, 1968, the purpura had cleared. The platelet count was 130,000/cu mm, blood hemoglobin level, 13.7 g/100 ml, and the white cell count, 6,800/cu mm with a normal differential count. The dosage of prednisone was reduced to 30 mg a day for two days, and then to 20 mg a day. The patient was examined on March 20, 1968, at which time his skin was clear and the platelet count was 250,000/cu mm. Prednisone was discontinued. At follow-up examination from 1970 to 1973 the patient reported no recurrence of the petechiae or rectal bleeding.

Comment. When the platelet count was 170,000/cu mm, the patient's serum was tested for platelet agglutinins. Various dilutions of the patient's serum, with and without the addition of a 10 mg/100 ml solution of pure acetaminophen, were mixed with normal platelet-rich plasma, incubated overnight at 5 C and examined microscopically for agglutination. No agglutination was seen in any mixture. Furthermore, the drug had no effect on clot retraction in normal blood to which the patient's serum had been added.

Discussion

Acetaminophen, an aniline derivative, is a physiologic metabolite of acetanilide and acetophenetidin, and is probably responsible for the pharmacologic action of the latter.[2] As an analgesic and antipyretic it is comparable to aspirin. One report[3] suggests that acetaminophen may be more effective than aspirin in painful musculoskeletal disorders; however, acetaminophen has no intrinsic antirheumatic properties.

Significant adverse effects and idiosyncratic reactions are rarely associated with the administration of acetaminophen. Gastrointestinal distress and tinnitus occur with the same frequency as with aspirin. Loss of blood from the gastrointestinal tract is associated with the use of acetylsalicylic acid; this seldom occurs with acetaminophen. Hepatic necrosis,[4, 5] renal toxicity,[6] and multiple system involvement, including hemorrhagic diathesis, have been associated with overdosage of acetaminophen.

Unlike other aniline derivatives, acetaminophen does not cause hemolysis or methemoglobinuria.[7] Agranulocytosis, not associated with the concurrent administration of acetophenetidin, has been reported.[8] Acetaminophen does not alter hemostasis in most normal individuals.[9] Eisner and Shahidi[10] have recently reported an example of immune thrombocytopenia in which a metabolite of acetaminophen and not the drug itself was the antigenic substance. Such a mechanism was not investigated in this case.

In the case reported here there was close temporal association between thrombocytopenia and the administration of acetaminophen. However, the drug had no effect on clot retraction and produced no platelet agglutination in vitro. The pure drug and not the commercially available tablet was used in those tests. The patient was also taking erythrityl tetranitrate, but there was no relationship between the ingestion of that drug and the throm-

bocytopenia. The patient has continued to take this medication without any complications. No other cause for the acute thrombocytopenia was found, and although idiopathic thrombocytopenic purpura, a rare disorder in a 61-year-old man cannot entirely be excluded, it seems an unlikely cause. The onset of thrombocytopenia coincided with the start of acetaminophen therapy, and a rise in the platelet count coincided with discontinuance of the drug and the start of steroid therapy. There seems to be presumptive evidence that the thrombocytopenia resulted from ingestion of acetaminophen.

Summary

A case of reversible thrombocytopenic purpura associated with acetaminophen therapy is reported. The history of toxicity and idiosyncratic effects of the drug are reviewed. An antiplatelet factor related to acetaminophen was not detected by in vitro studies.

References

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