Communications

Methylphenidate and Idiopathic Thrombocytopenic Purpura—Is There an Association?

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Methylphenidate (Ritalin) is a central nervous system stimulant widely used for the treatment of attention deficit disorders. Despite extensive pediatric use for more than 20 years, the paucity of reports in the literature of adverse side effects is notable. The *Physicians' Desk Reference* and approved drug package inserts list numerous "hypersensitivity" reactions including thrombocytopenic purpura among other adverse reactions.[1] There are, however, no substantiated reports in the English literature of the occurrence of idiopathic thrombocytopenic purpura (ITP) in association with methylphenidate usage, although the concern over hematologic side effects has been voiced elsewhere.[2,3]

A case report of a patient who developed idiopathic thrombocytopenic purpura while receiving methylphenidate therapy follows.

Case Report

A seven-year-old patient presented to the Pediatric Outpatient Department because of unexplained bruising, epistaxis, and gingival bleeding for $2^1/_2$ days. Her past medical history was positive for prematurity and mild neonatal asphyxia, child abuse, and frequent streptococcal pharyngitis, which had led to elective tonsillectomy one year prior to presentation. She had developed school and behavior problems including attention deficit disorder and, seven months prior to presentation, was begun on methylphenidate 10 mg twice a day. She had been examined two weeks prior to presentation for a mild upper respiratory tract infection. Her family history was positive for attention deficit disorder in a five-year-old brother, who was also treated with methylphenidate, but negative for bleeding problems or easy bruisability.

On physical examination she was a well-developed, well-nourished white girl in no distress weighing 23.2 kg, with a height of 118 cm. Her vital signs were normal. Her skin was notable for countless petechiae over the entire dermal surface, most concentrated over her buttocks. Numerous areas of purpura were noted, especially over the buttocks and extremities. There were multiple areas of buccal mucosal and gingival bleeding with a large hematoma present on the left lateral surface of her tongue. Clotted blood was seen in her nostrils and ear canals bilaterally. She did not appear pale. Her physical examination was otherwise normal. Her laboratory evaluation showed hematocrit 40 percent, hemoglobin 14.8 g/dL, white blood cell count $12.5 \times 10^3/\mu L$, with 66 percent neutrophils, 26 percent lymphocytes, 1 percent atypical lymphocytes, 4 percent monocytes, and 3 percent eosinophils. Platelet count was 26,000/mm^3, and the peripheral smear was notable only for a lack of platelets; red cell morphology was normal. Antinuclear antibody was negative.

The patient was admitted and methylphenidate was discontinued. Bone marrow aspiration showed normal to increased megakaryocytes with normal red and white cell precursors. A diagnosis of idiopathic thrombocytopenic purpura was made, and the patient was begun on 50 mg of

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prednisone daily. Her platelet count fell to 5,000/mm^3, and when continued epistaxis could not be controlled with local epinephrine and packs, she was transfused with three units of platelets with good results. Within one week her platelet count had risen to 123,000/mm^3, and her petechiae had begun to fade. She was discharged on 50 mg of prednisone daily, but this dosage was tapered to 2.5 mg daily within one month. At this point new petechiae were noted, and her platelet count fell to 43,000/mm^3; her prednisone dose was raised again to 50 mg daily, again with a noted rise in platelet count. Her prednisone dosage was then tapered more slowly on an every other day schedule and five months later, discontinued. There has been no recurrence of petechiae or bruising one year later. Because the family would not consent to a challenge test of methylphenidate following recovery, her behavior problems have been managed without the drug.

Comment

Various side effects have been reported with methylphenidate treatment including insomnia, abdominal pain, adverse behavior changes, and an increased incidence of seizures.[4] There is evidence of exacerbation of Gilles de la Tourette's syndrome in certain children while receiving the drug,[5,6] and Sverd et al[7] reported two cases of apparent allergic skin manifestations associated with methylphenidate usage. Probably the most well-known complications are the suppressive effects of methylphenidate on appetite and subsequent growth retardation as reviewed in 1979 by Roche and colleagues.[8]

Two cases of "easy bruisability" in patients receiving the drug were reported to Ciba-Geigy, manufacturers of Ritalin, one in 1960 and one in 1968. In 1976 they received a documented report of a 10-year-old boy who was noted to have easy bruisability with a platelet count of 10,000/mm^3 after receiving 20 mg of methylphenidate daily for six months. He responded to platelet transfusions and high-dose prednisone therapy (personal communication, Patricia M. Gibney, MD, April 19, 1982). None of these cases has been reported in the medical literature, and an extensive search has failed to locate any published reports of adverse hematologic effects noted with this drug.

Drug-induced thrombocytopenic purpura has been well known to occur with other therapeutic agents, including quinine, quinidine, diuretics, and sulfonamides.[9] In 80 percent of childhood idiopathic thrombocytopenic purpura, a viral infection, occurring three weeks prior to the appearance of purpura, is implicated in the pathogenesis of the disorder.[10] It is highly possible that in the case just presented the etiology of the patient's idiopathic thrombocytopenic purpura may well have been her preceding upper respiratory tract infection rather than the methylphenidate, which she had taken without difficulty for seven months prior to the onset of her hematologic disorder. Given the widespread occurrence of upper respiratory tract infections in school-age children, it may be possible that a viral illness, not methylphenidate, was etiologically related to the three other cases of idiopathic thrombocytopenic purpura reported to the drug manufacturer.

It is hoped that the report of this case will stimulate others to report their experience, or lack thereof, regarding the association of methylphenidate and idiopathic thrombocytopenic purpura. Because of the importance of this drug to the management of certain children with attention deficit disorder and its current widespread use in thousands of children, it seems important to justify with data the current precaution that "periodic CBC, differential and platelet counts are advised during prolonged therapy"[1] or eliminate the precaution as a recommendation to clinicians.

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