QUININE-ASSOCIATED IMMUNE THROMBOPENIA, NEUTROPENIA, AND RENAL FAILURE IN A PATIENT WITH KLINEFELTER'S SYNDROME

To the Editor:

Quinine-associated thrombocytopenia and hemolytic uremic syndrome (with renal failure and microangiopathic red blood cell changes) is a recently described entity.[1,2] I recently cared for a patient with a similar illness who developed varying degrees of leukopenia, thrombopenia, and renal failure after quinine ingestion. My patient had the incidental finding of Klinefelter's syndrome. Three of the four previously described cases occurred in phenotypic females; cytogenetics of the phenotypic male are not described.[1] The observation that four of the five described cases have occurred in patients who presumably have two X chromosomes may help define targets for further investigation.

A 20-year-old white man was initially hospitalized in January 1988 because of myalgia, fever, and pancytopenia. Laboratory studies are shown in Table 1. A bone marrow examination was normal; rheumatoid factor, antinuclear antibody, and human immunodeficiency virus antibodies were absent. An etiology was not found for either the pancytopenia or the fever; he was treated with empiric antibiotics, and recovered completely. I first evaluated him in February 1988. He had a history of asthma and periodic use of an epinephrine inhaler. He mentioned quinine ingestion in connection with his January 1988 hospitalization. Laboratory results are shown in Table 1.

In March 1988, he developed myalgia and diffuse arthralgia and took two nonprescription quinine tablets. Fever, nausea, vomiting, and frontal headaches developed, and he was hospitalized. His fever was 100°F. Meningismus, ecchymoses over the extremities without petechiae, and nonpalpable spleen and lymph nodes were found. Cerebrospinal fluid examination was normal; splenomegaly was present on abdominal scanning. Serum haptoglobin was undetectable; third and fourth components of complement (ie, C3 and C4) were low, but total hemolytic complement was normal. No pathogens were isolated. Schistocytes could not be found on multiple examinations of the peripheral blood. Bone marrow examination performed on the second hospital day was histologically normal. Chromosomal analysis (performed at SmithKline Bioscience Labs, Van Nuys, CA) showed a 47XXY chromosomal complement in all cells examined. Because of the suspicion of lymphoma and an undiagnosed abdominal catastrophe, diagnostic laparotomy was performed and findings were normal. Pathologic examination of splenic and lymph node tissue was unremarkable. He recovered completely after hemodialysis, plasmapheresis, and empiric antibiotics. A third hospitalization for neutropenic fever occurred in January 1991; no history of quinine ingestion could be elicited.

This young man had at least three eipsodes characterized by varying degrees of fever, pancytopenia, renal failure, shock, coagulopathy, and complement activation, which were unexplained. Quinine ingestion, either overt or surreptitious, temporally preceded each episode. The spectrum of quinine-dependent antibodies and their targets, whether endothelial membranes,[2] platelet glycoproteins,[3] complement-activating surfaces (as suggested by this case) remains to be defined. Patients who present with unexplained, episodic neutropenia, thrombopenia, or hemolytic uremic syndrome should be carefully questioned regarding the ingestion of quinine tablets, which may have been obtained without prescription.

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Table 1. Clinical Laboratory Values in a Patient With Episodic Quinine-Related Immune Thrombopenia, Neutropenia, and Renal Failure

Date	WBC (4.8-10 × $10^3/\mu L$)	Hb (14-18 g/dL)	Platelets (140-400 × $10^3/\mu L$)	Prothrombin Time	Partial Thromboplastin Time	Serum Creatine
3/8/83	7.0	12.9	NM			0.9
1/23/88	0.6	13.8	104	15.8/12.4	51.0/32	1.3
1/27/88	3.5	12.6	96	11.0/11.6	25.7/32	1.0
2/17/88	5.6	13.5	219			
3/13/88	2.0	13.9	22	11.9/11.9	33/27	2.9
3/17/88	1.1	10.7	64			9.2
4/4/88	4.5	11.4	NM			1.1
5/17/91	7.2	13.1	574			
1/5/91	1.2	13.4	260			1.2
1/19/91	7.8	14.4	254			1.2

Boxed areas represent periods of hospitalization. Prothrombin and partial thromboplastin times are expressed in seconds as patient specimen over control plasma.

Abbreviations: WBC, white blood cell count; Hb, hemoglobin; NM, not measured.

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