INTRODUCTION

Traditional Chinese medicines (TCMs) are commonly used for a wide range of conditions in east Asian countries, including Korea. TCMs contain heavy metals, such as arsenic, cadmium, mercury, and lead (1, 2). Of these, arsenic and lead can cause hematologic changes, including anemia, neutropenia, and thrombocytopenia (1, 2).

Exposure to arsenic compounds usually follows ingestion or inhalation, and can occur during the occupational exposure of metal workers or workers engaged in the manufacturing or application of arsenical pesticides and herbicides, or non-occupational exposure resulting from the ingestion of contaminated well water, dried milk, soy sauce, or moonshine whiskey (3-5). Short-term arsenic poisoning may cause neuropathy and intravascular hemolysis, while long-term exposure is associated with the development of cancer (3-7).

Here, we report a severe hemolytic anemia induced by arsenic intoxication after the long-term ingestion of TCM.

CASE REPORT

A 51-yr-old woman was admitted to Chonnam National University Hospital with exertional dyspnea and dizziness for 4 weeks. She also complained of tingling sensations in her palms and soles that had been present for a long time. Her family had no medical problems in the past. Twelve years before the admission, she was diagnosed as neurocysticercosis. She has ingested a TCM for about 12 yr instead of undergoing medical therapy for the disease. She was presented with a severe Coombs'-negative hemolytic anemia with hemosiderinuria. The urine arsenic level was elevated suggesting the arsenic intoxication as a cause of the anemia. She was treated successfully with therapeutic red cell exchange without any sequelae.
Antinuclear antibodies, anti-Sm antibodies, anti-DNA antibodies, anti-cardiolipin antibodies, lupus anticoagulant, and anti-2-glycoprotein IgG were all negative.

The peripheral blood smear showed polychromatophilia, anisocytosis, and macrocytosis. Both direct and indirect Coombs’ test results were negative. Osmotic fragility and glucose-6-phosphate dehydrogenase activity were appropriate to the reticulocyte count. Hemoglobin electrophoresis was normal. Sucrose lysis and Ham’s test were negative. The serum ceruloplasmin level and urine copper excretion were not elevated. A bone marrow biopsy showed a mild hypocellular marrow with 40% cellularity and erythroid hyperplasia (Fig. 1). However, numerous investigations failed to reveal a cause for the hemolysis.

She was treated empirically with prednisolone 1 mg/kg per oral daily in three divided doses for 6 weeks, but there was no improvements in the hemolytic anemia. Subsequently, four sessions of plasma exchange were performed as a salvage therapeutic intervention, resulting in mild improvement in the hemolysis. We measured the levels of some heavy metals found in TCMs. There was increased urinary excretion of arsenic of 67.2 μg/day (normal range; 0-25 μg/day). Other heavy metals included: serum cadmium 3.1 μg/dL (0-10 μg/dL), serum lead 5 μg/dL (0-60 μg/dL), and urine lead 6 μg/L (0-150 μg/L). Her hemolytic anemia improved gradually after therapeutic red cell exchange of 450 mL. After 1 month, her hemoglobin rose to 11.0 g/dL, and the reticulocyte count and urinary excretion of arsenic decreased to 2.2% and 13.0 μg/day, respectively. Her clinical course is described in Table 1. She is currently being followed monthly and there has been no deterioration in her condition.

**DISCUSSION**

Our patient was initially presented with severe intravascular hemolysis of unknown etiology. It is necessary to obtain a thorough history from patients, but physicians in east Asian countries often encounter difficulties in taking past histories from patients who frequently conceal traditional management method of diseases, including the ingestion of TCMs. Arsenic intoxication mainly occurs through occupational exposure.
Hemolytic Anemia Due to Arsenic Intoxication

exposure, including work with smelters, flue maintenance operations, pesticides, herbicides, and preservatives. In addition, non-occupational exposure, such as ingestion of contaminated well water, dried milk, soy sauce, and moonshine whiskey, has the potential to cause arsenic intoxication. In chronic arsenic intoxication, despite insufficient evidence of its effectiveness, the systemic absorption of arsenic, is measuring arsenic levels in the hair and nails (3, 4). Therapeutic red cell-exchange, non-occupational exposure, such as ingestion of contaminated well water, dried milk, soy sauce, and moonshine whiskey, has the potential to cause arsenic intoxication (3, 4). The hematologic manifestations of acute and chronic arsenic intoxication include intravascular hemolysis, leukopenia, and thrombocytopenia (3, 4).

Our patient ingested TCM for about 12 yr intermittently, and continuously for the most recent 6 months. Although hemolytic manifestations occur mainly in acute arsenic intoxication, it is unclear whether the hemolytic anemia in our patient was induced by the recent or long-term ingestion of TCMs. Her bone marrow hypocellularity, peripheral pancytopenia, and long-term peripheral neuropathy were thought to reflect chronic intoxication for 12 yr. In contrast, the intravascular hemolytic anemia was thought to reflect acute intoxication for the last 6 months. Our patient is therefore suggesting to have coexisting acute and chronic intoxication.

The most useful laboratory test for confirming recent arsenic exposure is the total urine arsenic level (1, 4, 10). Nonexposed persons have levels below 10 μg/g of creatinine (g Cr), while persons exposed to 0.01 mg/L have levels of 50 μg/g Cr, and acute poisoning is caused at 1,000 μg/g Cr or higher levels (4). Another diagnostic method for arsenic intoxication, especially the systemic absorption of arsenic, is measuring arsenic levels in the hair and nails (3, 4). Therapeutic red cell-exchange is used to treat patients with hemolytic anemia due to arsenic intoxication, despite insufficient evidence of its effectiveness (11). In addition, chelating agents, including D-penicillamine, dimercaprol, dimercaptosuccinic, or dimercaptopanesulfonic acid, used clinically in chronic arsenic poisoning, but the chelating agents are not effective for treating established arsenical peripheral neuropathies or arsine poisoning (3, 4).

Plasmapheresis given to our patient as an empirical treatment was not an effective intervention for the arsenic intoxication. However, the therapeutic red cell-exchange resulted in gradual improvement of her hemolytic anemia within a few weeks without any complications. In this patient, we performed the therapeutic red cell-exchange with half volume of total red cell, as described a previous report in a patients with malaria (12).

In summary, we report a case of arsenic intoxication after long-term ingestion of TCM presenting with intravascular hemolysis that was treated successfully with therapeutic red cell-exchange.

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