CASE REPORT

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Sudden Unexpected Death in a Patient with Splenic Sequestration and Sickle Cell-β^+-Thalassemia Syndrome

REFERENCE: Hutchins KD, Ballas SK, Phatak D, Natarajan GA. Sudden unexpected death in a patient with splenic sequestration and sickle cell-β^+-thalassemia syndrome. J Forensic Sci 2001;46(2):412–414.

ABSTRACT: Acute splenic sequestration crisis is a rare disorder that usually occurs in children, with sickle cell anemia, who are under the age of five years. A few cases have been described in adults with heterozygous sickle cell syndromes. Though this entity can be fatal there have been no reported cases associated with sudden death. We describe a case of sudden, unexpected death, associated with splenic sequestration, in a 29-year-old African-American man with undiagnosed sickle cell-β^+-thalassemia syndrome.

KEYWORDS: forensic science, forensic pathology, sudden death, acute splenic sequestration, thalassemia, sickle cell disorders

The expression of clinical severity in patients who are double heterozygotes for hemoglobin S and β-thalassemia depends on the production of normal β-globin (1). Patients with sickle cell-β^+-thalassemia produce some normal β-globin, and, consequently tend to be asymptomatic or have a mild clinical course (1). Unlike patients with sickle cell anemia, whose spleen eventually becomes fibrotic, patients with sickle cell-β^+-thalassemia continue to have splenomegaly into adulthood (2). Adults with splenomegaly are vulnerable to episodes of acute splenic sequestration; a disorder usually associated with children with homozygous, and rarely heterozygous, sickle cell syndromes (2,3). Physiologically, this phenomenon is due to the obstruction of the venous outflow of a distensible spleen by sickled red cells (4). Fatalities may occur as a result of anemia, hypoxemia, hypovolemia, and sepsis (4). Though there has been a reported fatal case of splenic sequestration crisis in a hospitalized adult patient with sickle cell-β^+-thalassemia, to our best knowledge this entity has not been associated with sudden, unexpected death in adults (5). We present a case of splenic sequestration in an adult with sickle cell-β^+-thalassemia and briefly discuss the causes of sudden death in the heterozygous sickle cell syndromes.

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Received 30 Nov. 1999; and in revised form 5 Jan, 22 Feb., and 7 April 2000; accepted 10 April 2000.

Case Report

A 29-year-old African-American man was found dead in his home. He visited his local physician the previous day complaining of cold, cough, and fever. On physical examination his temperature was 99°F and the oropharynx appeared reddened. Prescriptions were given for vitamins and cough suppressants. The next morning he complained of chest pain and 10 h later was found dead. The only past medical history was a diagnosis of sickle cell trait made when he was a child. There was no history of crises or other medical complaints due to this diagnosis. The postmortem examination revealed a well developed, well nourished, 262 lb, 70 in. man. Internal examination showed an 1132-g spleen measuring 25 × 15 × 10 cm. The heart weighed 404 g and the left ventricle was 1.5 cm in thickness. There was some myxomatous change of the mitral valve. Histologically, there was vascular dilatation and congestion with abnormally shaped and sickled red blood cells in the spleen and other parenchymal organs including the heart and brain. Macrovesicular steatosis was present within the liver sections. Examination of a postmortem blood smear revealed many abnormal and sickled red cells (Fig. 1). There was 29% hemoglobin A and 71% hemoglobin S on electrophoresis. Molecular diagnostics on genomic DNA isolated from peripheral blood white cells showed that the patient was doubly heterozygous for sickle cell and β-thalassemia genes leading to an accurate diagnosis of sickle cell-β^+-thalassemia. Blood and splenic cultures revealed only postmortem growth. Vitreous electrolytes were not diagnostic of dehydration. Toxicologic analysis on blood revealed trace amounts of Amitriptyline (0.06 mg/L) and Nortriptyline (0.01 mg/L).

Discussion

The major heterozygous sickle cell conditions include sickle cell trait, sickle cell-thalassemia (β,α), and sickle cell-hemoglobin C. Though these entities are described as either asymptomatic or having milder clinical expression than sickle cell anemia, fatal cases

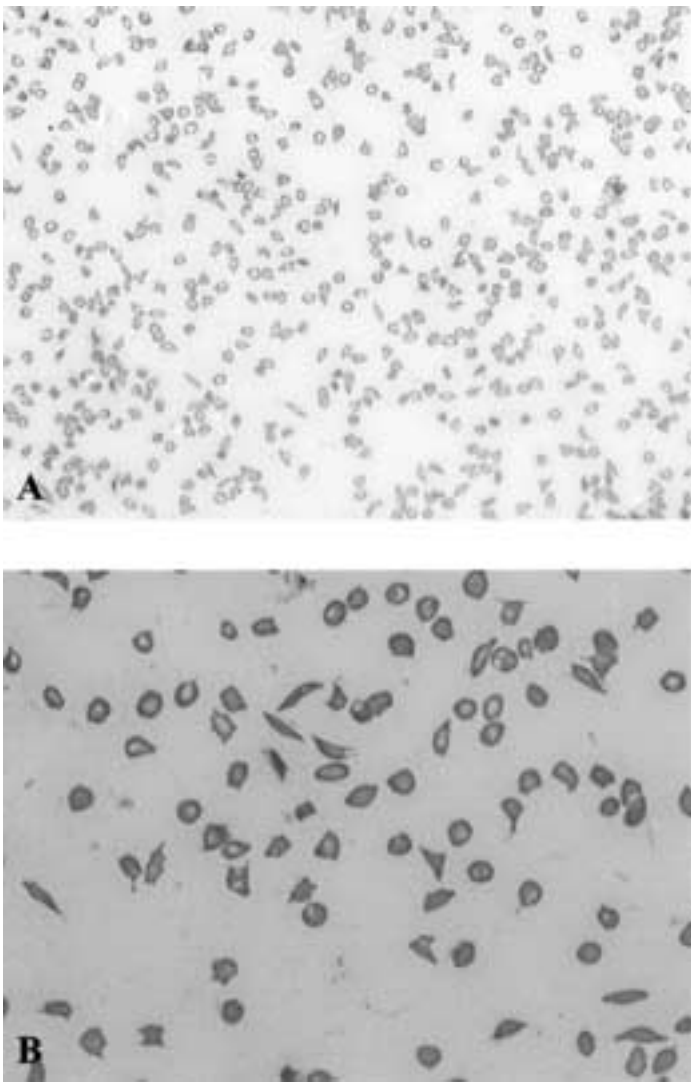

FIG. 1—*In panels A and B low and high power views of the patient's postmortem blood smear reveal many abnormal and sickled red blood cells (panel A original magnification × 100; panel B original magnification × 300).*

have been reported. Sudden death due to exertional collapse has been described in patients with sickle cell trait (6–8). Most of these cases have concerned military recruits who collapsed during exertion in basic training (9). Patients with sickle cell trait have also been reported to suffer from crises when under physiologic stress such as hypoxia, acidosis or dehydration (10). Fatalities with autopsy-proven massive fat and bone marrow emboli have been described in patients with both sickle cell-hemoglobin C and sickle cell-β^+-thalassemia (11–13). In relation to our case, reports of deaths due to splenic sequestration have been described in one adult patient with sickle cell-β^+-thalassemia and in a few patients with sickle cell-hemoglobin C (4,14,15). Other entities, which cause potentially life threatening illnesses in these disorders, include rhabdomyolysis, metabolic renal disorders and renal papillary necrosis, while the rare, aggressive neoplasm, renal medullary carcinoma, has been described in patients with sickle cell trait (16–19). The proposed etiologies of these various disorders have not been specifically defined, though vascular occlusion with sickled red blood cells may play a contributory role. In this case the patient had a previous diagnosis of sickle cell trait but the presence of splenomegaly, and the high hemoglobin S concentration, suggested some other sickle cell syndrome (2). Analysis of genomic DNA confirmed the presence of sickle cell-β^+-thalassemia. Pathologically, there was not only splenic sequestration, but also generalized vascular congestion and dilatation with sickled red blood cells. Hypovolemia due to the splenic sequestration and hypoxemia due to anemia and decreased oxygen carrying capacity may combine to contribute to vascular collapse in these patients. Also, any element of hypoxia, dehydration or sepsis may induce sickling and lead to an adjuvant fatal effect in these disorders (3). Unfortunately, the specific precipitating factors leading to death in this case are unknown. Because fatalities, though rare, have been described in association with these sickle cell syndromes, it is important, when appropriate, that these disorders be considered. A complete autopsy, histologic examination, hemoglobin electrophoresis, vitreous electrolytes, urine myoglobin, microbiologic studies and DNA analysis should be evaluated, and may confirm the presence of one of these rare syndromes. Prudent forensic practice would include these studies in any unexplained sudden death in a young African-American patient, especially in sensitive cases, such as those involving police custody, in which the initial cause of death seems a mystery (20).

Acknowledgments

We wish to thank Edilma Cervantes and Anita Horsey for their excellent photography, Maureen Gardner for review of this manuscript, and Patricia Vimieiro of Vimieiro Images for preparation of the figures.

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