H79 Sudden Death Due to Leukostasis in a Subject With Untreated Chronic Lymphocytic Leukemia (CLL)

Lorenzo Gitto, MD, State University of New York Upstate, Department of Pathology, Syracuse, NY 13210; Rohin Mehta, MD, State University of New York Upstate, Department of Pathology, Syracuse, NY 13202; Kanish Mirchia, MD, State University of New York Upstate, Department of Pathology, Syracuse, NY 13202; Christopher Ramos, MD, State University of New York Upstate, Department of Pathology, Syracuse, NY 13202; Serenella Serinelli, MD, PhD*, State University of New York Upstate, Department of Pathology, Syracuse, NY 13210*

Learning Overview: After attending this presentation, attendees will have a better knowledge of the pathophysiology of death due to leukostasis in subjects with a hematologic malignancy.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by providing an overview of the possible mechanisms of sudden death due to leukostasis in subjects with CLL in the absence of preceding symptoms.

CLL is a chronic lymphoproliferative disorder characterized by monoclonal mature B cell proliferation. It comprises approximately 25% of all leukemias in the United States, with a slight preference for the male sex. CLL is usually asymptomatic and the incidental finding of lymphocytosis or lymphadenopathy typically leads to the diagnosis. Typical symptoms such as fever, weight loss, night sweats, and fatigue are present in 5%–10% of cases.

Hyperleukocytosis (white blood cell count $>100\times10^9$/L) is present in a large proportion of patients at initial presentation, but symptomatic hyperleukocytosis (leukostasis; usually >400 x 10^9/L) is an extremely uncommon presentation. Clinical manifestations are secondary to the decreased tissue perfusion due to the intravascular accumulation of large aggregates of leukemic cells. These aggregates can be observed in virtually every organ, but the symptomatology is usually related to Central Nervous System (CNS) and pulmonary involvement.

The case of a 70-year-old White male with a medical history of dementia, bipolar disorder, hypertension, and obesity who was found unresponsive in his bed by his wife is reported. He did not have any symptoms before death.

Autopsy examination showed an obese male (BMI = 36.6kg/m2) with evidence of severe atherosclerotic-hypertensive cardiovascular disease, consisting of heart enlargement (570 grams) and critical (up to 90%) narrowing of the major coronary arteries. Massive enlargement of the spleen (2,100 grams) and numerous firm nodules within the spleen parenchyma were present. Diffuse lymphadenopathy and nodules in the left kidney and liver were also seen. Histology and immunohistochemistry were consistent with diffuse extranodal CLL/Small Lymphocytic Lymphoma (SLL). In addition, pulmonary, brain, cardiac, and renal small vessels were filled with leukemic cells, a finding highly suggestive of leukostasis. The leukostasis could have further reduced the blood supply to the heart muscle, which was already compromised by coronary artery disease, and to brain and lung, leading to fatal complications.

Two main theories have been proposed to explain the pathophysiology of leukostasis in leukemia: these are not mutually exclusive, and both eventually result in organ damage. The first theory centers on the idea that with a higher-than-the-standard-degree of viscosity, stasis can occur in the microvasculature due to adhesive interactions between leukemic blasts and their inherently rigid cell membrane compared to Red Blood Cells (RBCs). The second theory involves local tissue hypoxemia due to higher metabolic demand of the neoplastic cells coupled with the release of damaging cytokines.

Although extremely rare, leukostasis is a life-threatening complication in patients with CLL. Pathologists should be aware of this complication when investigating sudden deaths if autopsy evidence consistent with leukemia is observed.

Sudden Death, Leukostasis, Chronic Lymphocytic Leukemia