

# Leukostasis Presenting as Focal Hemorrhagic Lesions in the Brain: An Underrecognized But Life-threatening Complication of Leukemia

Singh Ria BS<sup>1,\*</sup>, Cotant Matthew B MD<sup>2</sup>, Krishnan Anant MD<sup>3</sup>

<sup>1</sup>Kansas City University College of Osteopathic Medicine 1750 Independence Avenue, Kansas City, Missouri, 64106

<sup>2</sup>Corewell Health William Beaumont University Hospital 3577 West 13 Mile Road, Royal Oak, Michigan, 48073

<sup>3</sup>Corewell Health William Beaumont University Hospital 3601 W 13 Mile Rd, Royal Oak, Michigan, 48073

\*Corresponding author: [ria.singh@kansascity.edu](mailto:ria.singh@kansascity.edu)

Received August 17, 2024; Revised September 19, 2024; Accepted September 25, 2024

**Abstract** Leukostasis, which refers to increased blood viscosity due to the increased white blood cell count, is a critical condition observed in acute myeloid leukemia and is associated with significant morbidity and mortality. The excessive accumulation of white blood cells can lead to the occlusion of small vessels in various body parts such as brain and lungs, resulting in corresponding clinical symptoms. We discuss a patient with history of breast cancer and newly diagnosed leukemia whose head CT revealed multiple defined hemorrhages that were suspected to represent hemorrhagic metastasis. Findings on serial imaging and correlation with patient's blood work, led to an alternate diagnosis of leukostasis with intracranial manifestations. This was also confirmed on the subsequent MRI. The intracranial involvement of leukostasis is rarely discussed in practice or literature such that we hope our case report will facilitate increased awareness of the condition.

**Keywords:** Acute myeloid leukemia, leukostasis, hemorrhages, white blood cells, blood viscosity

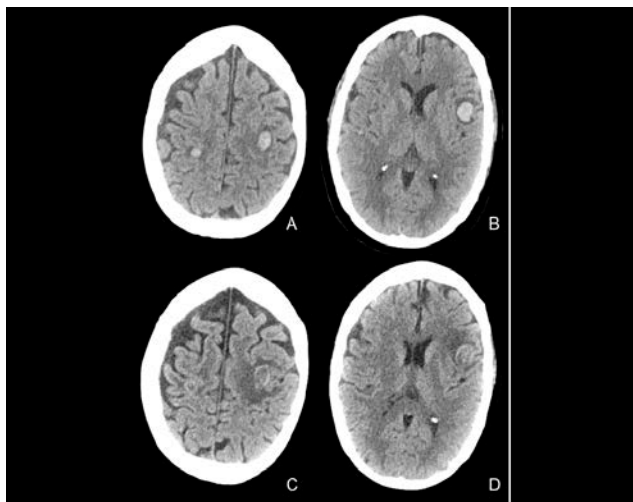
**Cite This Article:** Singh Ria BS, Cotant Matthew B MD, and Krishnan Anant MD, "Leukostasis Presenting as Focal Hemorrhagic Lesions in the Brain: An Underrecognized But Life-threatening Complication of Leukemia." *American Journal of Medical Case Reports*, vol. 12, no. 9 (2024): 138-140. doi: 10.12691/ajmcr-12-9-2.

## 1. Introduction

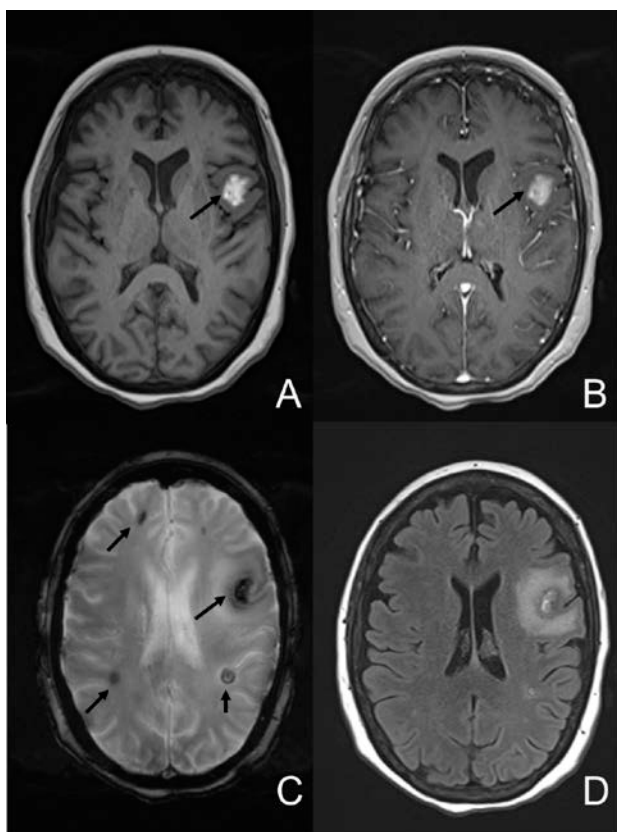
Leukostasis refers to the clinical syndrome that results from increased white blood cells (WBCs) circulating in the blood. This marked elevation in the number of WBCs, as seen in myeloid leukemia, results in the expansion of the fractional volume of leukocytes leading to an increase in blood viscosity. In addition, the relatively rigid nature of leukemic cells and their enhanced expression of surface molecules like selectins and intracellular adhesion molecules (ICAMs) lead to consequent stasis and aggregation of leukocytes in small blood vessels [1]. This can result in hypoperfusion of the involved organ and constitutes a medical emergency with a mortality rate up to 40% [2]. The associated signs and symptoms are nonspecific and include but are not limited to dyspnea, hypoxemia, dizziness, and visual changes [3]. We report a unique case of leukostasis in a patient with history of breast cancer and acute myeloid leukemia (AML). Initial head CT images revealed multiple hemorrhagic lesions that were suspected to represent hemorrhagic metastases but subsequently were identified as areas of hemorrhage associated with leukostasis. Our intent with this paper is to review the clinical presentation and imaging findings of this uncommon condition of leukostasis.

## 2. Case Presentation

A 66-year-old woman with medical history of breast cancer in remission, hypertension, hyperlipidemia, and chronic back pain was transferred to our hospital's intensive care unit (ICU) for severe shortness of breath and further management of newly diagnosed AML. In the next few days, she developed new-onset progressive right upper extremity and right lower facial weakness, prompting a non-contrast head CT to be ordered. The CT head (Figure 1) identified multiple somewhat rounded areas of hemorrhage within the cerebral hemispheres and the pons. Several follow-up CT scans showed no increase in the number or size of the hemorrhagic foci. By day 12, the areas of hemorrhage seen on the follow-up CT scans were observed to have improved. A brain MRI done two days later (Figure 2), confirmed lack of enhancement in the multiple subacute areas of hemorrhage, with improving edema; therefore, underlying metastatic lesions were considered much less likely as the cause of hemorrhage. The patient was subsequently treated with chemotherapy and leukopheresis for her AML. An additional follow-up MRI performed one month later (not shown) showed further improvement in the foci of hemorrhage.



**Figure 1.** Axial head CT images of patient from day of initial study (A, B) and 12 days later (C, D). Initial images (A, B) reveal multiple intracranial rounded areas of hemorrhage with surrounding edema. Follow-up study (C, D) demonstrates progressive decrease in density and size of hemorrhages without new hemorrhage or mass effect



**Figure 2.** MRI brain of the patient. Pre-contrast T1 (A), post-contrast T1 (B), gradient T2\* (C), and FLAIR T2 (D) images obtained on day 14. Multiple hemorrhages (black arrows) are seen within the brain with the largest in the left frontal operculum, which is surrounded by edema. There is no enhancement or mass associated with these hemorrhages

### 3. Discussion

AML is the most common adult leukemia [4]. It involves clonal expansion of blast cells in the peripheral blood and bone marrow resulting in ineffective erythropoiesis and bone marrow failure. As a result, the patient experiences a variety of symptoms including

recurrent infections, anemia, easy bruising, and bone pains. Depending upon the extent of anemia, a patient can also present with fatigue, lethargy, and dyspnea as seen in our patient [5]. Our patient presented with severe shortness of breath and subsequently developed right upper extremity and right lower facial weakness. A non-contrast head CT demonstrated multiple defined areas of hemorrhage. Considering her past medical history of breast cancer, these were initially thought to represent hemorrhagic metastasis.

However, in the subsequent CT scan performed 12 days later, the hemorrhages and surrounding edema improved, which is uncharacteristic of metastatic lesions. Following discussion of the improving intracranial hemorrhagic foci in the setting of very high number of blast cells, the neuroradiologist and oncologist favored leukostasis related intracranial hemorrhages as the most likely etiology and recommended an MRI. The lack of enhancement on MRI in any of the masses, along with the improved surrounding edema, effectively excluded metastases and myeloid sarcoma, the latter typically presenting as an enhancing, diffusion restricting T2 hyperintense mass [6]. Hyperleukocytosis is a medical condition characterized by a WBC count greater than 100,000 cells/ $\mu$ L and is found in 18% of patients with AML [7]. In some patients with AML, and rarely in patients with CML (chronic myeloid leukemia), there is a clinical condition called leukostasis that should be considered in the differential diagnosis. This refers to the reduction in blood flow as a result of increased viscosity due to the large number of circulating WBCs. The elevated white blood cell count seen in AML patients leads to intravascular accumulation of blast cells, resulting in the formation of small aggregates leading to stasis in the blood vessels and intravascular thrombosis [8]. Depending upon the site of thrombosis, this can result in severe respiratory distress, central nervous system abnormalities or other major organ dysfunction. Particularly regarding the nervous system, leukostasis can manifest as intracranial hemorrhage, focal neurologic deficit, coma and headache [9]. Imaging findings in leukostasis include areas of ischemia, foci of hemorrhages or CNS masses [10]. A definitive diagnosis of the condition is made by brain tissue biopsy but is not commonly performed due to the associated risks [11].

### 4. Conclusion

Leukostasis is an oncologic emergency resulting from the increased blood viscosity due to the extremely high white blood cell count seen in some leukemia patients. The associated aggregation and clumping of WBCs in the microvasculature results in intravascular thrombosis giving rise to neurologic, pulmonary or other major organ dysfunction symptoms. In our case presentation, the patient's foci of intracranial hemorrhage were found to be due to leukostasis given her high WBC count, history of breast cancer in remission and their improvement with in a relatively short period of time. Thus, in a patient with high attenuation or hemorrhagic lesions on head CT with an underlying history of AML, it is important to consider leukostasis in the differential diagnosis and discuss with the treating physician. Future studies should focus on

detailing the imaging criteria for leukostasis for its early diagnosis and treatment.

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