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Case Report

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Leukostasis With Isolated Central Nervous System Involvement in Chronic Phase of Chronic Myelogenous Leukemia

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Abstract

Chronic myelogenous leukemia (CML) is a hematologic malignancy with unique significance to the field of hematology and oncology, specifically due to the development of tyrosine kinase inhibitors (TKIs). CML often presents with nonspecific symptoms, and the quality of life in patients with CML has drastically improved as a result of TKIs. However, complications of CML including the risk of transforming into life-threatening blast crises continue to exist. Further, as most patients are asymptomatic in the chronic phase, patients often present with serious complications associated with noncompliance to TKIs. For example, central nervous system (CNS) manifestations of CML have been reported, both as the initial presentation of undiagnosed CML and as known complication of uncontrolled CML. Hyperleukocytosis is a manifestation of uncontrolled CML and leukostasis is a complication, occurring in cases of acute myeloid leukemia (AML). Here we present a rare case of leukostasis in a patient with known CML presenting on computed tomography (CT) as intracranial masses in the chronic phase. Our goal is to discuss this rare case of leukostasis in adult CML and describe its management.

Keywords: Chronic myelogenous leukemia; Hyperleukocytosis; Leukostasis; Central nervous system

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Introduction

Chronic myelogenous leukemia (CML) occurs in about 0.7 to 1 in 100,000 individuals per year according to several European registries and involves patients in the ages of 40 to 70s [1]. CML initially presents with nonspecific symptoms of fatigue, loss of appetite, weight loss, abdominal fullness and pain. Laboratory studies often exhibit leukocytosis with left shift. As a result of leukocytosis, patients develop splenomegaly, thrombosis, or abnormal bleeding [2]. Interestingly, some patients remain asymptomatic for long periods of time in the chronic phase (CP). According to the World Health Organization (WHO) criteria, CML is staged by the number of immature myeloid cells, or blasts, present in bone marrow (BM) or peripheral blood. The development of tyrosine kinase inhibitors (TKIs) has improved survival rates from < 15% to about 87% [2]. Furthermore, the progression of CML from CP to blast phase, leading to acute leukemia, has decreased from 20% to 1-1.5% [3]. Still, patients present with manifestations of noncompliance to TKIs, and untreated CML is associated with significant morbidity and mortality. In this case report, we discuss the case of a patient with known CML who presented with headache and hyperleukocytosis with findings of intracranial lesions. Upon pathology evaluation, the lesions were found to be the sequalae of leukostasis.

Case Report

We present the case of a 25-year-old male with known diagnosis of CML complicated by a history of hyperleukocytosis requiring leukapheresis and hearing impairment who initially presented to an outside institution with headache and associated nausea with vomiting and was transferred to our institution for higher level of care. Initial computed tomography (CT) of the head demonstrated multiple bilateral intracranial lesions, correlating with the patient's symptoms. Upon chart review, the patient had been diagnosed with CML about 10 years prior to his presentation and had been started on imatinib but reportedly was noncompliant. In addition, due to concern for resistance against imatinib, the patient had been started on dasatinib several years prior. The patient again reported he was

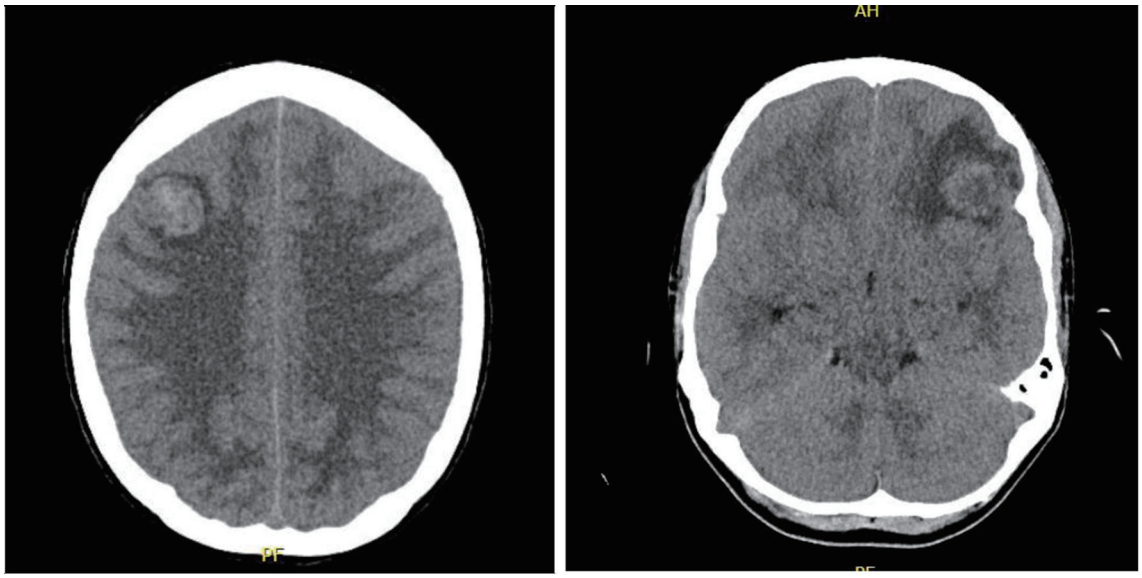

Figure 1. CT of head without contrast. Multiple lesions, prominently left frontal and right frontal lobe leukemic infiltrates with surrounding vasogenic edema and mass effect, concerning for a CNS manifestation of leukostasis. CT: computed tomography; CNS: central nervous system.

not taking dasatinib and had unfortunately missed many of his appointments in hematology clinic.

Upon presentation, the patient's laboratory findings were remarkable for leukocytosis with white blood cell (WBC) count of 4.95 × 10^{11}/L, anemia with hemoglobin (Hgb) of 5.6 g/dL, and thrombocytopenia with platelet count of 1.31 × 10^{11}/L. Upon initial examination, the patient was alert and oriented without focal neurologic deficits besides the known hearing impairment. Hematology and Oncology was consulted and given concern for leukostasis in the setting of hyperleukocytosis and brain lesions with the differential including myeloid sarcoma (MS), emergent leukapheresis was started with further cytoreduction by starting hydroxyurea 2,000 mg twice a day. The patient was also started on prophylactic allopurinol 300 mg daily with monitoring for tumor lysis syndrome (TLS) with daily complete metabolic panel, phosphorous, lactate dehydrogenase (LDH), and uric acid levels. By the time a dialysis line was placed for leukapheresis, the patient's WBC had worsened to 6.46 × 10^{11}/L but this improved to 6.05 × 10^{11}/L after the first session of leukapheresis.

Given the hemorrhagic intracranial lesions, Neurosurgery was consulted and recommended serial repeat CT imaging without emergent surgical intervention. Repeat CT of the head without contrast showed hyperdense/hemorrhagic multifocal rounded lesions (largest lesion of 2.2 × 2.5 × 2.6 cm in the left frontal lobe and 2.3 × 2.0 × 2.2 cm in the right frontal lobe) throughout the bilateral cerebral hemispheres with surrounding vasogenic edema and mass effect (Fig. 1). Temporizing measures including steroids was initiated due to evidence of cerebral edema and mass effect. The patient's serum WBC level peaked at 8.86 × 10^{11}/L and trended down with continued hydroxyurea. However, due to hemodynamic instability, the patient was unable to tolerate further sessions of leukapheresis and developed acute worsening of mental status with Glasgow coma scale (GCS) of 6, and intubated for airway protection. Due to further increase in the WBC to 6.66 × 10^{11}/L, the patient's hydroxyurea dose was subsequently increased to 2,000 mg three times a day. Repeat CT imaging of the head revealed new and developing uncal herniation. The patient became comatose with the lack of brainstem reflexes and determined to be clinically brain dead and an autopsy was requested by the patient's family.

The peripheral smear did not show any mutations associated with resistance against imatinib but otherwise demonstrated marked leukocytosis with left shift with only occasional blasts (1%) seen. In addition, flow cytometry was significant for 1.2% myeloblasts with no evidence of blast crisis, with findings consistent with the known CP of CML.

The neuropathology findings from the autopsy showed extensive microvascular and parenchymal involvement of the frontal lobe and brain stem by cells derived by the patient's known CML with marked leukemic infiltration concerning for leukostasis (Fig. 2). Histology further showed hemorrhagic lesions involving brain parenchyma with marked left-shifted myeloid cells and leukemic infiltrates, and congestion of blood vessels with white blood cells. Overall, early ischemic changes were noted, indicative of a global ischemic event. Immunohistochemical staining was obtained for further characterization of the intracranial lesions and was positive for myeloperoxidase (MPO), CD43, and CD68, further consistent with known CML (Fig. 3). Further, the intracranial masses stained negative for CD117, CD45, CD34, CD3, and CD20.

Discussion

CML arises from the fusion of the Abelson murine leukemia (ABL) gene with the breakpoint cluster region (BCR) gene

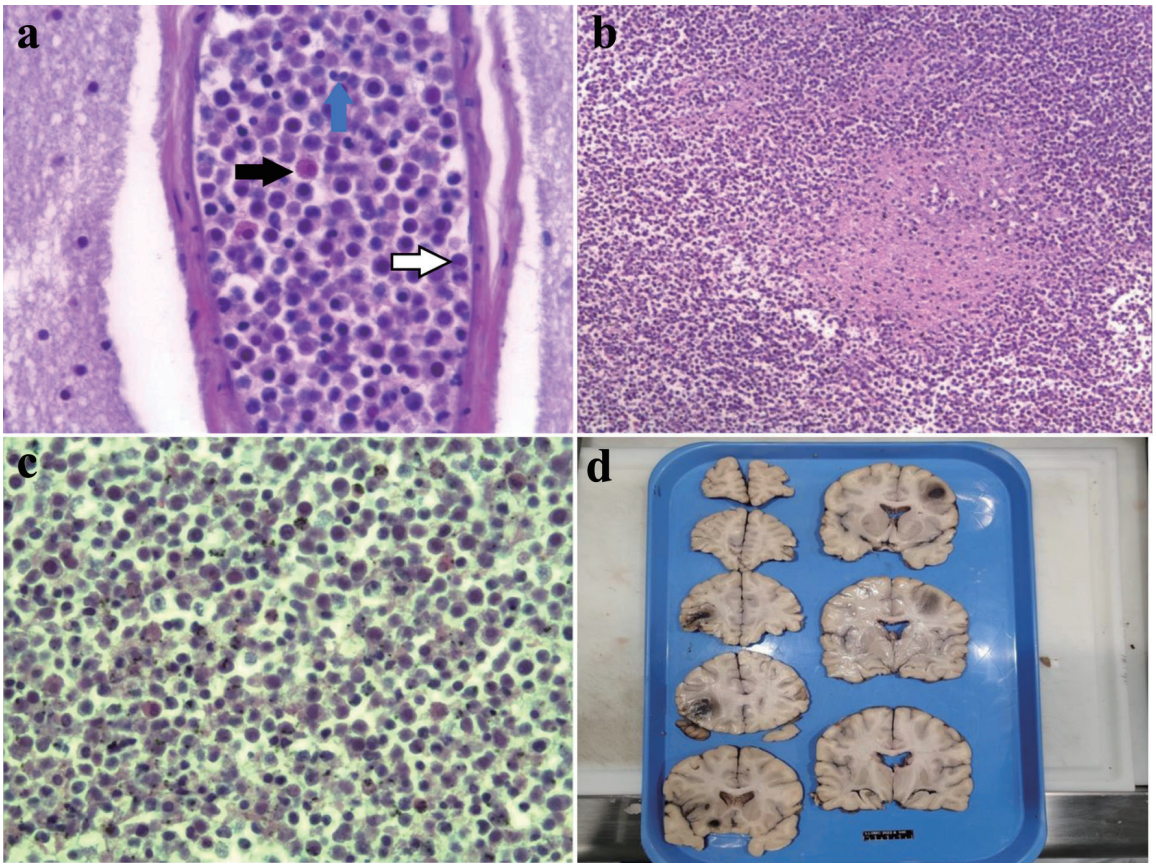

Figure 2. Autopsy images of hemorrhagic intracranial masses and pathology of mass lesions. (a) High power histology of the CML mass lesion in the brain. The black arrow represents an early myeloid cell (immature eosinophil), the blue arrow shows a neutrophil/band and the white arrow (with black outline) shows the monocytes. (b) Medium power histology of the CML mass with background of necrotic brain parenchyma. (c) High power histology of the tumor cells showing myeloid lineage including neutrophils and monocytes with myeloid precursors of various degrees of maturation. (d) Coronal sections of the patient's brain which demonstrates several hemorrhagic masses. CML: chronic myelogenous leukemia.

in the Philadelphia chromosome, a translocation of chromosomes 22 and 9 [4]. This fusion creates the oncoprotein which stimulates the tyrosine kinase pathway and further activates downstream pathways including the Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway. This leads to hematopoietic cell proliferation and resistance to apoptosis [4].

TKIs, which inhibit the adenosine triphosphate (ATP) binding site of the ABL-BCR oncoprotein, revolutionized the treatment and prognosis of CML. Currently, the Sokal, Hasford (Euro), and European Treatment and Outcome Study (EUTOS) prognostic scores are utilized to risk stratify patients into low, intermediate, and high risk of disease progression prior to starting TKIs [2, 4, 5]. For patients with intermediate or high-risk scores, second-generation TKIs are preferred over first-generation TKIs [6]. Unfortunately, BCR-ABL dependent and independent mutations and noncompliance lead to TKI resistance [4].

In current literature, there are cases of central nervous system (CNS) complications, including leukostasis and MS, associated with CML (Table 1) [3, 7-31]. Leukostasis occurs in the setting of hyperleukocytosis, defined as serum WBC greater than 1.00×10^{11}/L, which is a rare manifestation of several leukemias [32, 33]. Leukostasis is rare but most commonly associated with acute myeloid leukemia (AML) as an increased number of circulating leukemic blasts in the microvasculature cause vascular obstruction and tissue hypoxia [34-37]. The complications associated with the highest mortality risk of hyperleukocytosis are leukostasis, TLS and disseminated intravascular coagulation (DIC), with leukostasis being associated with a mortality rate of up to 40% [34, 38]. While the incidence of leukostasis is low in AML, leukostasis in patients with CML is extremely rare, occurring in the blast phase of CML compared to other phases [39]. A retrospective study of 256 pediatric patients with CML showed that 9.7% were diagnosed with leukostasis after developing symptoms such as headache, syncope, vision changes, and priapism [40]. In comparison, leukostasis in adults with CML has not been extensively studied due to its rare occurrence.

One proposed mechanism of leukostasis resulting in increased blood viscosity is the high fractional volume of leukocytes causing microvascular obstruction, ischemia, and endothelial dysfunction arising from damage to the vacular endothelium [41-43]. Patients often present with headache, diz-

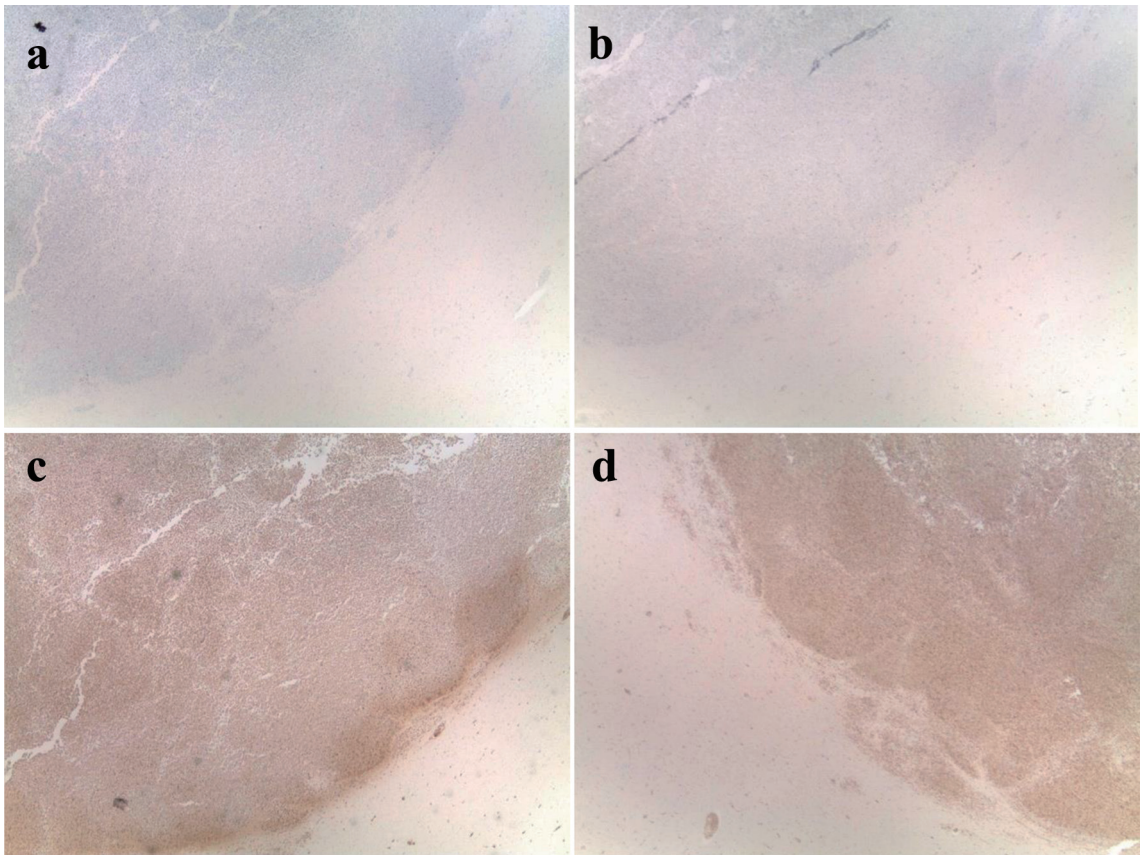

Figure 3. IHC staining of leukemic infiltrates in the frontal and brain stem lesions. IHC staining of the central nervous system lesions which was positive for MPO and CD68, consistent with known CML, and negative for CD20, confirming that the lesions do not originate from B-cell neoplasm. (a) IHC staining negative for CD20. (b) IHC staining negative for CD34. (c) IHC staining positive for MPO. (d) IHC staining positive for CD68. CML: chronic myelogenous leukemia; IHC: immunohistochemistry; MPO: myeloperoxidase.

ziness, confusion, tinnitus, blurred vision, delirium, ataxia, and coma, although other systems can also be affected [37]. Leukostasis may present on CT or magnetic resonance imaging (MRI) as hemorrhagic changes and areas of cerebral edema [44].

When hyperleukocytosis is suspected, prompt cytoreduction is recommended. Hydroxyurea is a commonly used medication along with systemic therapy [45]. Another key component of treatment of hyperleukocytosis is leukapheresis. Leukapheresis involves the immediate removal of the excess leukocytes via blood cell separators. However, hypercalcemia and thrombocytopenia are common complications of leukapheresis, and hemodynamically unstable patients may not tolerate leukapheresis as it can cause significant vasovagal response [45, 46]. Cranial irradiation can also be considered, though it is not a standard component of emergent management of leukostasis [47]. In general, TKIs such as imatinib, dasatinib, and nilotinib should also be started in the acute setting along with leukapheresis [48]. Other key factors for management of leukostasis include monitoring fluid balance and checking serum uric acid, electrolytes including potassium and phosphate, and renal function due to possible TLS [38].

Given the rarity of leukostasis in CML, when patients present with intracranial masses, the diagnosis of MS should remain in the differential [49]. MS, also known as granulocytic sarcoma or chloroma, describes an extramedullary tumor associated with myeloid leukemia [49]. In both AML and CML, MS presents as a distinct tumor mass with myeloid blasts, with or without maturation, occurring at any site outside of the BM and often considered equivalent to the diagnosis of AML [49]. However, in CML, MS may present with less percentage of blast cells compared to MS in AML, as MS may arise in various phases of CML including the CP [50]. MS is most often seen in AML, and histology shows increased blasts often staining positive for MPO, CD34, and CD68 [49]. MS is usually associated with progression of disease and with extramedullary manifestations, commonly arising in the soft tissue, bone, peritoneum and lymph nodes [51, 52]. The progression of CML from the blast stage to the CP increases the risk of MS by 7-17% [9]. The rate of misdiagnosis of MS is as high as 75%, with common misdiagnoses including infection, tumors, and hemorrhage [53].

Immunophenotypic analysis, especially of the cerebrospinal fluid (CSF), and flow cytometry are helpful tools in accurate diagnosis and distinguishing leukostasis from MS [42]. In our patient, the infiltrates in the brain parenchyma were posi-

Table 1. A Review of the Cases of CNS Involvement in CML in Current Literature

Authors	Age/gender	Diagnosis	Imaging/CSF/pathology	Treatment	Response/ outcome
Current case	25/M	Known CML	CT of head showing multiple parenchymal leukemic infiltrates with mass effect; lesions with positive staining for MPO, CD43, and CD68	Started on imatinib but changed to dasatinib due to concern for resistance; did not tolerate leukapheresis	Death
Jin et al [7]	5/M	Newly diagnosed CML	Extramedullary blast crisis in CNS. BM aspirate revealed active hyperplasia of BM. + BCR/ABL1	Methotrexate, dexamethasone, and cytarabine intrathecal injection therapy; HAD for three cycles, followed by second generation TKIs	CR
Radhika et al [8]	15/F	CML on imatinib	MRI of brain showed thrombosis of posterior part of superior sagittal sinus. CSF showed large atypical looking cells comprising 48%, with hyperchromatic nuclei; CSF cytospin showed > 90% blasts	BMT not possible, as the patient did not have an HLA matched sibling donor. Imatinib dose increased and underwent six cycles of triple intrathecal chemotherapy and cranial radiotherapy	Lost to follow-up
Radhika et al [8]	37/M	CML on imatinib	MRI of brain revealed bilateral multiple small infarcts with features of meningitis. CSF showed increased numbers of immature cells (30%); CSF cytospin showed 60% blasts.	BMT was not possible, as the patient did not have an HLA matched sibling donor. The dose of Imatinib was increased to 600 mg once daily, and six cycles of triple intrathecal chemotherapy and cranial radiotherapy were also given.	Death 3 months after CNS blast crisis due to CNS disease.
Abuelgasim et al [9]	29/M	Newly diagnosed CML	CT of head showed new 4 cm left frontoparietal subdural collection, 1.5 cm left frontotemporal lobe collection, and right frontoparietal subdural collection. CSF showed 95% blasts. Flow cytometry of CSF showed blast cells + for CD34, CD33, CD11b, CD71 and CD13/ CD117. BM showed chronic phase CML.	Whole brain radiation therapy and dasatinib therapy with AML induction with cytarabine and idarubicin + intrathecal methotrexate/ cytarabine/hydrocortisone (allo-HSCT not recommended due to multiple infections/pancytopenia)	CR
Jain et al [10]	35/M	Noncompliance in known CML	MRI of brain with heterogenous enhancement of falx cerebri and tentorium (pachymeningitis) and bilateral optic nerves. CSF flow cytometry showed myeloid blasts + CD13, CD33 (negative for CD10 and CD19). No mutation for TKI resistance. BM with 2% myeloblasts.	Imatinib and intrathecal methotrexate and dexamethasone	Death after two doses of intrathecal therapy
Healey et al [11]	23/F	Newly diagnosed CML	MRI of brain after imatinib showed enhancement of left posterior frontal lobe including subarachnoid space. BM with 14% blasts (accelerated phase of CML), CSF with 51% blasts	Imatinib initially then started on dasatinib due to relapse. Underwent unmatched donor HSCT	CR
Chiba et al [12]	30/M	Newly diagnosed CML	MRI of brain showed hypertrophic dura without obvious tumor. BM with increased myeloid cells (no specific number), CSF flow cytometry positive for CD10, CD19, HLADR, CD34	Hydroxyurea, dasatinib, and hyperCVAD/ MA therapy with dasatinib along with intrathecal methotrexate, cytarabine, and dexamethasone. Underwent allo-HSCT after whole brain radiation and total body radiation (with cyclophosphamide)	CR

Table 1. A Review of the Cases of CNS Involvement in CML in Current Literature - *(continued)*

Authors	Age/gender	Diagnosis	Imaging/CSF/pathology	Treatment	Response/ outcome
Atilla et al [3]	72/M	Progression of known chronic phase CML to blast crisis	MRI of brain showed enhancement of clivus and occipital condyles. BM with 42% blasts; CSF flow cytometry normal	Bosutinib with methotrexate, dexamethasone involvement. Radiotherapy and intrathecal methotrexate with cytarabine	CR
Gomez et al [13]	33/M	Known CML, CNS involvement on imatinib	Normal head CT. Normal brain MRI. Unavailable CSF and serum flow cytometry	Intrathecal methotrexate, cytosine arabinoside, dexamethasone; then started on dasatinib.	CR but with persistent severe visual impairment
Neumann et al [14]	25/F	CML with previous HSCT and relapses treated with DLIs and imatinib	Leptomeningeal relapse confirmed by CSF cytology and flow cytometry	Intrathecal methotrexate, cytarabine, and dexamethasone followed by high dose cytarabine for persistent neurological symptoms. DLI in increasing doses with addition of nilotinib	CR for 15 months followed by relapse and death
Park et al [15]	54/M	Known CML	Diffusion MRI of brain with MRA revealed abnormal leptomeningeal enhancement of both paramedian gyri. CSF confirmed CNS involvement	Dasatinib, intrathecal methotrexate, and cranial irradiation therapy	CR
Kim et al [16]	42/M	CML on imatinib	Craniotomy for increased intracranial pressure from mass of bilateral cerebellar hemispheres. Underwent partial resection with biopsy confirming isolated CNS lymphoid blast crisis	Cytarabine, methotrexate, and hydrocortisone with imatinib	Death 15 days after craniectomy
Beyazit et al [17]	46/F	CML treated with hydroxyurea and interferon-alpha/ cytarabine followed by imatinib at remission	Lumbar MRI suggested malignant infiltration of the spinal cord. LP showed blastic cellular infiltration	Intrathecal methotrexate and craniospinal radiotherapy	Death from pulmonary aspergillosis
Gaur et al [18]	30/M	CML on ponatinib	MRI of brain showed diffuse supratentorial and infratentorial leptomeningeal enhancement. CSF showed myeloblasts	Intrathecal cytarabine and craniospinal irradiation	CR; pending allogeneic SCT
Rajappa et al [19]	39/M	CML on Imatinib	MRI of brain showed meningeal enhancement and CSF positive for blasts	Cranial radiotherapy and triple intrathecal chemotherapy	CR
Bornhauser et al [20]	56/F	CML on imatinib	MRI of brain revealed minimal dural enhancement. LP revealed lymphoid blast crisis in CSF	Intrathecal cytosine arabinoside, methotrexate, and dexamethasone and irradiation of the total neuraxis	Death 22 days after HSCT
Bujassoum et al [21]	42/F	Known CML	MRI of brain showed increased signal intensity in the periventricular area with LP showing CML blast crisis. Flow cytometry showed an increase in myeloid blasts $CD34^+$, $CD117^+$. BM showed BCR/ABL1 fusion	Intrathecal methotrexate and cytarabine	CR
Johnson et al [22]	50/M	Known CML	CSF showed $CD19^+$, $CD10^+$, $CD34^+$	Intrathecal chemotherapy and HSCT	Death

Table 1. A Review of the Cases of CNS Involvement in CML in Current Literature - *(continued)*

Authors	Age/gender	Diagnosis	Imaging/CSF/pathology	Treatment	Response/ outcome
Matsuda et al [23]	17/M	CML on imatinib	CT of head demonstrated no specific signs of meningeal and cerebral involvement. LP revealed blasts in the CSF	Intrathecal chemotherapy with cytosine arabinoside, methotrexate, and dexamethasone and whole-brain radiation	CR
Aichberger et al [24]	52/M	CML on imatinib	CT of head and MRI of brain normal. LP showed myeloblasts. $CD34^+$, $HLADR^+$, $CD117^+$	Intrathecal liposomal cytarabine and intracranial radiation	CR
Aichberger et al [24]	73/F	CML on imatinib	CT of head showed leukoencephalopathy and microangiopathy without meningeal involvement. $CD117^+$, $CD13^+$, $CD33^+$, $CD34^+$	Intrathecal liposomal cytarabine	CR
Barlow et al [25]	68/M	CML on imatinib	CSF showed increased white blood cell count	Intrathecal methotrexate and dexamethasone; switched to dasatinib. Underwent cranial irradiation	Clinical improvement
Altintas et al [26]	39/M	CML on hydroxyurea and imatinib	MRI of brain showed meningeal enhancement at the frontoparietal region and tentorium. CSF showed lymphoblasts.	Radiation, intrathecal chemotherapy, and imatinib	CR
Lee et al [27]	39/M	CML on imatinib	MRI of brain with abnormal high signal intensity in the petrous region bilaterally	Intrathecal cytarabine and methotrexate and increased imatinib dose	CR
Isobe et al [28]	61/M	Known CML	CT of head showed swelling of cerebellar cortex and fourth ventricle dilatation. CSF showed lymphoblasts and flow cytometry showed blasts positive for CD10, CD19, and CD20.	Intrathecal methotrexate and dexamethasone, and allogeneic HSCT with thiotepa, etoposide and cyclophosphamide; also underwent optic nerve irradiation	CR
Thomas et al [29]	33/M	CML treated with hydroxyurea, cytosine arabinoside, dasatinib, and SCT	MRI of brain and spine unremarkable. CSF showed blast-like cells positive for MPO and *BCR-ABL* fusion signal in 91% of cells and flow cytometry showed myeloid associated antigens.	Intrathecal methotrexate and craniospinal irradiation. Started on nilotinib.	CR
Fuchs et al [30]	64/F	CML treated with imatinib followed by cytosine arabinoside and mitoxantrone and hydroxyurea	MRI of brain revealed leukemic infiltration of lateral ventricles walls and hydrocephalus. CSF with about 50% immature blasts with highly elevated BCR-ABL/ABL ratio	Intrathecal cytarabine, methotrexate, and dexamethasone followed by dasatinib	CR
Nishimoto et al [31]	22/M	CML on imatinib	CML blast crisis in CNS after 29 months of therapy	Allogeneic HSCT following combination therapy with dasatinib, intrathecal chemotherapy and cranial irradiation. Followed by dasatinib maintenance therapy	CR

The review of both pediatric and adult cases of CML in current literature including the case report of this study along with histopathologic and imaging characteristics of each case and outcomes based on varying treatment modalities. BM: bone marrow; BMT: bone marrow transplant; CML: chronic myelogenous leukemia; CNS: central nervous system; CR: complete remission; CT: computed tomography; DLI: donor lymphocyte infusion; HAD: homoharringtonine, cytarabine, daunorubicin; HSCT: hematopoietic stem cell transplant; hyperCVAD: cyclophosphamide, vincristine, doxorubicin, and dexamethasone; LP: lumbar puncture; MPO: myeloperoxidase; MRA: magnetic resonance angiography; MRI: magnetic resonance imaging; SCT: stem cell transplant; TKI: tyrosine kinase inhibitor.

tive for MPO and CD68 and only occasional blasts (around 1%), which suggested leukostasis in the setting of the CP of CML. The negative CD20 staining additionally confirms that the intracranial masses were not derivative of a B-cell neoplasm. Further, the negative staining for CD34 is consistent with leukostasis in the setting of CML and not acute leukemia in the form of MS. The lack of increased blasts in the flow cytometry as well as BM biopsy showing hypercellular marrow with evidence of maturation and without significant increase in blast cells both further support the diagnosis of leukostasis over MS.

Conclusion

Leukostasis is a rare complication of hyperleukocytosis which manifests in the CNS or respiratory system. Here we described a rare case of leukostasis presenting with intracranial lesions and correlated neurologic symptoms in the setting of known CP of CML. Interestingly, the patient's intracranial lesions were found to be leukostasis as there was no evidence of AML to point to MS or CML in the blast phase. Given the high mortality rate associated with leukostasis, patients presenting with suspected CNS manifestations of CML should be evaluated for leukostasis with the goal of prompt cytoreduction and leukapheresis as indicated upon initial diagnosis. Future studies should be directed at standardized surveillance strategies for patients with CML and development of prognostic scores to predict the development of CML, especially those in complete remission as a result of TKI response to first- and second-generation TKIs.

Acknowledgments

None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

The authors do not report any conflict of interest.

Informed Consent

Unable to be obtained due to deceased patient and next-of-kin unavailable for consent.

Author Contributions

WJ, MN, and SD conceptualized the manuscript and contributed to the writing of the manuscript. JM, BJ, and DC provided critical review and contributed to the revision of the manuscript. KP provided their expertise in the discussion of pharmacotherapy for this manuscript. JH and RR contributed to the pathology details included in the manuscript. AM and AP provided critical review of the manuscript and their expert guidance on the topic. All authors approve of submission of this manuscript for publication.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

Abbreviations

ABL: Abelson murine leukemia; AML: acute myeloid leukemia; ATP: adenosine triphosphate; BCR: breakpoint cluster region; BM: bone marrow; BMT: bone marrow transplant; CML: chronic myelogenous leukemia; CNS: central nervous system; CP: chronic phase; CR: complete remission; CT: computed tomography; DIC: disseminated intravascular coagulation; DLI: donor lymphocyte infusion; EUTOS: European Treatment and Outcome Study; GCS: Glasgow coma scale; HAD: homoharringtonine, cytarabine, daunorubicin; Hgb: hemoglobin; HSCT: hematopoietic stem cell transplant; hyperCVAD: cyclophosphamide, vincristine, doxorubicin, and dexamethasone; JAK: Janus kinase; LDH: lactate dehydrogenase; LP: lumbar puncture; MPO: myeloperoxidase; MRA: magnetic resonance angiography; MRI: magnetic resonance imaging; MS: myeloid sarcoma; RBCs: red blood cells; SCT: stem cell transplant; STAT: signal transducer and activator of transcription; TKIs: tyrosine kinase inhibitors; TLS: tumor lysis syndrome; WBC: white blood cell; WHO: World Health Organization

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