Case Report

DOI: 10.5582/irdr.2018.01045

Is it always cancer? A curious case of benign intracranial hypertension in chronic myeloid leukemia

Purva V. Sharma[1,*], Omar Ilyas[1], Yash Jobanputra[1], Teresita Casanova[2], Venkat Kalidindi[1], Napolean Santos[3]

[1] *Department of Internal Medicine, University of Miami Palm Beach Regional Consortium, Atlantis, Fl, USA;*
[2] *Department of Neurology, JFK Medical Center, Atlantis, Fl, USA;*
[3] *Department of Hematology/Oncology, JFK medical Center, Fl, USA.*

Summary **28-year-old African American female with chronic myeloid leukemia (CML) presented with blurry vision for 4-5 days prior to presentation associated with right-sided headaches. Patient was on treatment for the CML but never had hematological remission. Patient saw an ophthalmologist who told her that she has bilateral optic disc swelling and advised her to get an MRI of the brain. She came to the ER due to worsening headache and blurry vision. The funduscopic examination showed significant bilateral papilledema. Laboratory evaluation revealed a leukocytosis of 240 × 10^3/u**L **with platelet count of 1,202 × 10^3. The white cell differential count showed 17% blasts along with myelocytes and meta-myelocytes. MRI of brain revealed non-specific CSF flair signal. Lumbar puncture (LP) showed significantly elevated opening pressures. The CSF composition was however normal. The patient felt much relief of her symptoms following the LP. The papilledema was thought to be due to benign intracranial hypertension (ICH), which was attributed to poor CSF absorption due to resistance to flow of CSF caused by the high WBC count. She received 2 cycles of leukopheresis which dropped her WBC count. She was also started on acetazolamide for the benign ICH and her symptoms improved considerably. Patients with CML can thus present with symptoms mimicking CNS involvement of the disease such as headaches and blurry vision, but that could be attributed to the poor CSF resorption given the leukocytosis rather than spread of the disease itself.**

Keywords: Intracranial hypertension, chronic myeloid leukemia, papilledema

1. Introduction

Chronic myeloid leukemia (CML) is a myeloproliferative disorder characterized by overproduction of myeloid cells. CML accounts for approximately 15 to 20 percent of leukemias in adults (*1*). The median age at presentation is 50 years of age. It commonly presents in 3 different clinical courses – chronic phase, accelerated phase and blast crisis. CML in blast crisis has been shown to have a propensity for CNS involvement (*2*). This can cause seeding of the leukemic cells in the CNS especially with high WBC counts at presentation (*3*).

We present an interesting case of a young African American lady with CML who presented with blurry vision and headaches. She was found to have bilateral optic disc edema secondary to increased intracranial pressure.

2. Case Report

28-year-old African American female with history of CML presented to JFK Medical Center in November 2017 with symptoms of blurred vision for 4-5 days prior to presentation. Patient states the blurry vision started insidiously and is worse in the right eye. It gets worse with movement of her head. The blurry

Released online in J-STAGE as advance publication July 27, 2018.

**Address correspondence to:*
Dr. Purva V. Sharma, Department of Internal Medicine, University of Miami Palm Beach Regional Consortium, Atlantis, Fl 33462, USA.
E-mail: purva7sharma@gmail.com

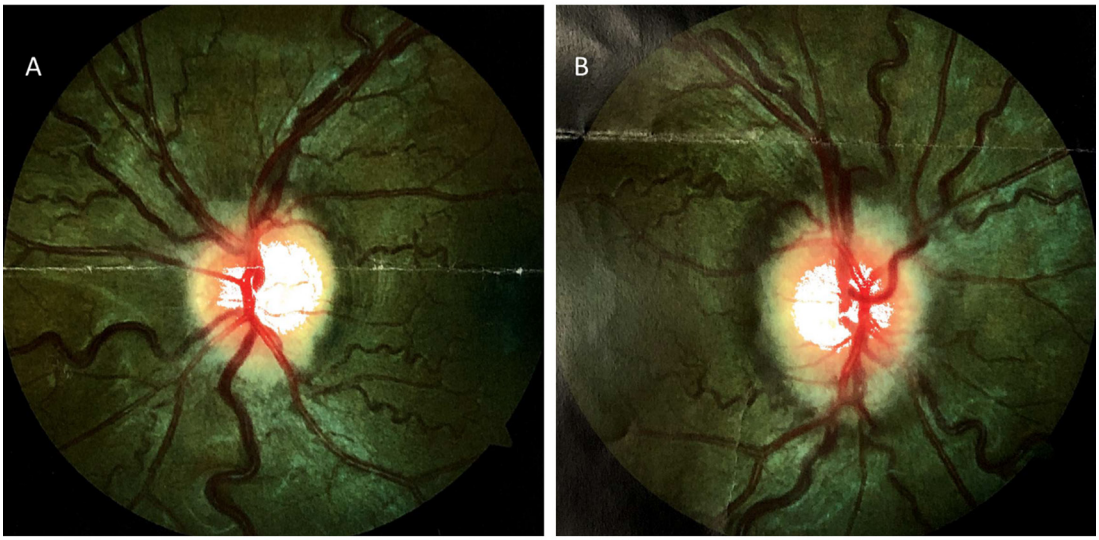

Figure 1 showing left (A) and right (B) optic disc edema visualized on the fundoscopic examination.

vision is associated with right sided headaches in the frontal, temporal and occipital region which have also been ongoing for 3-4 days prior to presentation. The headaches were described as continuous, sharp and relieved by OTC analgesics. The patient saw an ophthalmologist 2 days prior to presentation due to the blurry vision. She was told to get an MRI as there was bilateral optic disc edema visualized on the fundoscopic examination (Figure 1). Patient, however, was not able to have the MRI done until the time of presentation.

The patient was diagnosed with CML in chronic phase back in 2014. Since then she has received multiple lines of therapy including Imatinib, Dasatinib and Nilotinib. However, she never reached a durable hematologic remission. More recently she was started on Bosutinib.

At the time of arrival, patient was in mild to moderate distress due to the headaches. She was afebrile, with HR 92 and regular, BP- 138/68 mmHg and saturating well at 98% on room air. The physical examination was consistent with bilateral papilledema. Her head and neck examination was within normal limits, visual fields and remainder of neurologic exam was intact.

Her laboratory evaluation revealed white cell count of 240×10^3. The differential count showed 7% myelocytes, 12% meta-myelocytes and 17% blast cells. Her Hb was 8.7 g/dL and platelet count was $1,202 \times 10^3$. MRI of the brain showed non-specific abnormal specific CSF flair which was questionable for early signs of meningitis. This was followed by a lumbar puncture which showed clear, colorless fluid with 0 white cells and 0 red blood cells. The CSF analysis also showed normal protein and glucose. The lumbar puncture was remarkably significant for an elevated opening pressure of 65 cm H_2O. The patient felt much improvement of symptoms of headache and blurry vision after the lumbar puncture. MRA did not show any abnormality in the flow rate of venous filling of the dural sinuses. MRI did not show enlarged ventricles and the patient had no clinical signs or symptoms of meningitis which was suspected on the imaging. After multidisciplinary discussion between Neurology, Oncology and the primary team, the decision was made to start Acetazolamide to treat for elevated intracranial hypertension. Leukopheresis was initiated as well to reduce the white cell count. She received 2 cycles of leukopheresis and her white cell count steadily dropped to 27×10^3. Her symptoms of blurred vision and headaches also considerably improved. Patient was discharged on acetazolamide and Bosutinib. One month later she had a follow-up with Neurology and Oncology and no recurrence of her symptoms at that time.

3. Discussion

CML is a myeloproliferative neoplasm characterized by the uncontrolled proliferation of mature and maturing granulocytes. CML is associated with the fusion of two genes: BCR (on chromosome 22) and ABL1 (on chromosome 9) resulting in the BCR-ABL1 fusion gene. This abnormal fusion typically results from a reciprocal translocation between chromosomes 9 and 22, t (9;22) (q34; q11), that gives rise to an abnormal chromosome 22 called the Philadelphia (Ph) chromosome. If untreated, CML can progress from a chronic phase to an accelerated phase and then a blast crisis.

Blast phase of CML is defined by more than 20% blasts in the blood/bone marrow or 5-10% blasts in the extramedullary sites (*3*). Lymph nodes, skin and soft tissues, bone, gastrointestinal and genitourinary tract are the most common sites of extramedullary blast crises. CNS involvement by extramedullary crises is rare and involves systemic involvement.(*3,4*) Also, CNS involvement is commonly seen in patients who are

treated with Imatinib for several months. This is because the drug is shown to have poor penetration into the CNS and allows leukemic infiltration (*4*).

However, in CNS leukemia the CSF will show evidence of increased WBC count as well as blasts which is not the case in our patient. The MRI of our patient did show some non-specific CSF flair but the CSF had 0 WBC count, which makes CNS infiltration by the leukemia very unlikely. The most significant physical examination finding in our patient was the bilateral optic disc edema seen on funduscopic evaluation.

Optic disc swelling in leukemia may be due to either direct leukemic infiltration of the optic nerve or papilledema secondary to raised intracranial pressure (ICP). Direct leukemic infiltration however is more common in acute leukemias and the presentation is usually asymmetric or unilateral (*5,6*). The appearance of the disc is also very different in direct infiltration as compared to papilledema. The disc is more opaque and asymmetrically placed. Also, reducing the ICP should reduce the papilledema, but will not affect the disc appearance in direct leukemic infiltration. In our patient, the optic discs were bilaterally edematous and symmetrically enlarged. This also makes direct involvement of the CML through infiltration of the optic nerve very less likely.

Although it is possible to have CNS leukemia without detection of leukemic cells in the CSF fluid, it is extremely unlikely that our patient's presentation was as a result of that. We believe that the bilateral optic disc swelling was secondary to papilledema. This is consistent with the initial CSF opening pressure of 65 cm H2O with subsequent clinical course of reduction in papilledema with the reduction in ICP. The mechanism of raised ICP is most likely from obstruction to CSF outflow (*7*). The obstruction to CSF flow could be seen as a result of direct meningeal infiltration in CNS leukemia, with cells proliferating in the arachnoid space. However, the patient had no signs of a CNS leukemia on MRI or lumbar puncture. A patient with raised ICP and normal CSF composition and neuro-imaging, by definition, has benign intracranial hypertension. Thrombosis of the dural venous sinuses could result in raised ICP, however our patient's MRA showed no signs of thrombosis (*8*).

We therefore postulate that the increase in ICP was due to poor absorption of CSF into the patent sinuses. This is due to increased resistance to outflow secondary to the very high WBC count (*9*). Borgesen *et al*. have shown that there is a linear relationship between resistance to CSF outflow and ICP (*10*). Increased white count causes increased viscosity which in turn can lead to an increased resistance to flow of CSF from the arachnoid villi into the sinuses. The rapid resolution of papilledema with reduction of ICP after lumbar puncture also favors this hypothesis.

Additionally, the patient benefited from leukopheresis and her WBC count dropped considerably after two rounds of treatment. Leukopheresis is known to be an effective treatment modality, especially in cases of hyperviscosity syndrome in patients with CML and is able to achieve rapid cytoreduction (*11*).

4. Conclusion

Papilledema in a patient with leukemia with normal CSF and neuro-imaging is most likely due to benign intracranial hypertension. The most likely pathogenesis of the elevated ICP in such cases is that the elevated white cell count in leukemia causes hyperviscosity which decreases the absorption of CSF from the arachnoid villi. This results in increased intracranial pressures. It is significantly improved after reducing the ICP by lumbar puncture.

References

1. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin. 2017; 67:7-30.
2. Kim HJ, Jung CW, Kim K, Ahn JS, Kim WS, Park K, Ko YH, Kang WK, Park K. Isolated blast crisis in CNS in a patient with chronic myelogenous leukemia maintaining major cytogenetic response after imatinib. J Clin Oncol. 2006; 24:4028-4029.
3. Altintas A, Cil T, Kilinc I, Kaplan MA, Ayyildiz O. Central nervous system blastic crisis in chronic myeloid leukemia on imatinib mesylate therapy: A case report. J Neurooncol. 2007; 84:103-105.
4. Rajappa S, Uppin SG, Raghunadharao D, Rao IS, Surath A. Isolated central nervous system blast crisis in chronic myeloid leukemia. Hematol Oncol. 2004; 22:179-181.
5. Allen RA, Straatsma BR. Ocular involvement in leukemia and allied disorders. Arch Ophthalmol. 1961; 66:490-508.
6. Chalfin AI, Nash BM, Goldstein JH. Optic nerve head involvement in lymphocytic leukemia. J Pediatr Ophthalmol Strabismus. 1973; 10:39-43.
7. Ellis W, Little HL. Leukemic infiltration of the optic nerve head. Am J Ophthalmol. 1973; 75:867-871.
8. Foley J. Benign forms of intracranial hypertension; toxic and otitic hydrocephalus. Brain. 1955; 78:1-41.
9. Guymer RH, Cairns JD, O'Day J. Benign intracranial hypertension in chronic myeloid leukemia. Aust N Z J Ophthalmol. 1993; 21:181-185.
10. Børgesen SE, Gjerris F. Relationships between intracranial pressure, ventricular size, and resistance to CSF outflow. J Neurosurg. 1987; 67:535-539.
11. Shafique S, Bona R, Kaplan AA. A case report of therapeutic leukapheresis in an adult with chronic myelogenous leukemia presenting with hyperleukocytosis and leukostasis. Ther Apher Dial. 2007; 11:146-149.

(Received May 2, 2018; Revised July 4, 2018; Accepted July 10, 2018)