Case Report

Chronic Myeloid Leukemia Preceded by Tuberculosis

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Keywords

CML · Chronic myeloid leukemia · TB · Tuberculosis

Abstract

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm, classically described as a triphasic disease. However, little is known about risk factors for developing CML. Currently, ionizing radiation is the only established risk factor. Here, we report on a 37-year-old man treated for tuberculosis; 2 years later, he developed CML in a chronic phase. We would like to shed light on tuberculosis as a possible risk factor for CML.

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Published by S. Karger AG, Basel

Introduction

Tuberculosis (TB) is an infectious disease usually caused by *Mycobacterium tuberculosis* bacteria. TB generally affects the lungs, but it can also affect other parts of the body. Most infections do not cause symptoms, in which case the disease is referred to as “latent TB.” About 10% of all latent infections progress to active disease which, if left untreated, kills about half of those affected. The classic symptoms of active TB are a chronic cough with blood-containing mucus, fever, night sweats, and weight loss. Historically, it was called “consumption” due to the weight loss. Infections of other organs can cause a wide range of symptoms [1].

Chronic myeloid leukemia (CML, also known as chronic myelocytic, chronic myelogenous, or chronic granulocytic leukemia) is a myeloproliferative neoplasm characterized by the deregulated production and uncontrolled proliferation of mature and maturing granu-

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locytes with fairly normal differentiation. 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.

In the absence of treatment, CML follows a triphasic or biphasic clinical course as it progresses from a chronic phase to an accelerated phase and on to a terminal blast crisis. CML accounts for approximately 15–20% of all leukemia cases in adults [2]. It has an annual incidence rate of 1–2 cases per 100,000, with a slight male predominance [3]. The median age at presentation is approximately 50 years for patients enrolled in clinical studies, but the actual median age from cancer registry data may be 10 years older. Exposure to ionizing radiation is the only known risk factor for CML [4]. Tyrosine kinase inhibitors are a cornerstone in the management of CML around the world with good results [5–9]. This case is shedding light on a possible association between TB and the development of CML.

Case Presentation

A 37-year-old man, with no significant past medical or surgical history, developed fever and cough for 10 days, associated with nights sweats and 3 kg weight loss. Fever was on and off, the cough was with yellowish sputum. There was no shortness of breath, exertional dyspnea, or chest pain. He was treated for community-acquired pneumonia with IV antibiotics (ceftriaxone) + oral azithromycin without improvement of symptoms which warranted further evaluation. A chest CT was done showing multiple enlarged lymph nodes seen in the pretracheal, precarinal, and left hilar, the biggest measuring 2.3 cm. Those lymph nodes were heterogenous with hypodense areas representing necrosis. His PPD skin test was positive. Sputum for acid-fast bacillus smear was negative. Mediastinoscopy was done, and a biopsy was taken from a paratracheal lymph node which showed necrotizing granuloma, and the acid-fast bacillus smear was positive. Our patient was started on anti-TB medications (rifampicin 600 mg, isoniazid 300 mg, pyrazinamide 400 mg, ethambutol 275 mg) for 2 months with follow-up. Then, he received further treatment with two medications for 4 months (rifampicin and isoniazid).

Two years later, he developed blurry vision of sudden onset in his left eye, with no history of trauma, eye redness or swelling, focal neurogenic deficit, or headache. Systemic review was positive for early satiety. In the Emergency Department, he was seen by an ophthalmologist. The fundus examination of his right eye showed: diffuse retinopathy with spare macula; that of his left eye showed: diffuse retinopathy with maculopathy (membrane or cyst). He was referred to the Department of Medicine for further work-up.

Physical Examination

Vital signs: temperature 36.5°C, blood pressure: 113/71 mm Hg, pulse: 75 beats per minute, respiratory rate: 15 breaths per minute, O₂ saturation: 98%.

General look: normal, head, neck, eye, ENT was normal, no lymphadenopathy, no pallor or jaundice. Chest: good bilateral air entry, no added sounds. Cardiovascular: normal, abdomen and pelvic showed hepatomegaly 6 cm below the costal margin, no shifting dullness or ascites. No masses, genitourinary: not documented, neurological exam was normal. Musculoskeletal/spine was normal.

Complete blood count: WBC: 276,000/μL (reference range 4,000–10,000), Hb: 10.2 g/dL (reference range 13–17), MCV: 86 fL (reference range 83–101), platelets: 127,000 (reference range 150,000–400,000). Peripheral smear showed red cells: normocytic slightly hypochromic with anisocytosis, NRBCs were seen. Leukocytes: neutrophilic hyperleukocytosis with a marked shift to the left, different stages of maturation with peaks of the segmented and

myelocyte stages, eosinophilia, basophilia, and monocytosis. Platelets: mild thrombocytopenia.

Impression: morphology was consistent with a myeloproliferative disorder, most likely CML (in a chronic phase). Ultrasound abdomen showed splenomegaly 17.7 cm. Referral to hematology was done. A bone marrow biopsy was done: the overall peripheral blood and bone marrow aspirate findings were diagnostic for CML. Our patient was started on nilotinib (a tyrosine kinase inhibitor), with which he achieved complete hematological remission, complete cytogenetic response, and major molecular remission.

Discussion/Conclusion

Little is known about the risk factors for developing CML, with multiple risk factors having been proposed. Whether age per se is a risk factor is unknown. Despite the average age at diagnosis of CML being around 64 years, one cohort study concluded that CML presented more aggressively in adolescents and young adults as compared to older patients; however, there was no difference in outcome [10]. Obesity could play a role, since in one study [11] mean age at diagnosis was lower in obese patients compared with the control group (39.0 vs. 42.2). Obese patients had a lower WBC count and a higher Hb level at diagnosis (mean WBC 153.9 vs. 193.0; mean Hb 11.4 vs. 10.3), and obese patients showed a better response to treatment and were less likely to need a switch to tyrosine kinase inhibitors due to failure of treatment [11].

Autoimmune hemolytic anemia (AIHA) is idiopathic in around half of the patients. However, in the rest, it is known to be linked with autoimmune disorders, viral infections, drugs, or cancers. The most common associated hematological malignancies are lymphoproliferative disorders, especially chronic lymphocytic leukemia. The combination of CML and AIHA, in comparison to chronic lymphocytic leukemia, is extremely unusual. AIHA is a rare cause of anemia in CML. But when AIHA occurs, it develops after the diagnosis of CML in the chronic phase which usually responds to steroids. So far, there is no evidence that it can precede CML [12, 13].

The relationship between CML and TB has not been established. A national survey including 1,082 CML patients, identified from the Taiwan National Health Insurance database covering the period between 1998 and 2011, concluded that the incidence of TB is significantly higher in CML patients of male sex, aged ≥ 60 , and having received either stem cell transplantation or interferon- α treatment. Careful screening strategies for TB should be considered in CML patients with a high risk of infection [14]. Currently, exposure to ionizing radiation is the only known risk factor for CML [15].

We conclude that despite fast developments in treating CML, ionized radiation remains the only known risk factor. However, TB should be thought of as an additional risk factor in view of the emerging data. Further studies are needed to confirm these results.

Acknowledgement

The authors would like to acknowledge the internal medicine residency program for scientific support.

Statement of Ethics

The case was approved by the Hamad Medical Corporation Medical Research Center, and the patient gave written informed consent to publish his case information and details.

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

This work was supported by Qatar National Library.

Author Contributions

Bara M. Al-Qudah and Mohamed A. Yassin contributed equally to the writing and editing of this paper. All other authors were responsible for clinical care.

References

- 1 Khan FY, Dosa K, Fuad A, Ibrahim W, Alaini A, Osman L, et al. Disseminated tuberculosis among adult patients admitted to Hamad General Hospital, Qatar: a five year hospital based study. *Mycobact Dis*. 2016;6(212): 10.4172/2161-1068.1000212.
- 2 Turkina A, Wang J, Mathews V, Saydam G, Jung C, Al Hashmi H, et al. TARGET: a survey of real-world management of chronic myeloid leukaemia across 33 countries. *Br J Haematol*. 2020. <http://dx.doi.org/10.1111/bjh.16599>.
- 3 Sant M, Allemani C, Tereanu C, De Angelis R, Capocaccia R, Visser O, et al. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. *Blood*. 2010 Nov;116(19): 3724–34.
- 4 Faderl S, Talpaz M, Estrov Z, O'Brien S, Kurzrock R, Kantarjian HM. The biology of chronic myeloid leukemia. *N Engl J Med*. 1999 Jul;341(3):164–72.
- 5 Al-Dewik NI, Morsi HM, Samara MM, Ghasoub RS, Gnanam CC, Bhaskaran SK, et al. Is adherence to imatinib mesylate treatment among patients with chronic myeloid leukemia associated with better clinical outcomes in Qatar? *Clin Med Insights Oncol*. 2016 Jan;10:95–104.
- 6 Vezzalini M, Mafficini A, Tomasello L, Lorenzetto E, Moratti E, Fiorini Z, et al. A new monoclonal antibody detects downregulation of protein tyrosine phosphatase receptor type γ in chronic myeloid leukemia patients. *J Hematol Oncol*. 2017 Dec;10(1):129.
- 7 Yassin MA, Taher A, Mathews V, Hou HA, Shamsi T, Tuglular T, et al. MERGE: a multinational, multicenter observational registry for myeloproliferative neoplasms in Asia, including Middle East, Turkey, and Algeria. *Cancer Med*. 2020 Apr; DOI: 10.1002/cam4.3004.
- 8 Tomasello L, Vezzalini M, Boni C, Bonifacio M, Scaffidi L, Yassin M, et al. Regulative loop between β -catenin and protein tyrosine receptor type γ in chronic myeloid leukemia. *Int J Mol Sci*. 2020;21(7):2298.
- 9 Al-Dewik NI, Jewell AP, Yassin MA, Morsi HM. Studying the impact of presence of alpha acid glycoprotein and protein glycoprotein in chronic myeloid leukemia patients treated with imatinib mesylate in the state of Qatar. *Biomark Cancer*. 2015 Jan;7:63–7.
- 10 Yassin MA, Abdulla MA-J, Chandra P, Aldapt MB, Hamad Y, Akiki SJ, et al. Chronic myeloid leukemia in adolescents and young adults: a single institute experience. *Blood*. 2019;134(Suppl_1):5915.
- 11 Yassin MA, Abdulla MA-J, Abbas F, Chandra P, Nashwan AJ, Ghasoub RS, et al. Clinico-pathological profiles of obese patients with chronic myeloid leukemia (CML) and their response to therapies (TKIs). *Blood*. 2019; 134(Suppl_1):5912.
- 12 Hamamyh T, Yassin MA. Autoimmune hemolytic anemia after relapse of chronic myeloid leukemia: a case report. *Clin Med Insights Blood Disord*. 2019 Dec;12:1179545X19894578.
- 13 Yassin MA, Hamamyh T. Autoimmune hemolytic anemia in chronic myeloid leukemia from busulfan to the era of tyrosine kinase inhibitors. *Blood*. 2019;134(Suppl_1):5917.
- 14 Liu CJ, Hong YC, Teng CJ, Hung MH, Hu YW, Ku FC, et al. Risk and impact of tuberculosis in patients with chronic myeloid leukemia: a nationwide population-based study in Taiwan. *Int J Cancer*. 2015 Apr 15;136(8):1881–7.
- 15 Moloney WC. Radiogenic leukemia revisited. *Blood*. 1987 Oct;70(4):905–8.