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CASE REPORT

Co-occurrence of atypical chronic myeloid leukemia and prostate cancer in a 75-years old male

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Abstract

Atypical chronic myeloid leukemia (aCML) is a rare form of myelodysplastic syndrome/myeloproliferative neoplasm. This report presents a case of aCML in a 75-year-old man, diagnosed based on cytologic evidence of neutrophilia, presence of neutrophil precursors, thrombocytopenia on complete blood count and microscopy, and granular hyperplasia and dysgranulopoiesis on myelogram. The patient was in good clinical condition with isolated splenomegaly. With hydroxyurea, the hyperleukocytosis was controlled, and the splenomegaly disappeared. The lymphadenopathy identified on a CT scan led to the diagnosis of prostate cancer, while the general health condition of the patient was impairing.

Key words: atypical chronic myeloid leukemia; prostate cancer; hydroxyurea.

Abstract

Atypical chronic myeloid leukemia (aCML) is a malignant neoplasm that falls between myeloproliferative neoplasms and myelodysplastic syndromes. It was recently designated as myelodysplastic/myeloproliferative neoplasm with neutrophilia in the fifth edition of the World Health Organization (WHO) classification of neoplasms (1,2). ACML is characterized by hyperleukocytosis greater than or equal to 13 x 10^9/L with neutrophilia and dysgranulopoiesis, at least 10% immature granulocytes, and less than 20% blasts (3).

The median age of onset of aCML is between 69 and 73 years (4,5). The annual incidence of aCML is 1/100,000 inhabitants, corresponding to 1 to 2 cases per 100 patients with BCR-ABL1 rearrangement CML (6,7). The clinical features are non-specific and related to splenomegaly, hepatomegaly, and induced cytopenias (6,8). The overall survival rate ranges from 12 to 29 months (3,6).

The hematology department at Campus University Hospital registered a rise in the number of BCR-ABL-positive aCML patients from 25 in 2009 to 63 in 2013, with a frequency of approximately 3 cases per year (9,10). We report the first case of aCML diagnosed in the department, which presented with lymphadenopathy.

Case

In October 2022, a 75-year-old man was referred to a hematology consultation for hyperleukocytosis at 87 x 10^9/L with neutrophilia at 78.3 x 10^9/L and polymorphic myelemia. This was found in the context of a sudden onset of right-sided deficit with predominantly crural distribution four weeks earlier. The patient had also reported a progressive onset of asthenia a few weeks before the hemi-body deficit. The patient did not have a history of hypertension, diabetes mellitus, or any significant medical history. He underwent cataract surgery twice, five and two years ago.

Upon admission, the patient was in good general condition with a performance status of I. He weighed 74 kg, was 1.72 m tall, and had a 25.01 kg/m2 body mass index. He was fully conscious and had a Glasgow score of 15/15.

Walking was difficult due to akinesia. The patient had decreased muscle strength in the right upper and lower limbs. She had right pyramidal syndrome with positive Barré, Mingazzini, and Babinsky maneuvers on the right side. Clinical examination did not reveal splenomegaly, hepatomegaly, peripheral lymphadenopathy, anemia, or hemorrhagic syndrome.

The initial blood count revealed a hyperleukocytosis at 90.5 x10^9/L with neutrophilia at 60.64 x10^9/L, 1% of eosinophils, and 1% of basophils. The blood smear revealed 1% of blasts and 24% of granulocyte precursors, with 1% of promyelocytes, 8% of neutrophilic myelocytes, and 15% of neutrophilic metamyelocytes. Additionally, the platelet count was 99 x10^9/L.

One week later, a myelogram revealed 92.5% balanced granular hyperplasia associated with neutrophil lineage dysplasia. This consisted of abnormal nuclear condensation and degranulation of neutrophils (Figure 1) and their precursors, affecting 16% of the neutrophilic lineage. There were 2.5% of blasts in the bone marrow. The erythroblastic lineage was 2.5%, resulting in a ratio of granular cells to erythroblasts of 37. The monocytic lineage was 0.5%, and the lymphoid lineage was 4.5%.

The bone marrow aspirate sample had a normal karyotype. The BCR-ABL fusion gene was not identified by fluorescent in situ hybridization. PCR testing for JAK2 V617F, CALR, and MPL mutations was also negative.

Atypical CML was diagnosed at nine weeks of follow-up, and the patient was prescribed hydroxyurea at an initial dose of 500 mg twice a

day. For the first month, it was combined with 100 mg/d of allopurinol. The leukocytes and platelets were at their maximum, 97 $x10^9$/L and 104 $x10^9$/L, respectively, and there were no further blood blasts during follow-up. The hydroxyurea dosage was adjusted between 0 and 1500 mg/d based on cytological reduction and the extent of induced cytopenias. After 19 weeks of hydroxyurea treatment, the patient's blood count showed normalization of the leukocytes and neutrophil counts. Additionally, the myelemia disappeared. However, thrombocytopenia persisted at between 53 and 93 $x10^9$/L.

At the time of diagnosis, a thoracic-abdominal-pelvic CT scan showed multiple deep sub-diaphragmatic lymphadenopathies, measuring up to 30 mm in the short axis in the pelvic region, as well as bilateral para-aortic, aortocaval, para-caval, ilio-pelvic, and inguinal lymphadenopathies measuring 10 to 30 mm. The patient presented with homogeneous splenomegaly measuring 130 mm and bilateral pulmonary nodules. These nodules were located in the right dorsal and postero-basal segments, measuring 3 mm and 4 mm respectively, and in the left antero-basal and postero-basal segments. A follow-up scan in October 2023 revealed that the spleen size had normalized (107 mm) with no focal lesions, and there were pulmonary and subpleural micronodules with no specific features. The prostate gland was found to be enlarged, measuring 64mm x 60mm x 56mm (107 mL) with regular borders and heterogeneous structure after contrast injection. The prostatic protrusion index was grade 3, with intravesical protrusion of the median lobes and discrete infiltration of vesico-prostatic fat with pelvic lymphadenopathy.

Discussion

ACML was diagnosed based on neutrophilia and myelemia in the complete blood count with granular hyperplasia, and signs of dysgranulopoiesis on the myelogram, despite the presence of adenopathies. The absence of basophilia (6), eosinophilia (2), and monocytosis (2,6) was also noted. Additionally, thrombocytopenia was present at diagnosis. Cytopenia meeting the defined thresholds for myelodysplastic syndromes is one of the diagnostic criteria for ICC, in contrast to the WHO classification (2,6).

Neutrophilia and medullary granular hyperplasia may indicate a reactive or malignant etiology like myeloproliferative syndrome. The presence of dysgranulopoiesis and the absence of the most common genetic abnormalities found in myeloproliferative syndromes at the molecular level suggested a myeloproliferative/myelodysplastic syndrome. Myelemia greater than or equal to 10% suggested myelodysplastic/myeloproliferative neoplasia with neutrophilia rather than chronic neutrophilic leukemia (2,7). The patient did not present with any signs of inflammation or infection, and the general condition was maintained. Splenomegaly and/or hepatomegaly are present in 44.6% of cases (8). The diagnosis of aCML was further supported by the reduction of splenomegaly and leukocytosis with hydroxyurea-based cytoreductive therapy. Hydroxyurea is used in over 85% of aCML patients (4,11). Treatment for aCML is not standardized and may include erythropoiesis-stimulating agents for anemia, and cytoreductive agents such as acute myeloid leukemia protocols, hypomethylating agents, hydroxyurea, or pegylated interferon alpha. Allogeneic hematopoietic stem cell transplantation remains the only potentially curative therapeutic option for patients with aCML(3). However, this option is not available in our developing countries. Advances in the understanding of the molecular mechanisms involved in the pathophysiology of CML have paved the way for research into the efficacy of several targeted therapies, in particular, JAK inhibitors like ruxolitinib, SRC kinase inhibitors like dasatinib and MEK inhibitors like trametinib (3).

The patient exhibits three risk factors for reduced survival: age over 65 years, leukocytes over 50 G/L, and myelemia. On the other hand, being male, having monocyte levels less than 3%, and not requiring transfusions were identified as good prognostic factors. Additionally, the patient exhibited two risk factors for leukemic transformation, including splenomegaly and myelofibrosis. Other positive prognostic factors included the absence of hepatomegaly, monocyte levels less than 3%, medullary blasts less than 5%, and no evidence of dyserythropoiesis or transfusion requirements (11). At the one-year follow-up, the discovery of the heterogenous prostate tumor, which likely indicated metastasis in the presence of lymphadenopathy, an altered general condition, contributed to worsening the patient's vital prognosis.

Conclusion

ACML is a rare form of MDS/MPN that is primarily diagnosed cytologically. Hyperleukocytosis and splenomegaly were under control with hydroxyurea. The concomitant presence of lymphadenopathy, without evidence of leukemic transformation, should prompt further investigations. In the present case, prostate cancer was diagnosed, worsening the poor prognosis of aCML.

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