Adult chronic myelomonocytic leukemia with trisomy 11: a case report

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ABSTRACT

Chronic myelomonocytic leukemia (cMML) is an indolent disease in the category of myelodysplastic and myeloproliferative neoplasms, which can often evolve into acute leukemic neoplasms. Although cytogenetic abnormalities such as trisomy 8 or absence of chromosome Y are well known, few reports about cMML with trisomy 11 have been published. Here, we report a case of cMML with trisomy 11 as the sole chromosomal abnormality, resulting in a very poor outcome.

Based on a bone marrow specimen, cMML-1 with trisomy 11 was diagnosed in a 79-year-old man presenting with anemia and atypical peripheral blood cells. Because of the patient’s age, he was followed without receiving anticancer treatment. Two months after his diagnosis, the patient’s leucocytosis and anemia rapidly worsened, with increasing numbers of immature peripheral cells, which was strongly suggestive of leukemic transformation. Because of acute kidney injury superimposed on chronic kidney disease that led to poor performance status, cytotoxic chemotherapy was not considered feasible, and the patient was transferred to a hospice care facility.

Key Words Myelodysplastic syndrome, chronic myelomonocytic leukemia, trisomy 11, case reports

INTRODUCTION

Chronic myelomonocytic leukemia (cMML) is a rare disorder of hematopoietic stem cells that is associated with peripheral monocytosis. It is classified as one of the myelodysplastic and myeloproliferative neoplasms (MDS/MPN) by the World Health Organization. 1 The number of incident cases of cMML in Korea was 60 in 2012. 2 The survival of patients with cMML is poor, with a reported 5-year relative survival rate in Korea of 23.2%. 2

Although most cMML patients have genetic mutations occurring in the TET2, SRSF2, ASXL1, or RAS genes, up to 30% of patients present with cytogenetic abnormalities. 3 The most common alteration is trisomy 8, followed by the absence of chromosome Y, chromosome 7 abnormalities, complex and monosomal karyotypes, and trisomy 21. 4 However, few reports about cMML patients with trisomy 11 have been published. A few such cases appear in the literature from the late 1980s and 1990s, but no recent reports on the incidence, prognosis, and clinical significance of this uncommon cytogenetic abnormality have been published. Here, we report a patient with cMML having trisomy 11 as the sole chromosomal abnormality.

CASE DESCRIPTION

A 79-year-old man was seen at the emergency department of Seoul National University Boramae Medical Center with a chief complaint of non-vertiginous dizziness over a 2-month period. He also complained of anorexia and general weakness, and a 3-month history of a 10 kg weight loss. He had no nausea or vomiting.

The patient’s medical history consisted of hypertension and diabetes mellitus, both well-controlled with medications; benign prostatic hyperplasia; and stage IIa chronic kidney disease, based on the Kidney Disease Improving Global Outcomes guideline. He had no family history of hematologic disease. He had drunk a bottle of beer daily for 40 years, but then had stopped 20 years earlier. He was an ex-smoker, with a 3 pack–year smoking history.

Upon the patient’s initial presentation, his vital signs were normal. Physical examination was unremarkable, except for slightly pale conjunctiva. A complete blood count revealed hemoglobin 7.3 g/dL, hematocrit 24.6%,
white blood cells $6.5 \times 10^9/L$ (differential: neutrophils 64%, lymphocytes 26%, eosinophils 1%, basophils 0%, monocytes 9%, and nucleated red blood cells 1%), and platelets $320 \times 10^9/L$. A serum biochemistry panel revealed blood urea nitrogen 23 mg/dL, creatinine 2.1 mg/dL (estimated glomerular filtration rate by the Modification of Diet in Renal Disease formula: 30.6 mL/min/1.73 m²), total protein 9.1 g/dL, albumin 3.6 g/dL, total bilirubin 0.5 mg/dL, aspartate transaminase 21 IU/L, alanine transaminase 7 IU/L, alkaline phosphatase 51 IU/L, total cholesterol 150 mg/dL, and lactate dehydrogenase 317 IU/L. A serum electrolyte panel showed sodium 133.8 mEq/L, potassium 5.2 mEq/L, and chloride 101.1 mEq/L. Examination of a peripheral blood smear revealed normocytic hypochromic red blood cells with anisocytosis and left-shift neutrophils with atypical lymphocytes (<1%). Serum iron was 68 μg/dL, total iron binding capacity was 211 μg/dL, and ferritin was 573 ng/mL. Serum and urine electrophoretic analysis was negative for monoclonal gammopathy. Serology for hepatitis viruses B and C was negative. Esophagogastroduodenoscopy revealed chronic gastritis without evidence of active bleeding, and colonoscopy revealed nonspecific inflammation. Splenomegaly was not observed on abdominal and pelvic computed tomography. Chest computed tomography was unremarkable.

Based on the findings, the patient’s anemia was considered to be anemia of chronic disease, and he was discharged and followed in the outpatient clinic. However, 1 week after discharge, he was readmitted to hospital for further assessment of increased atypical lymphocytes (5%) and immature cells (1%) accompanied by leucocytosis on his complete blood count.

A repeated peripheral blood smear showed leucocytosis, neutrophilia with decreased granules, monocytes (16%) with immature monocytes, and immature cells (2%) (Figure 1). Bone marrow aspiration and biopsy revealed hypercellular marrow (90%–100% cellularity) with infiltrating immature cells, increased numbers of granulopoietic cells, and megakaryocytes (7–8 per high-power field, Figure 2). Cytogenetic analysis of bone marrow revealed the karyotype 46,XY,+11[19]/46,XY[1] (Figure 3). Fluorescence in situ analysis for chromosomal abnormalities in patients with MPN was performed, but was negative for abnormalities involving chromosomes 13 and 20 and for BCR-ABL1 rearrangements. The final diagnosis was MDS/MPN, CMML-1.

Because hypomethylating agents such as 5-azacitidine or decitabine are not covered by Korean National Health Insurance, and because the patient was elderly, he was monitored by the outpatient clinic and received intermittent transfusions of packed red blood cells.

Two months after his diagnosis, the patient complained of slowly increasing overall weakness, loss of appetite, and dizziness. His Eastern Cooperative Oncology Group performance status at that time was 3.

A complete blood count displayed markedly increased leucocytosis and anemia, with hemoglobin 5.7 g/dL, white blood cells $156.8 \times 10^9/L$ (differential: neutrophils 42%, lymphocytes 19%, eosinophils 5%, basophils 0%, monocytes 24%, myelocytes 1%, metamyelocytes 5%, and immature cells 6%), and platelets $111 \times 10^9/L$ (Figure 4). The patient’s renal function had also deteriorated, with measured blood urea nitrogen 78 mg/dL and creatinine 5.7 mg/dL (estimated glomerular filtration rate by Modification of Diet in Renal Disease: 9.6 mL/min/1.73 m²). His uric acid level was 18.3 mg/dL.

The findings were highly suggestive of leukemic transformation of CMML, with tumour lysis syndrome. Massive hydration and allopurinol were initiated for acute kidney injury superimposed on chronic kidney disease. Because of the patient’s poor kidney function, he did not receive 6-mercaptopurine. In addition, because of his poor performance status, cytotoxic chemotherapy was not considered feasible, and he was transferred to a hospice care facility.
The features of CMML overlap with those of MDS and MPN. In most CMML patients, the disease course is indolent. However, because 15%–20% of patients can progress to acute myeloid leukemia, CMML patients must be followed and managed carefully. Of all CMML patients, 30% have cytogenetic abnormalities. Various risk stratifications have correlated certain cytogenetic abnormalities [+8, –Y, –7/7q–, 20q–, +21, and der(3q)] with survival outcomes. However, none of the stratification models include trisomy 11, a rare chromosomal abnormality in CMML.

Estimating the prevalence or incidence of CMML harbouring trisomy 11 is difficult because of the scarcity of published studies and the infrequency of cases. In a large study of 1084 patients with MDS, trisomy 11 was found in 28 patients (prevalence of 3%), mostly as part of complex karyotypes instead of as an isolated abnormality. But the study did not report the prevalence of trisomy 11 in patients with CMML.

The prognostic features of CMML with trisomy 11 have not yet been well established. Studies revealing the survival outcomes of MDS patients with trisomy 11 are also few in number. A study of patients with MDS or MDS/MPN reported that median survival in the 31 MDS or MDS/MPN patients with trisomy 11 was 11.5 months, which was comparable to the median survival of 10 months seen in MDS patients with poor-risk cytogenetic abnormalities. Another study showed that, for MDS patients with trisomy 11, median overall survival was 6.6 months, which was much shorter than the median survival in the MDS population as a whole.

Based on earlier studies, MDS patients with trisomy 11 can be classified into high- or intermediate-risk groups, but the prognostic value of trisomy 11 is better established for hematologic malignancies other than CMML. In patients with acute myeloid leukemia, trisomy 11 is not uncommon and is associated with an intermediate or poor risk, with a median duration of complete remission of 17.5 months (range: 8.7–49.8 months), and with a median overall survival of 14.3 months (range: 0.5–50.7 months). In addition, a study of acute myeloid leukemia with clonal isolated trisomy 11 revealed mutational landscapes that included the partial tandem duplication of KMT2A (formerly MLL), the internal tandem duplication of FLT3, and mutations in DNMT3A, U2AF1, IDH2. However, the presence of those genetic alterations has not been established for MDS and CMML. Further study is needed to determine whether CMML patients with trisomy 11 have such genetic mutations.

Hypomethylating agents currently constitute the optimal treatment for CMML. The overall response rate varies from 25% to 75%, in association with the genetic alterations. The only curative option is allogeneic stem-cell transplantation, but that therapy is associated with marked morbidity and mortality. The novel agent ruxolitinib, which is a Janus kinase 1 and 2 inhibitor, is being studied in a phase I trial that is enrolling patients with CMML.

Regardless of available treatments, response and survival outcomes are still not favourable in patients with CMML. The effects of trisomy 11 on response to treatment and survival have yet to be clarified, but physicians might decide that CMML patients with trisomy 11, which is often associated with a poor outcome, should not be treated aggressively.

**SUMMARY**

Our patient presented with ongoing anemia and atypical peripheral blood cells that suggested indolent leukemia. The findings on bone marrow biopsy led to a diagnosis of CMML with isolated trisomy 11. The patient developed manifestations suggestive of leukemic transformation 2 months after that diagnosis. This case report helps to better the understanding of the clinical manifestations and prognosis of patients with CMML featuring trisomy 11.

**ACKNOWLEDGMENTS**

We gratefully acknowledge the participation of our patient. Informed consent was not given, but was waived by the institutional
ethics committee because the patient was deceased without any next-of-kin, beneficiary, or legal guardian. All details that might result in identification of the patient have been omitted.

CONFLICT OF INTEREST DISCLOSURES
We have read and understood Current Oncology’s policy on disclosing conflicts of interest, and we declare that we have none.

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