Chronic Myelomonocytic Leukaemia Primarily Presenting as Life-Threatening Pericardial Effusion, Eldoret, Kenya: A Case report

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Title Page

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Key Clinical Message

Chronic myelomonocytic leukaemia, a rare case of haematological malignancy mainly affects the elderly and may present with life threatening pericardial effusion as an initial manifestation. High index of suspicion is hence key for early management.

Abstract

We present a case of an 81-year-old African male who presented with progressive cough, respiratory distress and bilateral lower limb swelling, and was diagnosed with life-threatening pericardial effusion resulting from chronic myelomonocytic leukaemia following complete blood count, peripheral blood film, bone marrow aspirate with trephine biopsy, and flow cytometry studies.

Keywords: *Chronic myelomonocytic leukaemia, pericardial effusion, heart failure, ascites, pleural effusion*

Introduction

Chronic myelomonocytic leukaemia (CMML) is a haematological malignancy characterised by both clinical and pathological features of myeloproliferative and myelodysplastic syndrome. It is evidenced by peripheral monocytosis and myeloid precursor cell dysplasia.[1] According to 2016 World Health Organisation (WHO) classification of myeloid neoplasms and acute leukaemias, CMML is classified under the group of myelodysplastic/myeloproliferative neoplasms (MDS/MPN), together with juvenile myelomonocytic leukaemia, atypical chronic myeloid leukaemia, and ring sideroblasts with thrombocytosis. This group also constitutes the MDS/MPN unclassified type.[2,3]

CMML is relatively a rare disorder, with a current reported incidence of 4 cases per 100,000 persons/year [4]. It mainly affects the elderly with a median age of 71 – 73 years. CMML presents heterogeneously, with clinical features ranging from constitutional symptoms, splenomegaly to cytopenias as well as extramedullary disease, but rarely causes life threatening extramedullary complications such as pericardial and pleural effusion as well as ascites.[5–7] We report a case of an 82-year-old male patient with CMML who presented with pericardial effusion and acute heart failure.

Case presentation/examination

An 82-year-old male patient was admitted to Moi Teaching and Referral Hospital, Eldoret on 1st April 2022 with progressive cough, difficulty in breathing and bilateral lower limb swelling for 4 weeks. He had a previous history of on and off cough since June 2021. The cough was mostly dry, but sometimes associated with whitish sputum. It was not variable by time of the day and was initially not associated with hotness of body, paroxysmal nocturnal dyspnoea, orthopnoea, easy fatiguability or lower limb swelling. However, four weeks prior to admission, the cough became persistent and associated with difficulty in breathing, dyspnoea on mild exertion, progressive bilateral lower limb swelling, abdominal distension, and early satiety. He also reported unintentional weight loss, but no history of other known chronic illnesses such as diabetes mellitus, hypertension, asthma, chronic obstructive pulmonary disease, and tuberculosis.

On physical examination, he had bilateral non-tender pitting oedema up to the knee level. His BP was 120/70mmHg, PR 79bpm, RR 18bpm and SPO_2 75% room air (which improved to 96% on 7L of O_2 via non-rebreather mask), and temperature of 36.8°C. Cardiovascular exams revealed warm extremities, normal volume peripheral pulses, muffled heart sounds but no cardiac murmurs. Abdominal examination revealed non-tender abdominal distension, hepatomegaly (4 cm below the costal margin), shifting dullness but no splenomegaly. Respiratory and central nervous systems were unremarkable.

Methods (Differential diagnosis, investigations and treatment)

Complete blood count revealed WBCs of $75.32*10^9$/L, absolute neutrophils: $50.56*10^9$/L (67.6%), monocytes: $18.50*10^9$/L (24.0%), lymphocytes: $4.76*10^9$/L (6.6%), Hb 12g/dl and platelets of $142*10^9$/L. NT-proBNP was 4,800pg/ml (normal <125pg/ml). Renal, liver and thyroid function tests were largely unremarkable. Blood culture yielded no growth, ruling out sepsis.

Electrocardiography showed low voltage QRS complexes with electrical alternans **(Fig 1).** Echocardiography showed large circumferential pericardial effusion (3.0cm), swinging heart, RA/RV free wall collapse with evidence of pulmonary hypertension (RVSP of 43mmHg), dilated non-collapsing IVC with normal left and right ventricular function.

[**Fig 1**]

Chest and abdominal CT scan showed pericardial and bilateral pleural effusion, and moderate ascites with multiple para-aortic and mesenteric nodes **(Fig 2).** Peripheral blood film showed monocytosis, and left shift with less than 1% blasts. Bone marrow aspirate with trephine biopsy showed hypercellular marrow with myeloid hyperplasia but no excess blasts, while flow cytometry was 94% positive for CD14, with remarkable monocyte population with aberrant CD123 (94%) and CD56 (83%), highly suggestive for CMML. Based on these findings, we arrived at a diagnosis of CMML presenting with acute heart failure (HF) due to life threatening pericardial effusion.

[**Fig 2**]

Pericardiocentesis with placement of pigtail catheter was done, draining a total of 1,800mls of haemorrhagic fluid (800mls on day 1, 750mls day 2, 150mls day 3 and 100mls day 4). This resulted in the relief of the patient's symptoms, including weaning from oxygen supplementation. Pleural fluid was exudative, with the total protein of 63.5g/L against total serum protein of 74.7g/L (pleural fluid: serum total protein ratio of 0.85). Both pericardial and pleural fluid culture and gram-staining for acid-fast bacteria were negative ruling out pericardial tuberculosis. The patient was therefore started on diuretics: frusemide and spironolactone for the heart failure, and hydroxyurea 1g twice daily for the CMML.

Conclusion and Results (Outcome and follow-up)

The patient clinically improved and was discharged from hospital on day 21, with the discharge WBC being $36.92*10^9$/L, neutrophils $18.58*10^9$/L (50.3%), monocytes $10.44*10^9$/L (28.3%), lymphocytes $7.02*10^9$/L (19.0%), Hb 10.6g/dl and platelets $35*10^9$/L. He was scheduled for follow-up at the MTRH haemato-oncology clinic in two weeks, for which he returned and was doing well, with the WBC having reduced to $15.21*10^9$/L, neutrophils $8.35*10^9$/L, monocytes $3.44*10^9$/L, lymphocytes $2.66*10^9$/L, Hb 11.2g/dl and platelets $100*10^9$/L. Further details on the laboratory findings are as shown in supplementary document.

Discussion

CMML is a rare haematological disorder, with most of the cases being asymptomatic at presentation. This makes the diagnosis of CMML challenging, especially in the low and middle-income settings where diagnostic resources could be limited. Noting that CMML has an inherent risk of transforming to acute myeloid leukaemia (AML) and this is associated with poorer outcomes,[8,9] high index of suspicion is therefore primal for early recognition and initiation of treatment. Our patient presented with acute HF from life-threatening pericardial effusion, which is a much rare manifestation of CMML,[6,7] Therefore, the diagnosis of CMML as the primary cause of our patient's complaints could have been missed were it not for the attention paid to the pericardial effusion as well as white blood cell counts. This necessitated further investigations and exclusion of common potential causes of pericardial effusion in our set up such as tuberculosis and other bacterial infections. Further, other causes of reactive monocytosis such as infections, chronic myeloid leukaemia (CML), essential thrombocythemia, polycythaemia vera and primary myelofibrosis were excluded by blood culture, PBF, bone marrow biopsy and flow cytometry. This led to early intervention for the HF and recognition as well as treatment of CMML in our patient. Consequently, he clinically improved significantly and was discharged from the hospital.

CMML diagnosis should therefore be guided by high index of suspicion, supported by suggestive findings from complete blood count and bone marrow. According to the 2016 WHO diagnostic criteria, CMML is diagnosed by: peripheral blood and bone marrow morphological findings of peripheral monocytosis of $>1*10^9$/L, with monocytes comprising >10% of the total WBC persisting more than 3 months, <20% blasts in peripheral blood and bone marrow, and dysplasia affecting [?]1 myeloid cell lines.[5,10,11]

Clinical presentation of CMML is quite variable, ranging from being asymptomatic to constitutional symptoms such as malaise, weight loss and night sweats, as well as symptoms of specific cytopenias such as headache among those with anaemia, bleeding tendencies among those with thrombocytopenia and recurrent infections due to white blood cell dysfunction [12]. On the other hand, polyserositis, which refers to the inflammation of the serous membranes (pericardium, pleura and peritoneum) and formation of serous

effusions is a rare presentation of CMML.[6,13,14] Fauci et al. reported that polyserositis affected up to 20% of the cases.[15]Of the 9,723 cases analysed by Kaur et al., only 0.4% (n =40) had leukemic involvement of the serous membranes ,with only 1 case being due to CMML.[16] The most common site was pleural cavity (n=30), followed by peritoneal cavity (n=7), then pericardial cavity (n=3). Therefore, our patient primarily presenting with life-threatening pericardial effusion with acute heart failure was a much rarer case of CMML.

WHO recommends that the diagnosis of CMML be made after the exclusion of other causes of reactive monocytosis such as chronic myeloid leukaemia (CML), essential thrombocythemia and polycythaemia vera. Multiparameter flow cytometry is key in excluding these differentials. The presence of [?]94% of classical human monocytes which express a high positive CD14 and high negative CD16 surface markers in flow cytometry has a sensitivity and specificity of 91.9% and 94.1% respectively in distinguishing CMML from the aforementioned differentials.[4,11,17] Notably, our patient expressed 94% CD14 in flow cytometry. Further, he showed 94% CD123 and 83% CD56, which are also highly suggestive of CMML.[4]

Further diagnosis of CMML would require elicitation of the absence of*BCR-ABL1* fusion for CML through RT-PCR or FISH. However, we could not conduct these tests due to resource limitation, although CML would very rarely present with more than 10% monocytes.[5]Our patient had 24% monocytes. Additional molecular studies to rule out genetic rearrangements such as *PCM1-JAK2, PDGFRA, PDGFRB, FGFR1*for very rare cases which would also have eosinophilia and monocytosis would be important,[3–5] and form part of WHO diagnostic criteria for CMML. We could however not do these tests in our set up due to their unavailability. Notwithstanding, the evidence from our PBF, bone marrow and flow cytometry results was sufficient for the diagnosis of CMML in our case.

In conclusion, CMML is a rare haematological disorder, with a highly variable presentation. Its diagnosis requires high index of suspicion especially in low resource setting where advanced diagnostic tools are not readily available. Further, pericardial effusion is a rare but a fatal complication of CMML that clinicians need to be cognisant of. Noting that CMML has a high propensity to transform to AML with poor prognosis, early recognition and initiation of treatment would be highly recommended.

Author contributions

Victor M. Wauye: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, visualization, writing – original draft, and writing – review & editing. **Evangeline Njiru:** Conceptualization, investigation, methodology, project administration, supervision, validation, visualization, and writing – review & editing. **Angela K. Amadi:** Investigation, methodology, project administration, and writing – review & editing.

Mildred N. Hagembe: investigation, methodology, project administration, and writing – review & editing. **Gabriel Kigen:** Supervision, validation, visualization, and writing – review & editing.

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Images/figures

Submitted as separate files.