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Case Report

Dissemine intravasculary coagulation may be the presenting feature for chronic myelomonocytic leukemia: Special case report

Chronic myelomonocytic leukemia (CMML) is a malignant myeloid stem cell disease accompanied by dysplasia in the context of myeloproliferative disease. Peripheral cytopenias (mainly anemia and thrombocytopenia) and hepatosplenomegaly are common findings.

Dramatic leukocytosis can also be seen without transformation to acute myeloid leukemia (AML); in some cases, this leukocytosis is associated with leukostasis and end organ damage. Splenomegaly is present in up to 25 percent of patients with CMML and is often accompanied by hepatomegaly, lymphadenopathy, or nodular cutaneous leukemic infiltrates. Gingival infiltration is occasionally observed but is much rarer than in AML with monocytic differentiation; central nervous system involvement is rare. Pleural and pericardial effusions and ascites can occur in CMML with very high monocyte counts and these signs often resolve with antileukemic therapy. Constitutional symptoms (ie, fevers, unexplained weight loss, and night sweats) are seen in some CMML cases and are similar to the symptoms associated with primary myelofibrosis.

The acquired cogulation defect may be due to factor X binding to atypical monocytes,resulting with acquired factor X deficiency.We report this case of CMML , who presented symptomatic multiple hemorrhagic skin lesions, echimosis and hematomas. Despite the rarity, Dissemine intravascular coagulation (DIC) may be presenting clinical feature for CMML. The treatment is challenging and considering the high risk of bleeding because of thrombocytopenia, acute Dissemine intravascular coagulation (DIC) also aggrevates the complications.

Case Report

Eighty-two years old female is having a car accident in May. She had no bone fracture but multiple echymosis were existing. She is discharged with preventive suggestions and supportive treatment. One week later she was admitted to internal medicine outpatient clinic for weakness and shorthness of breath. Anemia and low fibrinogen levels were detected. She is referred to the hematology department for further examination and eventual treatment. The patient goes to her daughter outside the city and afterwards being examined there. Bone marrow biopsy was performed and she continued bleeding at the biopsy region for hours. Coagulation tests were requested and fibrinogen level was <50 mg/dL. She was hospitalized for treatment, after 2 weeks the patient is discharged for financial reasons after blood product replacement. In January 2019 the patient admitted to our hospital's emergency department with multiple echymosis again. Her laboratuary results are summarized in table 1. She rejected a second bone marrow biopsy and decided to go home after plasma infuison.

However, she was referred to our hospital for diagnostic tests and treatment a month later. Peripheral smear,bone

Table 1: Laboratuary results at diagnosis and the last results after treatment.

	Diagnosis	After 3 cycles of Decitabine
PT	19.6 sn	14.4
aPTT	36 sn	39.4
INR	1.7	1.11
Fibrinogen	53 mg/dL	243
WBC	11.97 10e6/uL	4.49 10E6/uL
Mon	2.53	0.24
Neu	6.38	2.07
Hgb	13 gr/dL	9.9 gr/dl
Plt	43.000 10e3/uL	42.000 10e3/uL
Peripheral smear	Myelomonocytic atypical cells %19 %2 myelocyte Platelet count is smilar to CBC Normochrome normocytic RBC	No abnormal myeloid cell

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marrow biopsy and aspiration was performed. Cytogenetic tests and caryotype analysis were ordered.

She was diagnosed with CMML with bone marrow biopsy and decitabine treatment protocole was started. After the second course of treatment she was transfusion independent. She is still ongoing the same protocole. The latest laboratuary results are listed in table 1.

Conclusion

Cases of CMML have a persistent peripheral blood monocyte count >1000/microL that makes up >10 percent of the entire leukocyte differential. Despite a relative increase in monocytes, the total white blood cell count is not increased in many CMML cases. Myeloid dysplasia may be seen in all myeloid subsets, and unique abnormal mononuclear cells exhibiting features intermediate between myelocytes and monocytes, termed "paramyeloid cells," are often apparent [1].

The World Health Organization (WHO) criteria for the diagnosis of CMML is revised in 2016 as shown in table 2 [2].

CMML is also stratified into different forms according to WBC count, peripheral and bone marrow blast and promonocyte counts which is summarized in table 3.

Here we report an unusual case of CMML , presenting with DIC during diagnosis. The diagnosis in most cases is usually based upon peripheral blood and bone marrow abnormalities and clinical non-spesific features may co-exist. However bleeding or coagulopathy is extremely rare in the diagnostic period. All patients suspected as myeloid neoplasia should be evaluated for bleeding diathesis.To date, there has been a few cases describing bleeding diathesis in CMML patients and these cases were under treatment for CMML. Distinctly, our case has been referred to us for Dissemine intravascular coagulation (DIC) and later was diagnosed for CMML.

Table 2: WHO criteria for diagnosis of CMML.

persistent PB monocytosis >1 × 10e9/L, with monocytes accounting for ≥10% of the white blood cell (WBC) count;
not meeting WHO criteria for BCR-ABL1 CML, PMF, PV, or ET;
no evidence of PDGFRA, PDGFRB, or FGFR1 rearrangement or PCM1-JAK2 (should be specifically excluded in cases with eosinophilia);
<20% blasts in the blood and BM;
dysplasia in 1 or more myeloid lineages. If myelodysplasia is absent or minimal, the diagnosis of CMML may still be made if the other requirements are met and;
an acquired clonal cytogenetic or molecular genetic abnormality is present in hematopoietic cells or the monocytosis (as previously defined) has persisted for at least 3 months and; all other causes of monocytosis have been excluded

Table 3: Subgroups of CMML.

WBC count	The percentage of blasts plus promonocytes in the PB and BM
Myelodysplastic, with WBC count <13 × 10e9/L;	CMML-0, (with <2% blasts in PB and <5% blasts in BM);
Proliferative, with WBC count >13 × 10e9/L	CMML-1 (with 2–4% blasts in PB and/or 5–9% blasts in BM);
	CMML-2 (with 5–19% blasts in PB, 10–19% in BM, and/or when any Auer rods are present)

Many patients with cancer suffer from hypercoagulability. There may only be abnormal coagulation tests in the absence of thrombosis but also the patient may refere with massive thromboembolism [3].

Monocytes express a small amount of procoagulant activity (PCA). However, they can be stimulated to produce tissue factor and other direct factor X activators. This activation can be triggered by T lymphocytes, various antigens, cytokines, some lipoproteins, immune complexes, endotoxins [4-11]. Monocytes may also be activated by tumor-specific antigens and immune complexes or other cytokines containing them. For example, in lung cancer, pulmonary alveolar macrophages adjacent to tumor increased tissue factor activity in vitro compared to cells from normal controls or macrophages from the contralateral side of the tumor [12]. In CMML patients similar to these malignancies monocytes may provocate hypercoagulation as in our case.

Due to the heterogeneity of the disease, the clinical course and outcomes of patients with CMML are variable. To date, a number of clinical parameters have been reported to be associated with poor survival time of patients with CMML, including age, sex, Eastern Cooperative Oncology Group performance status , Hb level, WBC count, number of circulating immature myeloid cells, proportion of BM blasts, karyotype and β2-microglobulin/lactate dehydrogenase levels . Furthermore, previous reports have demonstrated that a high proportion of BM blasts, elevated lactate dehydrogenase, male sex and a low Hb level were independent prognostic factors. Most recently, cytogenetic status and specific gene mutations have been identified as important prognostic factors, and have been incorporated into the CMML risk stratification system.

The general prognosis of patients with CMML is poor, with an expected median survival of approximately 30 months. Several risk stratification models are available for estimating the prognosis of patients in clinical practice. Patients with low risk disease by both the MDACC and Mayo scoring systems can delay transplant until progression.

For those who are not candidates for allogeneic HCT and who decide not to participate in a clinical trial, we suggest symptom-directed therapy with either cytoreductive therapy (eg, hydroxyurea) or hypomethylating agents (eg, azacitidine, decitabine). Cytoreductive therapy is usually preferred for patients with dramatic proliferative symptoms, while hypomethylating agents are preferred for patients with cytopenias and those with myeloproliferative symptoms in whom hydroxyurea is ineffective [13-16].

As hematologists, emergency doctors and internal medicine doctors should be alert for elderly patients presenting with Dissemine intravascular coagulation (DIC) regarding chronic myeloid neoplasias. Especially CMML may imitate more frequent hypercoagulative diseasessuch as acute promyelocytic leukemia. However, it would be very helpful just to recall the possibility and analyse the peripheral smear for differential diagnosis in detail. Remembering and diagnosing CMML in this group patients may lead a remission status after hypometillating agent protocol.

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