

Chronic Lymphocytic Leukemia (CLL)

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INTRODUCTION:

Chronic Lymphocytic Leukemia (CLL) is a monoclonal disorder characterized by a progressive accumulation of functionally incompetent lymphocytes. It presents with lymphocytosis, progresses to lymphadenopathy, hepatosplenomegaly and bone marrow failure. The cells of origin in the majority of patients are clonal B cells arrested in the B-cell differentiation pathway. Morphologically in the peripheral blood, these cells resemble mature lymphocytes².

As in the case of most malignancies, the exact cause of CLL is uncertain however the protooncogene bcl2 is known to be over expressed, which leads to suppression of apoptosis (programmed cell death) in the affected lymphoid cells. CLL is an acquired disorder, and reports of truly familial cases are exceedingly rare. CLL is the most common form of leukemia in the western world with an average incidence of around 62 years. About 10-15% of cases are below 50 years and males are affected more than females with a male-to-female ratio of 1.7:1.1.

CASE:

A 46-year old male referred from Ngara district, Kagera region with chief complaints of painful multiple swellings on the neck, armpit and groin for 6 months, abdominal pain and abdominal distention. The patient was well until 6 months ago when he started noticing growing nodules on the neck, axilla, and groin, which were painful from the onset. One month later, he had abdominal distention which was of gradual onset and bilaterally symmetrical.

Abdominal pain was dull in nature, more prominent on the upper part and did not respond to ordinary analgesics. He also complained of tiredness and fatigue. There was no history of fever, bone/joint pain, excessive bleeding or easy bruising, difficulty in micturition, constipation. Review of other systems indicated history of dry cough, difficulty in breathing and awareness of heart beats (palpitations). The man was a peasant and a refugee from Burundi.

On examination the patient appeared to have good nutritional status, was moderate pale, he had visible multiple enlarged lymph nodes on the neck, axilla and groin. The patient was not dyspnoeic, no jaundice and was afebrile (37^o C). On palpation of

the nodules, some were discrete, hard & some were matted, tender, 5-8cm in size, mobile and not fixed to the skin.

Pulse rate was 80 bpm, Blood pressure (BP)-120/80 mmHg and the apex beat was detected in the 4th intercostal space, mid-clavicular line. Chest examination revealed fine crepitations on the right lung base. The abdomen was distended, more above the umbilicus, but moved with respiration. The spleen was enlarged 4cm below the left costal margin. The liver was also enlarged 3cm below the right costal margin mid-clavicular line.

Laboratory studies revealed mild anemia (9.5 g/dL), leucocytosis (3.48x10⁹/L), lymphocytosis (1.47x10⁹/L), neutropenia (1.59x10⁹/L), thrombocytopenia (113 K/ μ L), basophilia (9.94 x 10⁹/L) and low hematocrit (19.7 %). Erythrocyte Sedimentation Rate (ESR) was normal.

Peripheral blood smear showed poorly fixed and haemolysed RBC's, numerous mature lymphocytes and smear cells with slightly reduced platelets. Complete chemistry indicated low levels of Calcium with increased levels of alkaline phosphatase, chloride, potassium, phosphate, lactate dehydrogenase (LDH), creatinine and urea. Prothrombin time (PT), Activated partial thromboplastin time (APTT) were normal and international normalized ratio (INR) was low. ELISA was negative for HIV.

Chest x-ray indicated irregular ribs on both sides (ribs no. 2, 3 & 4). Slightly increased diploic space with hair on end appearance (at occipital lobe) was seen on skull x-ray. Ruggier Jersey sign was positive at distal end humerus with osteoporosis. X-ray of femur was normal. These findings were suggestive of early bone manifestation of CLL.

Abdominal ultrasound showed hepatomegaly with smooth margins and homogenous echoes without intrahepatic duct dilatation. Spleen was enlarged (18cm below left costal margin) with smooth margins and homogenous echoes. The kidneys were normal in size, slight hyperechogenicity with loss of corticomedullary differentiation (nephritis) and

no hydronephrosis. Para aortic lymph nodes were enlarged. No ascites was seen and the gall bladder & pancreas were normal.

Fine Needle Aspiration Cytology (FNAC) of the lymph nodes revealed mature lymphocytes, macrophages and plasma cells. This picture was suggestive of chronic inflammation. Bone marrow aspirate showed no particles. Sheets of mature lymphocytes predominated (98%) with marked reduction of other marrow cells. Iron stain was not suitable. CLL was diagnosed. The signs and symptoms of the patient together with the investigations indicated the patient was in stage B (Binet staging system)³.

Tablets Diclofenac for pain relief, Capsules Amoxicillin to treat the chest infection were prescribed. Prednisone and Chlorambucil was prescribed to treat CLL.

DISCUSSION

The natural history of CLL is heterogeneous. Some patients die rapidly, within 2-3 years of diagnosis, the majority of patients live 5-10 years. During the later phase, morbidity is considerable, both from the disease (eg Immunosuppression) and from complications of therapy¹.

Onset is insidious, and it is not unusual for this disorder to be discovered incidentally after a blood cell count is performed for another reason. This patient presented with multiple swellings, abdominal pain and distention. Other symptoms and signs include sinusitis, bacterial pneumonia, bruising and bleeding, petechiae, night sweats, fever and weight loss are uncommon but may occur¹.

A number of autoimmune phenomena may occur in patients with CLL. The most common manifestations are autoimmune haemolytic anemia (AIHA) and autoimmune thrombocytopenic purpura (ITP)². In the above case, the patient did not present with obvious bleeding tendency. However, he had thrombocytopenia thus necessitating further investigations to rule out autoimmune phenomena.

Differentials include Non-Hodgkin's Lymphoma, Hairy Cell Leukemia, Lymphoblastic Lymphoma, Diffuse Large Cell Lymphoma, Follicular Lymphoma and Chronic Myelogenous Leukemia¹.

FBP shows absolute lymphocytosis with more than 5000 lymphocytes/ μL (as seen in the case above). Microscopic examination of the peripheral blood smear usually shows the presence of smudge cells.

Peripheral blood flow cytometry is the most valuable test to confirm CLL¹. This is not done in our setting.

Bone marrow aspiration is not required in all cases but may be necessary in selected cases to establish the diagnosis and to assess other complicating features such as anemia and thrombocytopenia. Lymph node biopsy is indicated if lymph node(s) begin to enlarge rapidly in a patient with known CLL to assess the possibility of transformation to a high-grade lymphoma. When such transformation is accompanied by fever, weight loss, and pain, it is termed Richter syndrome⁴.

The patient developed anemia and thrombocytopenia possibly due to secondary bone marrow involvement. Other complications include splenic sequestration of red blood cells. Extremely high white blood cell counts ($>300,000/\mu\text{L}$) may produce a hyperviscosity syndrome with altered central nervous system function and/or respiratory insufficiency¹.

None of these other complications were seen in this case. Main stay for treatment of CLL is chemotherapy. Some patients require admission if they develop febrile neutropenia.

More intensive treatment including bone marrow transplantation is sometimes attempted in young patients¹. This patient being a refugee prevented follow up of further management since he had to be returned to the camp.

CONCLUSION

This case advocates the basic mixture of signs and symptoms that could be directing to an infectious (eg Commonly HIV in our setting). High index of suspicion would be required to catch the disease early. Early diagnosis of CLL leads to prevention of further complications that could have required palliative care only.

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