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Case Report

Oncology Section

Haematological Malignancy Presenting in an Unusual Manner

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ABSTRACT

Chronic lymphocytic leukaemia is a haematological malignancy that occurs due to an increased proliferation of mature B lymphocytes. It is considered to be the most common leukaemia in adults. Hyponatraemia is commonly seen in such patients. This case report is about a 75-year-old male, who presented with giddiness, followed by altered sensorium. However, the patient had no motor weakness or sensory loss. Initially, a diagnosis of posterior circulation stroke was made but Magnetic Resonance Imaging (MRI) brain did not show associated signs. The routine investigations showed highly elevated total leukocyte count and Hyponatraemia. The patient was worked up for malignancy and diagnosed with chronic lymphocytic leukaemia. Oncology reference was taken and treated with tablet Ibrutinib. On discharge, the patient's mentation improved, and he is on regular follow-up.

Keywords: Chronic lymphocytic leukaemia, Flow cytometry, Fluorescence in-situ, Hyponatraemia, Ibrutinib

CASE REPORT

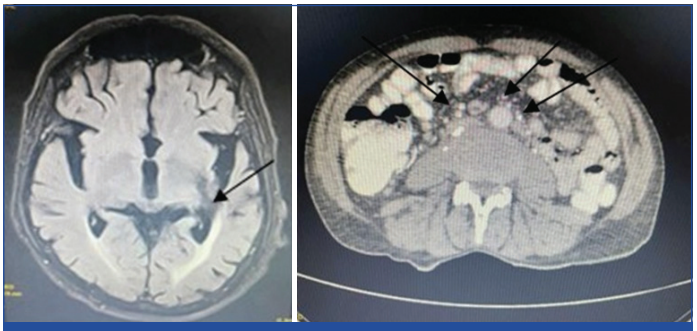
A 75-year-old male patient, known hypertensive, reported to the Emergency Department with complaints of an episode of sudden onset of giddiness the previous night, in the washroom. The episode lasted for a few minutes followed by which the patient had a fall. However, there was no head injury. According to the companions, the patient had developed in-coherent speech after this incident and was not able to identify the people around him. The patient had no weakness of any limbs, there was no sensory loss or involuntary movements. No history of loss of consciousness, headache, fever, vomiting, bowel or bladder disturbances. The patient was diagnosed to have cerebrovascular accident and seizure disorder in 2018 since then he was on regular medication. He was a known hypertensive taking tablet amlodipine 5 mg twice daily.

All vitals like temperature (98°F), pulse rate (72/min), blood pressure (150/90 mmHg), and respiratory rate (20/minute) were within normal limits. No signs of respiratory distress was seen. There were no pallor, icterus, cyanosis, clubbing, lymphadenopathy and pedal oedema. On Central Nervous Examination (CNS) examination, the patient was conscious. His sensorium was altered and he was not oriented to time, place, and person. Glasgow Coma Scale was 13/15. However, there were no cranial nerve palsies and no motor weakness or sensory loss in any of the limbs. Both plantars were down going and meningeal signs were absent. Initially, the differential diagnosis of meningoencephalitis or a form of posterior circulation stroke was made in view of altered sensorium and vertigo.

Routine investigations, on the day of admission, revealed an elevated total count (57000 cells/mm^3) with normal haemoglobin and platelet count. Hyponatraemia was present (107 mEq/L) with normal potassium. Both serum and urine osmolality were low (226.5 and 135 mOsm/kg), respectively. Urinary sodium was low (35 mmol/L). Serum cortisol was (15.6 mcg/dL) which was normal. Peripheral blood smear was suggestive of marked leukocytosis, atypical lymphocytes, and few smudge cells. Chest X-ray and electrocardiogram did not show any obvious abnormality.

Serum Adrenocorticotrophic Hormone (ACTH) was 49.49 pg/mL, serum aldosterone was 40.67 pg/dL, and he was Coronavirus Disease-2019 (COVID-19) Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR)-negative. Computed Tomography (CT) brain revealed no fresh bleed. The Magnetic Resonance Imaging (MRI) brain showed chronic ischaemic changes, gliotic changes due to old bleed in left thalamo-capsular, posterior limb of internal capsule [Table/Fig-1].

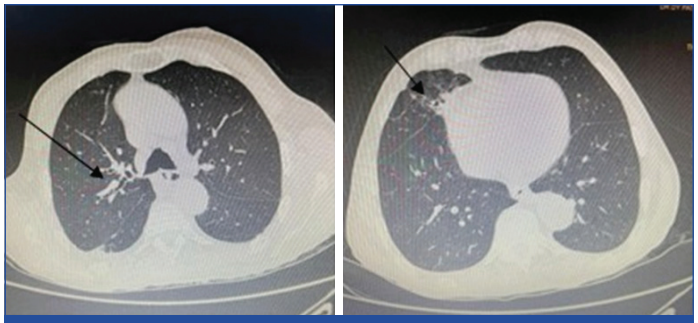
Magnetic Resonance (MR) angiography and venography were normal. Cerebrospinal fluid was clear in appearance, cob web appearance was absent, proteins of unit 52.5, glucose of unit 64, no Red Blood Cells (RBC) and Total Leukocyte Count (TLC) was 2 of which 100% were lymphocytes. Echocardiography was within normal limits. Contrast Enhanced Computed Tomography (CECT) Antero-posterior (AP) showed multiple enlarged discrete lymph nodes showing homogenous postcontrast enhancement in preaortic, bilateral para-aortic, retroaortic and retrocaval region, in the neck region enlarged Lymph Nodes (LN) were seen in level Ia, bilateral level Ib, II, IV and V [Table/Fig-2].



[Table/Fig-1]: Magnetic Resonance Imaging (MRI) brain showing old bleed in left thalamo-capsular region. **[Table/Fig-2]:** Contrast Enhanced Computed Tomography (CECT) Antero-posterior (AP) showing multiple enlarged discrete lymph nodes in pre aortic, bilateral para-aortic, retroaortic and retrocaval region. (images from left to right).

High Resolution Computed Tomography (HRCT) thorax revealed fibrotic infiltration with traction bronchiectasis in medial segment of right middle lobe along with fibrotic infiltrates in apical and apico-posterior segment of bilateral upper lobes. Enlarged pretracheal and precranial lymph nodes were also seen [Table/Fig-3,4].

The patient was started on Injection (Inj.) Ceftriaxone 1 gm i.v. bd, Tablet (Tab) Telmisartan and amlodipine (40/5) bd, Tab Metoprolol 25 mg od, Inj. Levetiracetam 500 mg i.v. bd Hyponatraemia was corrected with 3% NaCl. For further work-up of leukaemia, bone marrow examination was done which revealed mature lymphocytes (37%) replacing the normal haematopoietic cells, erythroid series showed normoblastic erythropoiesis, myeloid series showed



[Table/Fig-3]: High Resolution Computed Tomography (HRCT) thorax showing traction bronchiectasis in the medial segment of the right middle lobe.
[Table/Fig-4]: HRCT thorax showing fibrotic infiltrates in apical and apico-posterior segment of bilateral upper lobes. (Images from left to right).

maturation arrest, megakaryocytes were normal. These features were suggestive of Chronic lymphocytic leukaemia (CLL). Flow cytometry revealed 70% mature lymphocytes and 95% of total lymphoid cells expressed Cells of Differentiation (CD)5, CD19, CD20, CD22, CD23, CD200, Human leukocyte antigen (HLA)-Dendritic (DR) and lambda light chain, SmIgM, SmIgD. Co-expression of CD5 and CD19 was seen in 91% of total lymphoid cells. Findings were consistent with B-Chronic lymphocytic leukaemia/small lymphocytic leukaemia (stage 5).

The CLL panel fluorescence in-situ hybridisation was suggestive of B- chronic lymphocytic leukaemia with the following features:

1. DEL (Deletion)13 Q: positive for deletion of 13q.14.3 locus
2. DELATM: positive for deletion (DEL) of Ataxia-Telangiectasia Mutated (ATM) 11q22.3 locus
3. DEL (Deletion) TP53 (Tumour Protein 53): negative for TP53 (17p13)
4. Trisomy CEP 12: negative for trisomy 12.

Oncology opinion was taken and due to age and other associated conditions, considering the patient would not be able to tolerate chemotherapy, he was advised to start tablet Ibrutinib 420 mg daily for 7 days at the same time after food and to monitor for bleeding tendency, renal function tests and cardiac status. The patient was successfully treated with Ibrutinib. During discharge, he was conscious and well-oriented to time, place, and person. His total leukocyte count dropped to 34000 cells/mm and serum sodium increased to 128 meq/L.

DISCUSSION

In the western countries, CLL is considered to be the most common adult leukaemia. Various case studies have reported that the median age at diagnosis of CLL ranges from 70-72 years [1-3]. However, this patient's age at diagnosis was 75 years. Genetic factors play an important role in the etiopathogenesis of CLL as compared to environmental factors. Around 17% of first-degree relatives of patients with CLL had monoclonal B cell lymphocytosis, a precursor of CLL. Such patients with monoclonal B-cell lymphocytosis have increased risk of eventually being diagnosed with CLL [4,5]. However, this patient had no such positive family history of any carcinoma.

A study on CLL had reported that the presentations of CLL range from being asymptomatic at the time of diagnosis to having fatigue, excessive night sweats, involuntary movements and abdominal fullness [6]. However, this patient had presented in an unusual manner with altered sensorium and giddiness. Several studies reported that the incidence of hyponatraemia may be encountered in both benign and malignant haematological malignancy [7,8]. Hyponatraemia is considered as a negative prognostic factor in cancer patients. Asymptomatic patients can be treated with fluid restriction and symptomatic patients with Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) are treated with hypertonic saline [9].

Several studies have reported that the patients who are classified as high risk (Rai and Binet classification) have higher tumour load and more advanced disease [10-12]. The index patient falls under the intermediate to high-risk category. A study mentioned that bone marrow examination in CLL characteristically shows more than 30% of mature lymphocytes [13]. The index patient had 37% of mature lymphocytes. A study reported that in CLL flow cytometry typically expresses CD5, CD19, CD23 and CD200 [6]. This patient expressed CD5, CD19, CD20, CD22, CD23, CD200, HLA-DR, SmIgM, SmIgD. Studies have reported that rarely both kappa and lambda light chains are expressed, which is termed as "biclonal CLL" [14]. However, this patient expressed only lambda chain.

Ibrutinib is an irreversible inhibitor of Bruton's tyrosine kinase, which is approved for the treatment of CLL [15,16]. Patients with chromosomal aberrations of del (17p) and del (11q) are considered to have an aggressive disease. Studies have shown that early initiation of Ibrutinib in the course of management of CLL for such patients has improved the prognosis and hence have shifted ibrutinib to frontline therapy [17-19].

CONCLUSION(S)

It is important for treating physicians to recognise. Hyponatraemia in CLL and arrange for appropriate and timely intervention for a better outcome.

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