International Journal of Medical and Pharmaceutical Research
Website: https://ijmpr.in/| Print ISSN: 2958-3675 | Online ISSN: 2958-3683
NLM ID: 9918523075206676
Volume: 4 Issue:3 (May-June 2023); Page No: 338-343

Case Report

IJMPR

Chronic Lmphocytic Leukaemia with Pituitary Hypophysitis: A Case Report

Dr. Sujoy Mukherjee[1], Dr. Deep Das[2],Dr. Subham Bhattacharya[3], Dr. Aditi Munmun Sengupta[4]

[1]HOD of Internal Medicine and Critical Care, CMRI Hospital, Kolkata, India
[2] Senior Consultant Neuromedicine, CMRI Hospital, Kolkata, India
[3] Senior Consultant, Hematology, CMRI Hospital, Kolkata, India
[4]Principal Medical Officer, Critical Care Unit, CMRI Hospital, Kolkata, India;
Post Graduate Association Member, Harvard Medical School

ABSTRACT

A 55 years old man came to emergency department of a tertiary care hospital in Kolkata India with complaints of anorexia, weakness and vomiting with no prior history of fever or any significant medical comorbidities. On admission diagnosis was hyponatremia. During hospital stay he was also detected with Type 2 diabetes mellitus. Immunopheno typing (Flow cytometry) findings were consistent with Chronic lymphocytic leukaemia with CD38 expression. CECT whole abdomen and thorax showed features of multiple enlarged lymph nodes. CT Brain (Plain) showed normal study and MRI of pituitary gland showed bulky pituitary gland and infundibulum with homogenous enhancement in post contrast study. With just five examples of pituitary or hypothalamic involvement previously recorded, this case emphasizes an unusual presentation of chronic lymphocytic leukaemia (CLLBinet type A) with pituitary involvement.

Key Words: *CLL, Hyponatremia, Lymphocytic leukocytosis, Pituitary infundibulum*

***Corresponding Author**
Dr. Aditi Munmun Sengupta
Principal Medical Officer, Critical Care Unit, CMRI Hospital, Kolkata, India

INTRODUCTION:

A diverse range of disorders that present with reduced pituitary gland function are included in the hypophysitis, which is an inflammation of the pituitary gland. Pituitary insufficiency in adults is typically brought on by extracranial radiation, pituitary surgery, or pituitary or hypothalamus space-occupying tumours. Adenomas and cysts are just a couple of the many etiologies of a mass in the sella that can be differentiated. autoimmune conditions, primary or metastatic cancers, aneurysms, and parasellar lesions are among examples of granulomatous inflammation[1].

Case Study:

We present a clinically proven case of pituitary or hypothalamic involvement by CLL which is extremely rare and the delay in identification and therapy may be caused by unfamiliarity with this illness complication.

Graphical Representation of the Case

PROCEEDINGS

- A 55 YEARS OLD MALE PATIENT CAME IN EMERGENCY IN FEBRUARY 2022 WITH COMPLAINTS OF ANOREXIA, WEAKNESS AND VOMITING FOR 2 DAYS WITH NO HISTORY OF FEVER; DECREASED URINE OUTPUT FOR 2 DAYS; PATIENT DID NOT HAVE ANY SIGNIFICANT MEDICAL COMORBIDITIES.RECEIVED 2 DOSES OF COVISHIELD VACCINE.

- ON EXAMINATION: IN ER , PATIENT WAS CONSCIOUS , ORIENTED,(GCS- E3V4M5), TEMP=97.1F(NORMAL), PR=86(NORMAL), BP=136/80 MM OF HG(NORMAL RANGE),RR=20/MIN(NORMAL), SPO2=99%(RA), CBG=129MG/DL(LAST MEAL TIME=12:30 PM), PAIN SCORE=1/10, FACIAL PUFFINESS +, CHEST=B/L VBS, CVS=S1, S2 AUDIBLE, ABD=SOFT, NON- TENDER.

- COVID ID NOW: Negative

- ABG(RA): pH= 7.44/pCO2=30/pO2=80/HCO3=20.4/BE(B) = - 2.8/LACT=0.3/**Sodium=102**/K=3.7/Glucose=109/SO2=96%/ Hb=12.7

- ECG(ON ADMISSION) : NORMAL SINUS RYTHM.

- TREATMENT GIVEN IN ER : 3% Sodium chloride -100 ml *iv* over 7 hours (over 6 hours), Injection Pantoprazole (40 mg) *iv*, Injection Ondansetron(8 mg) *iv*.

- PROCEDURE DONE: Foley's catheterization(uneventful)

- INVESTIGATIONS SENT: CT Brain(Plain)

Patient was advised admission under Internal Medicine Consultant at ICU as per protocol

ADMISSION DIAGNOSIS: HYPONATREMIA UNDER EVALUATION

INITIAL INVESTIGATIONS

Pathological Investigations:

Routine Blood: Complete Blood Count, CRP, LFT, Urea, Creatinine, Sodium, Potassium, Serology, Blood grouping, Thyroid profile- T3, T4, TSH

Serum Cortisol(8 am/ 6 pm), PSA(Prostate specific antigen), Urine Routine

Radiological Investigations:

Chest X-Ray(PA view), USG abdomen, Echocardiography(2D)

ADMISSIONS ASKED FOR DURING THE COURSE OF STAY IN ICU:

Pathological Investigations:

Blood tests: Calcium, Magnesium , Phosphorus, LDH (Lactate Dehydrogenase), Uric acid,HbA1c, Prothrombin time

Hormonal profile: FSH(Follicle Stimulating Hormone), LH (Luteinizing Hormone), Prolactin, ACTH(Adrenocorticotrophic hormone), HGH(Growth hormone), Testosterone.

Special tests: Immunophenotyping (Flow Cytometry), CSF routine

Radiological Investigations: Contrast Enhanced CT Abdomen+Thorax, MRI of Pituitary gland.

INVESTIGATION FINDINGS

Blood Investigation Tests:

Hemoglobin=11.9 g/dl (initial) -12.4 (3 days later) ; **Total Leucocyte Count**=109800/cu mm (raised) N05, L75, E1, M1(initial) B0,Atypical mononuclear cells-18% -81300(3rd day of admission), N11, L75, E1, M3, B0, atypical mononuclear cells-10% ; **Platelets**-170x10^3/µL(initial)-150x10^3(3 days later); **ESR**=4 mm/1st hr(initial)-11mm/1st hr (3 days later); **Peripheral blood smear** (RBC: normocytic, normochromic; WBC: Leucocytosis, occasional smudge cells seen, platelets-adequate);

CRP=0.971mg/dl(raised)(initial);**Urea**=10mg/dl(initial); **Creatinine**=0.67mg/dl(initial); **Sodium**=111.2mEq/L(low)(initial)-112.9(1 day later)-115.30(2 days later)-127.3(3 days later); **K**=4.42mEq/L(initial)- 4.20(1 day later)-4.88(2 days later)-4.36(3 days later);**Calcium**=7.4 mg/dl(2nd day of admission); **Mg**=1.9mg/dl (2nd day of admission); **Phosphorus**=2.2 mg/dl(2nd day of admission); **LDH**=289U/L(2nd day of admission); **Uric acid**=2.9 mg/dl(2nd day of admission)

Liver Function Test(initial):Bilirubin(Total)= 0.6 mg/dl, Bilirubin(Direct)-0.3 mg/dl, ALP(Alkaline Phosphatase)=143U/L(raised), SGOT(serum glutamic oxaloacetic transaminase)/AST(asparte aminotransferase)=78U/L(raised), GGT=69U/L, Protein(T)=6.32gm/dl, Albumin=4.10g/dl, Globulin=2.22 gm/dl, Albumin:Globulin=1.85;

HbA1c=10.4%(4th day of admission)

Serology- non reactive; **Blood group**= "B" positive;

Prothrombin time (4th day of admission)- Patient=12.5, Control=11.6, INR=1.08;

Hormonal Profile: T3=0.553ng/ml(low), T4=2.91µg/dl(low), TSH= 0.601µlU/ml, Cortisol(AM)=0.695µg/dl(low), PM=0.534µg/dl(low) FSH=7.19, LH=3.77,

Prolactin=25.66ng/mL(high);ACTH-Adrenocorticotrophic hormone=9.95 pg/ml(within normal limits); HGH-Human Growth Hormone= 0.801ng/ml(within normal limits); Testosterone= 6.08ng/ml(within normal limits)

PSA(8/2)=0.472ng/ml(low)

Urine R/E: (initial) Colour= straw, Reaction=acidic(pH==6.5), Sp. Gravity=1.005, Sugar=trace, 100 mg/dl, Ketone bodies, bilirubin, bile salts, urobilinogen, chyle=nil; Blood(+) 10 RBC/MICROL, RBC=40-45/HPF, WBC=1-23/HPF; Casts, Crystals, Macrophages, Epithelial cells, Parasite=nil.

CSF R/E:(4th day of admission) Colour=clear, Xanthochromia, Clot, Coagulum, -absent, Total count=05, RBC=occasional, Protein=27, Sugar=120

Immunophenotyping (Flow Cytometry)(2nd day of admission)- The findings are consistent with Chronic lymphocytic leukemia with CD38 expression.

CHRONIC LYMPHOCYTIC LEUKAEMIA

RADIOLOGICAL INVESTIGATIONS

CT Brain (Plain)(on the day of admission) - Normal study of brain

Chest X-ray(Portable)(on the day of admission) –

USG (Whole abdomen- Portable) (2nd day of admission) – Hepatomegaly with grade II fatty liver, multiple enlarged periportal and peripancreatic lymph nodes, largest one measures 30x24 mm in size, No ascites or effusion.

Echo cardiography with Color Doppler(Portable)(3rd day of admission) – Left ventricle shows concentric hypertrophy, no RWMA, Good systolic function with EF=64%, reduced diastolic compliance. Good right ventricular systolic function.

- Cardiac valves show aortic valve sclerosis with trivial aortic regurgitation , mild mitral and mild tricuspid regurgitation. Normal pulmonary valve.
- Normal pulmonary arterial pressure(PA pressure=30 mm of Hg – systolic),
- No intracardiac shunt/mass, no pericardial pathology.
- IVC normal in size with normal respiratory variation.

Contrast Enhanced CT Abdomen + Thorax (2nd day of admission)- Multiple homogenously enhancing enlarged lymph node noted in bilateral axillary, left supraclavicular region, periportal region, peripancreatic region, aorto-caval window, paraaortic , mesenteric, and bilateral inguinal region largest measuring (2.9x2.7 cm) at periportal region.

- Hepatosplenomegaly.
- Features suggestive of lymphoma.

MRI of Pituitary Gland (2nd day of admission) – DCE MR of brain with particular reference to pituitary gland shows mildly bulky pituitary gland and infundibulum with homogenous enhancement in post contrast study.

LYMPHOCYTIC HYPOPHYSITIS

CLL BINET TYPE A

TREATMENT RECEIVED BY THE PATIENT DURING HOSPITAL STAY

Diet: Soft diet

Injection Cefoperazone and Sulbactam(2 gm) iv (APST) twice daily X 5 days

Injection Pantoprazole (40 mg) iv once daily before meals X 1day f/b Tab Pan(40 mg) per oral once daily before meals X continued till discharge

Injection Ondansetron (4 mg) iv thrice daily X 1 day) then SOS
Extra salt (2 gms) per oral thrice daily –continued till discharge

Syrup Lactulose (20 ml) per oral once daily at night-continued till discharge

Tablet Allopurinol (100 mg) per oral thrice daily- continued till discharge
Tablet Metformin(1 gm) per oral twice daily(after breakfast, after dinner) X continued
Tablet Glimepiride(1 mg) per oral once daily (before breakfast) X continued
Injection Insulin Glargine (10 units) subcutaneous once daily (before breakfast) X continued

Tablet Levothyroxine (25 µg) per oral once daily before meals x 1week f/b (50 µg) x continued.
Tablet Hydrocortisone (20 mg) per oral twice daily X 5days f/b (15 mg) at 7 am and (5 mg) at 4 pm- continued

Length of ICU stay=7 days; Length of Stay in General Ward=3 days.
Total days of stay in the hospital=10days

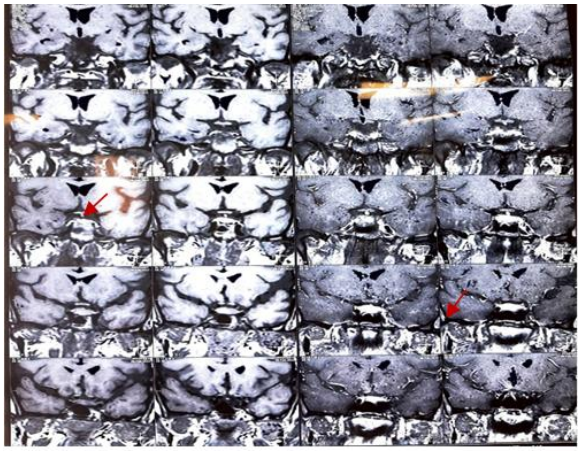
FINAL DIAGNOSIS: CHRONIC LYMPHOCYTIC LEUKAEMIA- BINET A WITH LYMPHOCYTIC HYPOPHYSITIS

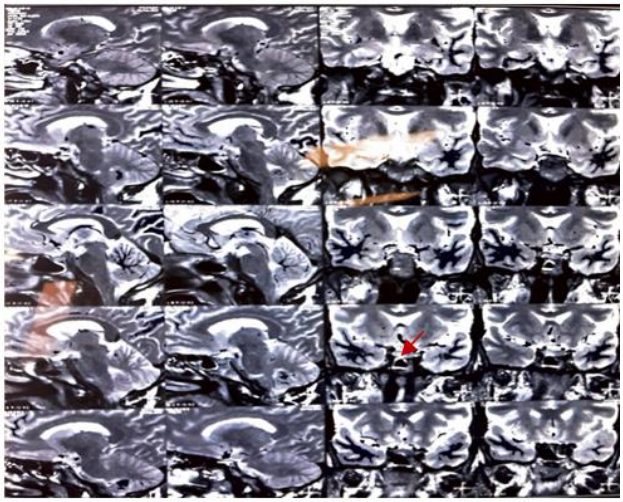
Patient was discharged with Tablet Ibrutinib (Tyrosine kinase inhibitor) in the dose of 3 tablets(140 mg each) to be taken per orally once daily as a life long medication.
Patient is under follow up.

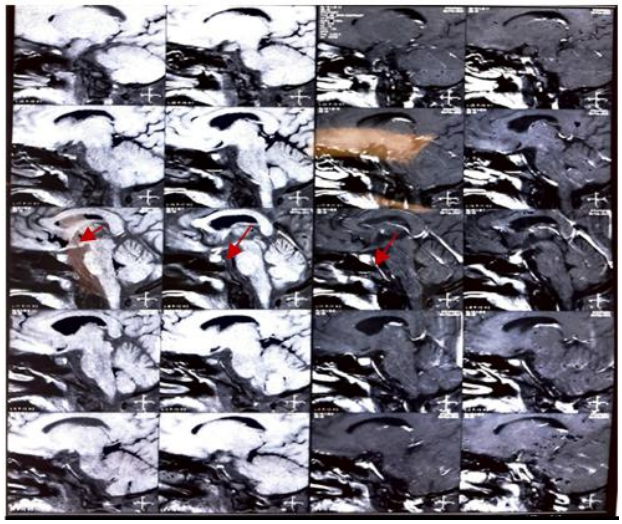
DISCUSSION:

Chronic lymphocytic leukemia (CLL) is a clonal sickness of B lymphocytes, characterized by proliferation and accumulation of small mature-appearing lymphocytes in the blood, bone marrow, and lymphoid tissues.[2] The presence of clinically considerable infiltration of CLL lymphocytes outside of these ~~web~~ sites is distinctly rare and is described as extramedullary CLL. Although the central nervous system (CNS) is one of the most observed extramedullary manifestations of CLL,[3] much less than one hundred instances of CNS involvement by means of CLL are described in the literature; all are case reviews or small case series.[4,5] Despite the low frequency of clinically sizeable CNS involvement by using CLL, post-mortem studies of patients with CLL indicate that occult CNS involvement via CLL is an exceedingly common finding, with an occurrence of 7%–71%.[6,7] This discrepancy between clinical manifestations and autopsy findings illustrates the truth that, whilst CLL cells can also frequently be existing in the CNS, they not often reason clinically vast manifestations. This makes the evaluation of neurological signs in sufferers with CLL challenging, considering the mere identification of CLL cells in CNS does no longer necessarily indicate that CLL is the etiology of the patients' neurological symptoms. In addition, the spectrum of neurological prerequisites that occur in patients with CLL is wide and includes infections, other malignancies, autoimmune/inflammatory diseases, and non-CLL-related medical conditions [8]. Here, we report the first study of patients with CLL undergoing evaluation of neurological symptoms in Eastern part of India. In India, chronic lymphocytic leukaemia (CLL) is not very frequent. Studies on CLL from the Indian subcontinent are few and far between. In India, there are 0.41reported cases of CLL for per 100,000 people [9]. In conclusion, although neurological signs happen frequently in patients of CLL, clinically significant CNS involvement by CLL is an uncommon condition.

Figures with Descriptions:







ABMagnetic resonance imaging(MRI) is the investigation of choice for suspected hypophysitis,

An enlarged triangular or dumb-bell shaped pituitary gland with a thickened without an obvious deviated stalk (marked in red).

This is supported by the absence of posterior pituitary bright spots on T-1 weighted images.

Acknowledgement:

To The Calcutta Medical Research Institute Department of Medicine, Department of Neurology, Department of Hematology, Department of Critical Care.Mr. Amit Kumar Sengupta for his diligent supervision and Dr. BrijeshEshpuniyani, for his academic advices.

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