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Case Report

A Rare Case of Hodgkin's Lymphoma Presenting as Multiple Paraneoplastic Syndromes: Autoimmune Haemolytic Anaemia, Polymyositis, Celiac Disease, and Venous Thromboembolism

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Abstract

Hodgkin's lymphoma (HL) is a lymphoid malignancy of mature B lymphocytes. Based on morphology and immunophenotype, HL is classified into two types: classical HL (cHL), and nodular lymphocyte-predominant HL (NLPHL). cHL usually present with asymptomatic lymphadenopathy and Constitutional symptoms ("B" symptoms, i.e., fever, night sweats, or unintended weight loss). In a minority of cases the clinical presentation of cHL is atypical. Here, we report a rare case of Hodgkin's lymphoma (HL) presenting as combined of multiple unusual manifestations of autoimmune haemolytic anaemia, polymyositis, celiac disease, and venous thromboembolism before the diagnosis.

Keywords: Hodgkin's Lymphoma (HL), Paraneoplastic Syndromes (PNS) Autoimmune Haemolytic Anaemia, Polymyositis, Celiac Disease, And Venous Thromboembolism.

INTRODUCTION

Most of the patient of HL present with lymphadenopathy in supradiaphragmatic areas, which are usually non tender [1]. Majority of the patients present with "B" symptoms (fevers, night sweats, and/or weight loss). Occasionally, HL can present as a pyrexia of unknown origin [2]. Rarely HL is associated with unusual manifestations like severe and unexplained itching, erythema nodosum and ichthyosiform atrophy, paraneoplastic cerebellar degeneration, demyelinating peripheral neuropathy, nephrotic syndrome, immune haemolytic anaemia and thrombocytopenia, hypercalcemia, and pain in lymph nodes on alcohol ingestion [3, 4]. Association of polymyositis, celiac disease, and venous thromboembolism with HL are very rare but these can be sometime presenting features of an underlying Hodgkin's lymphoma (HL) [5], posing a diagnostic challenge. Here, we report one such rare case of a 34-year female who presented with a complex paraneoplastic syndrome of autoimmune haemolytic anaemia, polymyositis, celiac disease, and venous thromboembolism and was eventually diagnosed with classical Hodgkin's lymphoma.

CASE PRESENTATION

38 years old female presented with history of easy fatiguability, exertional breathlessness and waxing, weaning jaundice over last 2 years. She complained difficulty in getting up from sitting position for last 6 months. She also developed gradually progressive bilateral lower limbs swelling over last 3 months. There was no history of fever, skin rashes, alopecia, oral ulcer, myalgia, oliguria, abdominal distention, haematemesis and Malena. She gave history of several episodes of loose motion after taking cookie, chapati, and breads. The patient lost around 6-8 kg weight over last 2 years, her menstrual cycles were irregular in the form of hypomenorrhea and oligomenorrhea for the same duration. On examination, the patient was icteric and had moderate pallor, mild bilateral pitting pedal oedema and grade - 2 clubbing all ten digits. Her BMI was 19.63 kg/m^2. She had mild non tender hepatomegaly. Others physical examinations were unremarkable except she had mild proximal myopathy of bilateral lower limbs.

Complete hemogram revealed severe anaemia with reticulocytosis. Unconjugated hyperbilirubinemia

and hypoalbuminemia were found on liver function test. LDH (650 U/L) was elevated and DCT (IgG) was also positive. For etiological evaluation of AIHA, we did viral serology (HCV and HIV) and ANA but all of them came to be negative. Inflammatory markers (ESR and CRP) were raised. Routine urine examination was normal. Low serum iron alone with relatively elevated TIBC were found on iron study. She also had hypocalcaemia. For proximal myopathy, we did serum CPK, which came to elevated (3000IU/L). For further evaluation, MRI of bilateral thigh **(Fig 1a)**, EMG **(Fig 1b)** and muscle biopsy **(Fig 1c)** were done, all of them suggested inflammatory myopathy i.e., Polymyositis. No muscle specific antibodies were found on Myositis profile. 2DEchocardiography and USG Abdomen and chest imaging were inconclusive. To evaluate possible cause of hypoalbuminemia in the background of low serum iron, hypoalbuminemia and gluten sensitive episodic diarrhoea, Upper GI Endoscopy and D2 biopsy were done. D2 biopsy showed partial villus atrophy and crypt hyperplasia alone with increased intraepithelial lymphocytes, suggested celiac disease **(Fig 2)**, but serology (Total IgA & Anti TTG) was negative**.**

No conclusive etiological associations were found, which could explain all the of three facets of AIHA, polymyositis and celiac disease. Initially, the patient was treated prednisolone 50mg daily and others conservative measures.

Three months later, our patient again presented with gradually progressive bilateral lower limbs swelling and pain over last 3 months. This time, we found two significant right supraclavicular lymphadenopathy on physical examination.

With a strong suspicion for DVT, we did venous doppler study, that revealed DVT in right femoral, popliteal, external iliac and common femoral vein.

CECT abdomen and thorax revealed multiple retroperitoneal and mediastinal lymph nodes as well as linear filling defect in right pulmonary and interlobar artery suggested pulmonary embolism **(Fig 3A&B)**.

For better evaluation, we did [18]. FDG whole body PET-CT scan, which confirmed multiple metabolically active lymphadenopathy in both sides of diaphragm, right supraclavicular region showed maximum FDG uptake (SUVmax -17.35) **(Fig 4)**. To find out possible link of issues of the patient histopathological and Immunophenotyping study of right supraclavicular lymph node were done, which showed several binucleated and multinucleated reed Sternberg cells with positive for CD30, CD15 and CD29 but negative EMA in the background of multiple inflammatory cells of lymphoid, plasma cells and histocytes, suggested classical Hodgkin lymphoma **(Fig 5)**. So, for this patient, the presentation of autoimmune haemolytic anaemia, polymyositis, celiac disease, and venous thromboembolism could be explained as paraneoplastic syndromes of Hodgkin lymphoma, presented combinedly in a single patient, before the diagnosis of Hodgkin lymphoma.

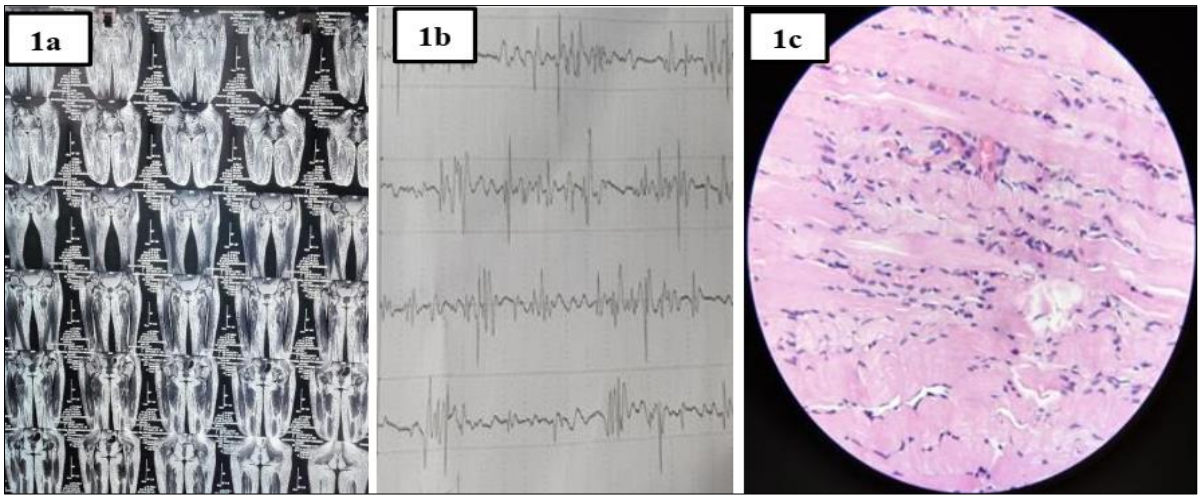

Figure 1: Evidence of Polymyositis

Fig 1a: T2WI FSE coronal section showing marked signal changes in bilateral thigh muscles – s/o inflammatory changes

Fig 1b: EMG Showing presence of polyphasic motor unit action potentials with early recruitment, suggested myogenic pattern

Fig 1c: Muscle biopsy from left vastus lateralis showing endomysial lymphomononuclear cells infiltration with perivascular inflammation and perivascular atrophy are lacking, features suggestive of polymyositis

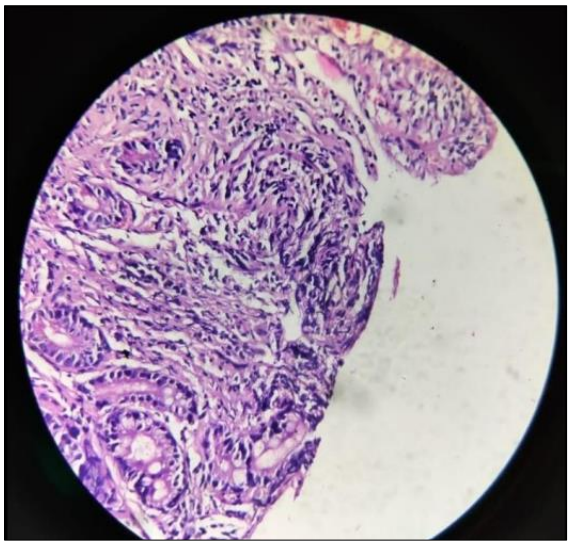

Figure 2: Celiac Disease

Showing partial villus atrophy and crypt hyperplasia alone with increased intraepithelial lymphocytes. Marked inflammation of lamina propria consisting of lymphocytes and plasma cells are seen, suggested celiac disease.

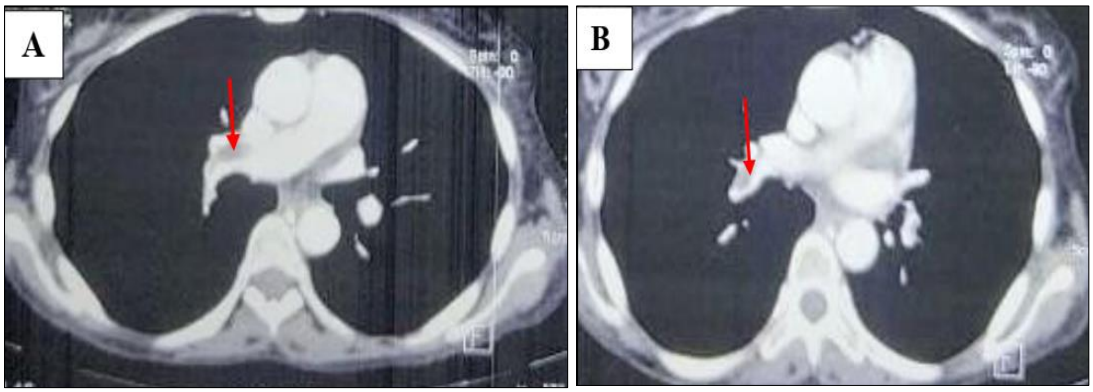

Figure 3 (A&B): Pulmonary embolism

CECT Thorax showing linear filling defect in the right pulmonary artery (red arrow) and interlobar artery suggestive of pulmonary embolism.

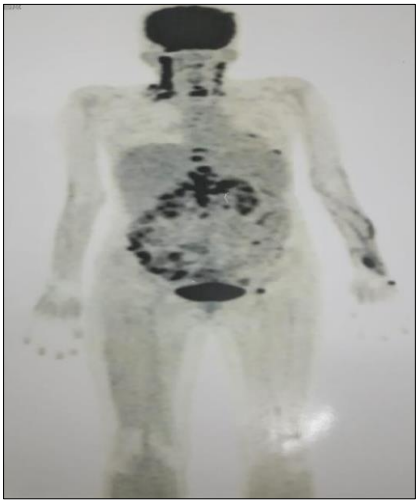

Figure 4: [18]. FDG Whole body PET-CT scan

Whole body PET-CT Scan findings are suggestive of metabolically active lymphadenopathy in both sides of diaphragm – bilateral cervical and intraabdominal region, possibly lymphoproliferative disease. Right supraclavicular region showing increased FDG uptake Dmax -1.44cm, SUVmax -17.35.

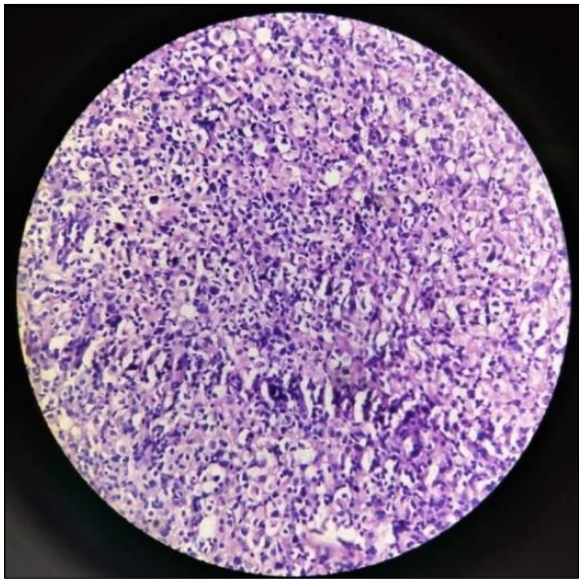

Figure 5: HPE of Lymph node biopsy from right supraclavicular region

Section shows binucleated and multinucleated Reed Sternberg cells and large mononuclear cells having vesicular nuclei with eosinophilic nucleoli scattered in the background of reactive lymphocytes, plasma cells, eosinophils and histiocytes, suggested Hodgkin Lymphoma (x400, H&E).

DISCUSSION

Paraneoplastic syndromes (PNS) are a heterogenous group of disorders, may affect several organ systems. Paraneoplastic syndromes are more commonly occur in people with lung, ovarian, lymphatic, or breast cancer. The pathophysiology of PNS is not well understood. in some syndromes, specific paraneoplastic antibodies have been isolated [3].

Most reported PNS has been described in association with Hodgkin lymphoma (HL) are unexplained itching, erythema nodosum and ichthyosiform atrophy, cerebellar degeneration, demyelinating peripheral neuropathy, nephrotic syndrome, immune haemolytic anaemia and thrombocytopenia, pain in lymph nodes on alcohol ingestion and hypercalcemia [3, 4]. These PNS has been reported before, concurrent and after the diagnosis of lymphoproliferative disease. In our case, autoimmune haemolytic anaemia, polymyositis, celiac disease, and venous thromboembolism are the rarely reported PNS of Hodgkin lymphoma, which manifest in a single patient, before the diagnosis of Hodgkin lymphoma. Ongoing haemolysis and falling of Hb despite adequate immunosuppressive therapy and development of other manifestations, help us to find out a common underlaying aetiology. A high index of suspicion is necessary when recognizing these clinical syndromes, for underlying malignancy to avoid a diagnostic delay. Appropriate therapy of the HL appears to be the most effective treatment to reverses the manifestations of PNS. Initially upon hospitalization, the patient was treated with oral prednisolone for autoimmune haemolytic anaemia, polymyositis, and celiac disease with no clinical improvement. However, after the diagnosis of Hodgkin's lymphoma was made, she was put on chemotherapy with ABVD regimen (Adriamycin, bleomycin, vinblastine and dacarbazine). After taking, initial 3 cycles of ABVD regimen, the patient was improving in respect to resolution of diarrhoea and correction of anaemia and weakness.

CONCLUSION

Polymyositis, celiac disease, and venous thromboembolism are uncommon Paraneoplastic syndromes in HL, which are rarely reported in literature. Sometimes, this can be the only presenting manifestations of an underlying Hodgkin's lymphoma, posing a diagnostic dilemma. So, in dealing new and unexplained clinical presentations, to prevent diagnostic delay, clinicians must maintain a high index of suspicion for an underlying malignancy. Successful treatment of the underlying malignancy reverses the manifestations of PNS.

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Conflict of Interest Statement: The authors report no conflicts of interest for this case report.

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Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Guarantor: Prof. Dr. Soumitra Ghosh

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