

8p11 associated myeloid/lymphoid neoplasms: An illustrative case report of this rare entity and review of literature

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Abstract

This report describes a unique case of 8p11 myeloproliferative syndrome (EMS), also known as stem cell leukaemia-lymphoma syndrome. A 13 years old male was referred from a tertiary care hospital after cervical lymph node biopsy. The disease mechanism of this neoplasm is to either evolve into acute myeloid leukemia or mixed lineage leukaemia, and less frequently of T or B lymphoid lineage. However, here we show a case of a rare simultaneous presentation of T lymphoblastic lymphoma on cervical lymph node and B lymphoblastic leukaemia on bone marrow biopsy along with t (8; 13) on karyotype testing.

Keywords: t (8; 13), T lymphoblastic lymphoma, B lymphoblastic leukemia, FGFR1, karyotype.

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Introduction

8p11 myeloproliferative syndrome (EMS), also known as stem cell leukaemia-lymphoma (SCLL), is a multilineage disease characterized by a BCR/ABL-negative myeloproliferative disease and a lymphoma, often precursor-T lymphoblastic lymphoma (TLBL). This is an aggressive and rare disease with a crucial cytogenetic aberration of translocation at the 8p11 locus which primarily involves the fibroblast growth factor 1 (FGFR1) gene.^{1,2}

The most frequent presentation is myeloproliferative neoplasm or TLBL, associated with eosinophilia.³ Patients who present with myeloproliferative neoplasm may subsequently suffer from myeloid or lymphoblastic transformation, or even both. Its presence in both myeloid and lymphoid malignancies suggests bi-lineage differentiation from an affected pluripotent stem cell.

Here, we report a rare case showing simultaneous presentation of TLBL on cervical lymph node and

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Blymphoblastic leukaemia (B-LL) on bone marrow biopsy along with t (8; 13) on karyotype.

Case Report

This is a case of a 13 years old male, referred from a tertiary care hospital after cervical lymph node biopsy. He had a history of fever, multiple neck swellings and abdominal distention for 1 - 2 months. On physical examination, he was febrile and tachycardic with bilateral cervical and axillary lymphadenopathy and massive splenomegaly. Biopsy of cervical lymph node demonstrated infiltration by sheets of mononuclear cells. Immunohistochemistry results showed positivity for TdT, CD3 and BCL2 and negativity for B-cell markers, consistent with T-cell lymphoblastic lymphoma/leukaemia (Figure-1).

No mediastinal widening was appreciated on chest X-ray. CBC revealed leukocytosis (TLC: 38.7 x 10⁹/L) and thrombocytopenia (32 x 10⁹/L). Peripheral smear showed a leucoerythroblastic blood picture, moderate eosinophilia and 14% blasts. Bone marrow biopsy revealed 30% blasts and 14% eosinophils. Blasts were negative for cytochemical myeloperoxidase. Trepine was hyper cellular (98-100% cellularity) exhibiting infiltration by blast cells along with prominent eosinophils. Immunophenotyping by flowcytometry showed positivity for TdT, CD34, CD79a, CD19, CD20 and negativity for CD3, MPO, and CD117 (Figure-2A). Hence, the diagnosis was established B-LL. Immunohistochemistry on trephine biopsy was also consistent with B-LL (Figure-2B). Due to this discrepant presentation of T cell process in lymph node and B cell phenotype in marrow, lymph node block was reviewed again and concurred with the reported results of T cell process. Bone marrow cytogenetic by Fluorescent In Situ Hybridization (FISH) was negative for BCR-ABL1, MLL gene rearrangement and ETV6/RUNX1. However, karyotype showed t(8;13) (p11.2; q12) (Figure-3)

The patient was treated according to high risk ALL protocol, post induction Minimal Residual Disease (MRD) was positive (2.3%). However, high risk consolidation chemotherapy continued. As post consolidation MRD also showed residual disease with 9% blasts, family was

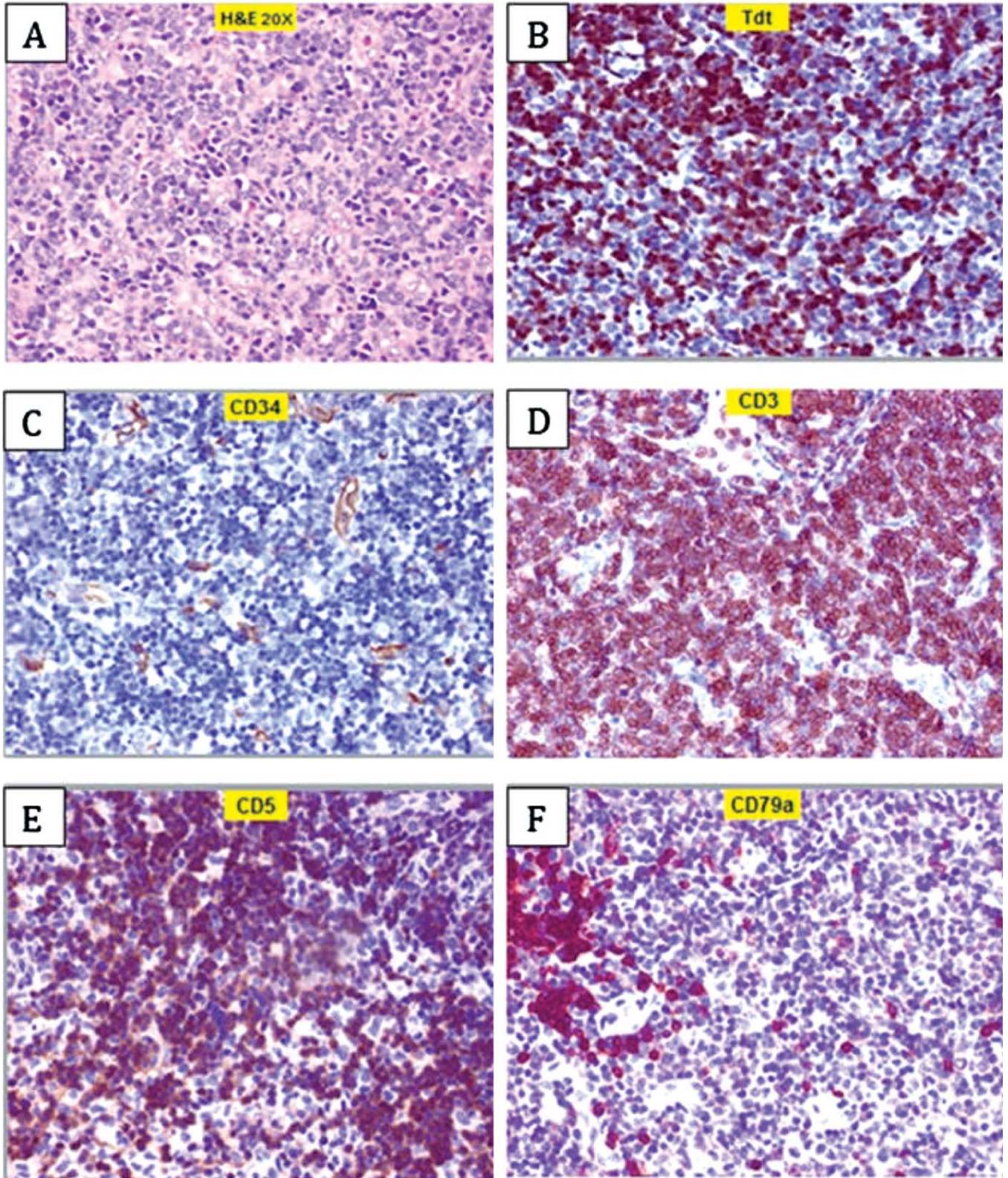


Figure-1: (A) Hematoxylin and Eosin (H&E) stained section of Cervical Lymph node biopsy, showing partial effacement of normal architecture. (B) Tumor cells showing positivity for TdT. (C) Negative for CD34. (D) Diffuse bright positive for CD3. (E) Diffuse bright positive for CD5. (F) Negative for CD79a.

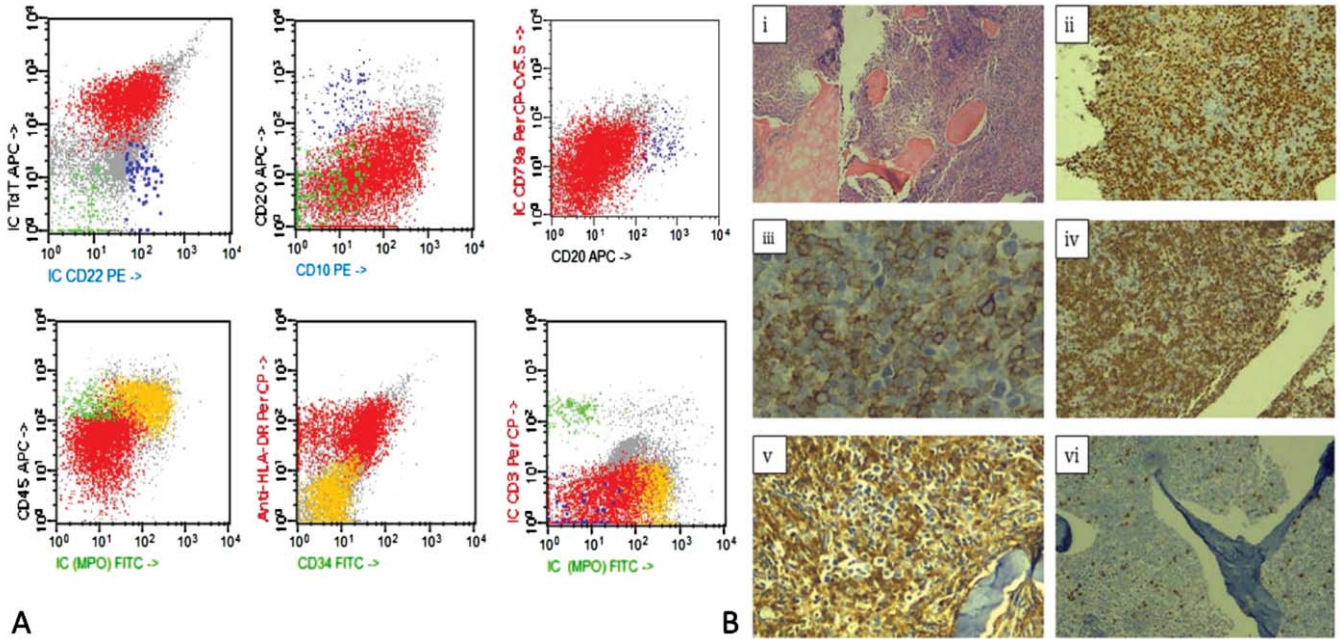


Figure-2: (A) Immunophenotypic analysis by flowcytometry showed 48.9% of the blasts positive for TdT, CD34, CD79a, cytoplasmic CD22, CD20 and CD10 while negative for CD3 and Intracytoplasmic Myeloperoxidase (MPO). (B) (i) H & E stained section of bone marrow biopsy showing infiltration by blasts (ii)TdT bright positive in blasts (iii) CD34 showing variable positivity (iv) CD79a diffuse bright positive in blasts (v) CD19 bright positive in blasts (vi) CD3 negative in blasts.

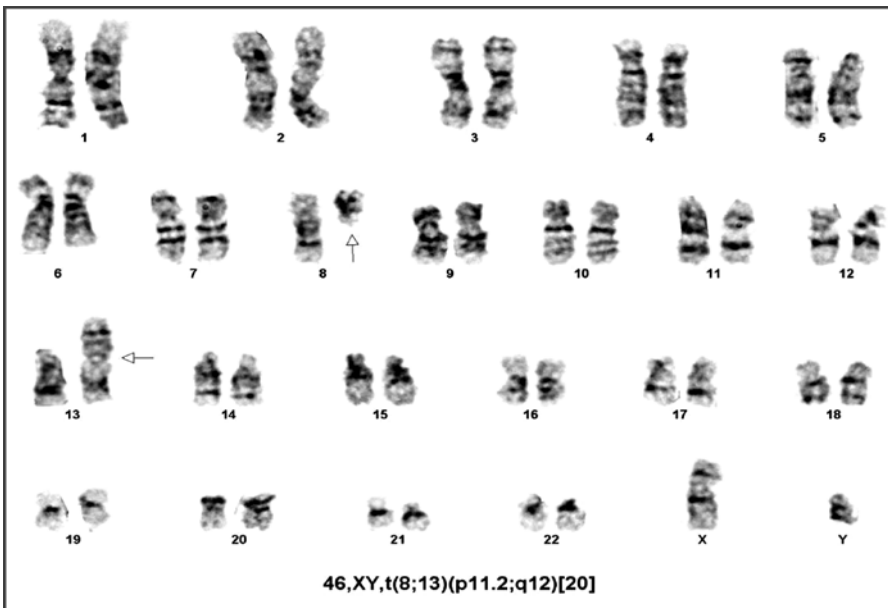


Figure-3: 20 cells were counted; all cells showed 46 chromosomes and bone marrow karyotype showed translocation between chromosomes 8p11 and 13q12.

counseled for palliative chemotherapy. The patient, deceased in due course because of the progressive nature of the disease.

Discussion

This distinct case of EMS/SCLL exhibits specific features of disease like localized lymphadenopathy, splenomegaly, an aggressive lymphoma, peripheral blood leukocytosis, eosinophilia and development of acute leukaemia resistant to standard chemotherapy.² Yet, there are some unusual variations in our case i.e. identification of concurrent TLBL and B-LL on lymph node and bone marrow biopsy respectively. Most cases reported previously show particularly TLBL immunophenotype with progressive or subsequent development of myeloproliferative disorder.⁴

The 8p11 associated myeloid/lymphoid neoplasm is a haematological and cytogenetic heterogeneous disorder.⁵ Literature reports less than 100 diagnosed cases till now. The neoplasm affects predominantly male (male to female ratio 1.5:1) and people that are between 3-84 years of age with a mean of 32 years.^{6,7}

Often, patients with 8p11 disorders show constitutional symptoms including fever, night sweats, and weight loss. They are also reported to have generalized or localized lymphadenopathy. Similarly, our patient showed enlarged cervical and axillary lymph nodes and had a massive splenomegaly. Literature shows, mediastinal lymphadenopathy is usually absent or a very rare feature at the time of presentation¹. Hepatosplenomegaly, is reported in 30-50% of cases of which isolated splenomegaly has the highest incidence (58%).¹ As reported in literature, bone marrow biopsy of our patient also revealed hyper cellular marrow, eosinophilia, and infiltration by blasts.

One other case of concurrent B-LL and TLBL has been reported until now.⁶ In contrast to this case, most of the reported cases show myeloproliferative disorder in bone marrow, either alone, parallel with T-LL or as a bi-lineal acute leukaemia. On lymph node biopsy, most common entity reported in literature is TLBL associated with eosinophilia as in our case whereas B-LL and myeloid sarcoma is rare.⁸ Findings consistent with chronic myeloproliferative disorders have also been reported in association with 8p11 neoplasm.^{5,9,10}

This patient's bone marrow karyotype revealed translocation between chromosome 8p11 and 13q12 that results in a fusion transcript composed of the zinc finger and proline rich motif of ZNF198 and the tyrosine kinase domain of FGFR1. Numerous partner genes are described in patients with FGFR1 associated neoplasms, and depending on the partner gene, different manifestations may be apparent.¹¹ To date, 13 translocations and 1 insertion involving chromosome 8p11 have been identified. Trisomy 21 is also reported in patients of EMS/SCLL and associated with rapid disease progression.¹²

EMS has a low survival rate of 15 months, as it evolves into chemo-resistant leukaemia. Various therapeutic modalities are applied, including chemotherapeutic protocols for acute lymphoblastic leukaemia, acute myeloid leukaemia and chronic myeloid neoplasms, but the results are unfavourable. The only potential curative therapeutic option for these patients is allogenic stem cell transplant. Furthermore, tyrosine kinase inhibitors such as FGFR1, TKI258 and PKC412 can also be used as targeted therapeutic agents.³ However, these modalities are not widely available in developing nations.

Amongst 8p11 cases, concurrent presence of B and T lymphoproliferative disorder is very rare and such cases pose

not only diagnostic but therapeutic challenges. Further research is required on these genetic alterations for targeted therapy and improvement of prognostic outcome.¹³ In conclusion, this case highlights both classical and unique features of disease and reinforces multidisciplinary approach in evaluation and management of such patients.

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Conflict of Interest: None to declare.

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