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Unusual Morphology in A Case of AML With t(8;21):A Diagnostic Dilemma

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Abstract: *An18 year old boy presented with paraparesis and retention of urine. General examination and nervous system examination revealed both upper and lower motor neurone signs at respective spinal levels. Peripheral blood smear examination revealed bicytopenia and increased total WBC count.MRI of dorsal spinal column revealed paravertebral collection. FNAC and bone marrow aspiration studies led to a provisional diagnosis of Acutepromyelocyticleukaemia,based on morphology.*
However, Flow cytometry and cytogenetics revealed a diagnosis of Acute myeloid leukaemia with t(8;21)(q22;q22) and extramedullary involvement. Here, we present an unusual case of acutemyeloblastic leukaemia with t(8;21), masquerading as Acute promyelocytic leukaemia cytologically, optimally diagnosed on immunophenotyping and cytogenetics.
Keywords: *AML, Morphology, t(8;21)*

I. Introduction

Globocan estimates the worldwide total leukaemia incidence of AML for 2012 as 351,965. The prevalence of AML increases with age. The median age of onset is approximately 66 years.Cytogeneticsconstitute one of the most important prognostic factors. Patientswith t(8;21), inversion 16, t(15;17) have the best prognosis, with long term survival rates of 65%. Acute promyelocyticleukaemia(APL)is characterized by t(15;17)(q22;q12) giving rise to PML-RARA fusion gene product.APL is particularly sensitive to All trans retinoic acid(ATRA) which should be administered once the disease is suspected clinically or on peripheral blood smear. This prevents coagulopathy which continues to be the most common cause of early death.On the other hand AML with t(8;21) is usually associated with high complete remission rate and long term disease-free survival when treated with repetitive cycles of high dose cytarabine. So it becomes imperative to diagnose the cytogenetic variant of AML so as to decide the line of management.

II. Case Report

An 18 year old boy presented with paraparesis of lower limbs for one week and retention of urine for three days. There was no history of fever, weight loss and bleeding tendencies.
General examination revealed mild pallor. Nervous system examination revealed mildly increased tone, decreased power (grade 4/5) and bilateral extensor plantar response in both the lower limbs. There were no sensory abnormalities, spinal tenderness or spinal deformity. Next complete blood count was done on two occasions (Table 1),ten days apart.

Biochemical investigations revealed no significant findings. Cerebrospinal fluid study was done but no blasts or atypical mononuclear cells were found. Next Magnetic resonance imaging (MRI) of dorsal spinal column (Figure 1) was done which showed left paravertebral collection seen from D6-D9 along with erosion of ribs and extradural extension from left causing cord compression.

Following this CT guided Fine needle aspiration cytology (Figure 2) from left sided soft tissue SOL(Space occupying lesion) at D6 vertebrae showed smears consisting of immature myeloid cells, atypical promyelocytes, erythroid precursors, lymphoid cells, and myeloid maturation uptometamyelocytes, which were suggestive of leukaemic cell infiltration. Bone marrow aspiration(Figure 3) corroborated the Fine needle aspiration findings. The predominant population consisted of medium sized to large myeloid cells having largeround ,oval or reniform nucleus with multiple prominent nucleoli, abundant primary coarseazurophilic granules in cytoplasm along with multiple Auer rods. The provisional diagnosis was thus Acutepromyelocytic leukaemia. Cytochemistry for MPO (Myeloperoxidase)showed brilliant positivity.(Figure 3).

Following this Flow cytometry and Cytogenetic analysis were done. Flow cytometry (performed on peripheral blood) revealed the following:

- CD 45- Brightly positive
- CMPO - Dim to moderate expression
- CD 117 – Moderate expression

- CD 13 – Dim expression
- CD 14 - Negative
- CD 15- Heterogenous
- CD33 – Moderate expression
- HLA-DR – Moderate expression
- CD34 – Moderate expression

Cytogenetic analysis of bone marrow aspirate showed the karyotype as 45,X,del Y, t(8;21)(q22;q22). Considering the clinical history,examination and above investigations the final diagnosis was made as **Acute myeloid leukaemia with t(8;21)(q22;q22) and extramedullary involvement.**

III. Discussion

Acute myeloid leukemia (AML) is a heterogeneous bone marrow malignancy, and patients with the cytogenetic t(8;21) abnormality represent a subset with specific clinical and biological characteristics [1]. The translocation fuses the AML1 gene (also called RUNX1) on chromosome 21 with the ETO gene (also referred to as the RUNX1T1 gene that encodes the CBFA2T1 protein) on chromosome 8 [1]. It was the firstcytogenetic abnormality discovered in AML [2]. The t(8;21) abnormality is found in approximately 5%–10% of all AML cases and 10%–22% of AML cases with maturation corresponding to the previous FAB class M2 [3,4,5].t(8;21) is most common in children/younger patients [6]. This type of AML has a high complete remission rate with standard chemotherapy and a prolonged survival when sequential high dose cytarabine was administered [1].Cytogenetically, t(8;21) AML is frequently associated with a loss of the sex chromosome Y in males and inactive X in females [1], which was also found in our case; 3.4% of the cases show variant translocations [1].

Nishii K et al documented that most of the cases of AML with t(8;21) shows FAB M2 morphology with a minority of the cases showing M1 and M4 morphology [1]. In the present report the blasts with t(8;21) showed morphology consistent with atypical promyelocytes.

Acute promyelocytic leukaemia is a distinct entity with distinct clinical features, cytogenetics and biological characteristics [7]. Morphologically it is consistent with FAB M3 [7].The cells from almost all patients have a balanced reciprocal translocation between chromosomes 15 and17, which generates a fusion transcript joining the PML (promyelocyte) and RAR-α (retinoic acid receptor-α) genes [8]. Leukemicpromyelocytes have the unique ability to undergo differentiation with exposure to retinoic acid and both differentiation and apoptosiswith exposure to arsenic trioxide (ATO) [9]. Thus, over the past 50 years APL has transformed from a highly fatal disease to highly curable one [9].

In contrast to almost every other disease for which treatment is started only after the correct diagnosis is established, treatment must begin before the diagnosis is confirmed in patients with suspected APL(clinically and morphologically on peripheral blood smear or bone marrow smear) due to the potentially rapidly fatal coagulopathy so characteristic of this disease [7,9].

IV. Conclusion

Acute myeloid leukaemia with t(8;21) is one of the most common subset of AML with good response to high dose cytarabine therapy. APL, on the other hand, is a highly curable disease and is most commonly diagnosed either on peripheral blood smear or bone marrow smear. Appreciation of the details of the morphology in APL is critical because this is one subtype of AML for which immediate treatment must begin when the disease is first suspected.In the present case of AML with t(8;21), morphology was characteristic of atypical promyelocytes (FAB M3), which is a very rare cytological presentation. We thus report this unusual case of Acute myeloid leukaemia.

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