

6-30-2016

Unusual Extramedullary Presentation of Mixed Phenotype Acute Leukemia – A Case Report

Hasmukh Jain

Department of Medical Oncology, Tata Memorial Centre, Department of Medical Oncology, E. Borges Road, Parel (E), Mumbai 400012., dr.hkjain@gmail.com

Manju Sengar

Department of Medical Oncology, Tata Memorial Centre, Department of Medical Oncology, E. Borges Road, Parel (E), Mumbai 400012., dr.hkjain@gmail.com

Hari Menon

Department of Medical Oncology, Tata Memorial Centre, Department of Medical Oncology, E. Borges Road, Parel (E), Mumbai 400012., dr.hkjain@gmail.com

Tanuja Shet

Department of Pathology, Tata Memorial Centre, Department of Medical Oncology, E. Borges Road, Parel (E), Mumbai 400012., dr.hkjain@gmail.com

Raajit Chanana

Department of Medical Oncology, Tata Memorial Centre, Department of Medical Oncology, E. Borges Road, Parel (E), Mumbai 400012., dr.hkjain@gmail.com

Follow this and additional works at: <https://impressions.manipal.edu/mjms>

 Part of the [Medicine and Health Sciences Commons](#)
See next page for additional authors

Recommended Citation

Jain, Hasmukh; Sengar, Manju; Menon, Hari; Shet, Tanuja; Chanana, Raajit; and Dangi, Uma (2016) "Unusual Extramedullary Presentation of Mixed Phenotype Acute Leukemia – A Case Report," *Manipal Journal of Medical Sciences*: Vol. 1 : Iss. 1 , Article 8.
Available at: <https://impressions.manipal.edu/mjms/vol1/iss1/8>

This Case report is brought to you for free and open access by the MAHE Journals at Impressions@MAHE. It has been accepted for inclusion in Manipal Journal of Medical Sciences by an authorized editor of Impressions@MAHE. For more information, please contact impressions@manipal.edu.

Unusual Extramedullary Presentation of Mixed Phenotype Acute Leukemia – A Case Report

Authors

Hasmukh Jain, Manju Sengar, Hari Menon, Tanuja Shet, Raajit Chanana, and Uma Dangi

Case Report

Unusual Extramedullary Presentation of Mixed Phenotype Acute Leukemia – A Case Report

Hasmukh Jain*, Manju Sengar, Hari Menon, Tanuja Shet, Raajit Chanana, Uma Dangi

E-mail dr.hkjain@gmail.com

Abstract

Mixed phenotype acute leukemia (MPAL) is a rare subtype of acute leukemia. The clinical manifestations are both due to bone marrow failure and extramedullary sites of involvement which can lead to protean manifestations. Accurate and timely diagnosis needs clinical suspicion as well as collaboration with the hematopathologist. Extramedullary (EM) disease poses a unique therapeutic challenge. There is a need for more data to guide treatment decisions and justify the usefulness of radiation and allogeneic stem cell transplant. We present 3 cases of MPAL with unusual EM sites of involvement.

Keywords: Mixed phenotype, acute leukaemia, clinical presentation, extramedullary site, therapeutic challenge

Mixed phenotype acute leukemia (MPAL) is an uncommon disease and comprises 2-5% all acute leukemias¹. Similar to other subtypes of acute leukemia, the clinical features in MPAL are attributed to the bone marrow failure, presenting with fatigue, infections, and bleeding manifestations. Higher incidence of extramedullary disease at presentation as compared to other subtypes of acute leukemia has been reported in one series². Here we present three cases of MPAL with unusual extramedullary manifestations at diagnosis.

Patient 1 is a 17-year-old boy, who presented with bilateral painless progressive testicular enlargement of six months' duration. He had undergone an incisional biopsy from the testicular swelling prior to reaching our centre and was diagnosed to have embryonal carcinoma. On examination, he had bilateral testicular enlargement, right being larger

than left, measuring about 10x12 cm, firm, painless and a palpable lump about 4x4 cm in right lumbar region. His complete blood count was normal, renal function and liver function tests were normal. His tumour markers were normal, with α -FP-1.62ng/ml (0-13.4ng/ml), α -HCG-<1.2mIU/ml (0-25mIU/ml), LDH-196U/L (100-190U/L). The biopsy was reviewed and it revealed cells with blastic morphology, the atypical cells were diffusely positive for TdT, CD 79a, myeloperoxidase and focally positive for CD20, establishing a diagnosis of mixed phenotype acute leukemia with myeloid/B-lymphoid phenotype (Figure 1, a,b). Bone marrow aspirate and biopsy was uninvolved on morphology and flow cytometry. FISH for Bcr/Abl and MLL translocations were negative. Cerebrospinal fluid was involved at baseline. An 18-FDG PET CT scan was done. It revealed active disease in bulky bilateral scrotal masses (Right – 7.4 x 11.1 x 11.8 cm, SUV 12.1, Left – 6.2 x 7.8 x 10.8 cm, SUV 11.2.), penile deposits, and bulky aortocaval nodal mass (4.8 x 3.7 x 7.5 cm, SUV 9.6), diffuse thickening of the lumbar spinal canal with thickened nerve at the L4/L5 exit site (Figure 2). He was started on modified BFM 90 protocol, and has attained complete remission after induction as documented clinically and on 18-FDG PET CT scan. Allogeneic stem cell transplantation

Hasmukh Jain, Manju Sengar, Hari Menon, Raajit Chanana, Uma Dangi

Department of Medical Oncology, Tata Memorial Centre, Department of Medical Oncology, E. Borges Road, Parel (E), Mumbai 400012.

Tanuja Shet

Department of Pathology, Tata Memorial Centre, Department of Medical Oncology, E. Borges Road, Parel (E), Mumbai 400012.

*Corresponding Author

How to cite this article: Jain H, Sengar M, Menon H, Shet T, Chanana R, Dangi U. Unusual Extramedullary Presentation of Mixed Phenotype Acute Leukemia – A Case Report. *MJMS*. 2016; 1(1): 46-48.

is not feasible and currently he is eight months into his maintenance therapy.

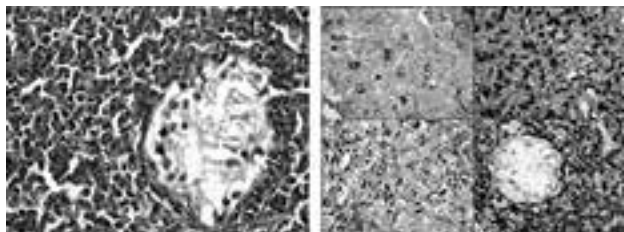


Figure 1: a. H & E image showing atypical cells with blastic morphology and seminiferous tubule. b. Immunohistochemistry images showing positivity with CD20, TdT and MPO, CD3 highlights reactive cells.

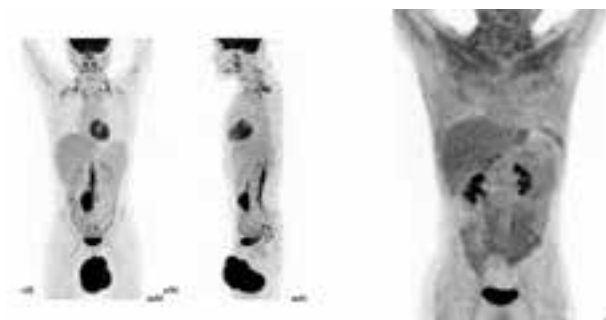


Figure 2: Baseline PET CT scan showing bulky testicular disease, retroperitoneal nodes, penile deposits and spinal canal thickening, and post induction PET CT scan with no metabolically active disease.

Patient 2 is a 21-year student who presented with a history of acute onset pain over left hip region for three weeks. His clinical examination was unremarkable. MRI of the pelvis and thigh revealed a lesion in the left proximal femur extending upto 16.5cm and he was subjected to biopsy, which was suspicious of primitive neuroectodermal tumour. His haemogram was normal. The biopsy blocks were reviewed at our centre that showed positivity for Mic2, Tdt, Fli-1, CD-20, and CD-10 with an impression of High grade Non-Hodgkin's lymphoma. An 18-FDG PET CT was done which showed uptake in the bone marrow of head neck and proximal one-third shaft of left femur (SUV max 7.60) and proximal end of left fibula (SUV max 3.59). Bone marrow studies revealed 43% blasts positive for CD10, CD19, Cd20, CD34, CD22, Cd123 and MPO consistent with a mixed phenotypic leukemia (B/Myeloid) FISH for Bcr/Abl and MLL translocations were negative. Cerebrospinal fluid was uninvolved. We started on modified BFM-90 protocol, and he had achieved complete remission on bone marrow

examination. The 18-FDG PET CT scan showed a partial metabolic response with uptake in the bone marrow of head neck and proximal one third shaft of left femur (SUV max 3.53) and of proximal end of left fibula (SUV max- 1.68). He has a 6/6 HLA match with his sister and is planned for allogeneic stem cell transplant. Currently he is two months into his maintenance phase.

Patient 3 was an 18-year-old engineering student who presented with multiple pruritic erythematous macular lesions with central hyperpigmentation all over the body, painless progressive right testicular swelling, multiple joint pains and generalized lymphadenopathy. He also had hypothyroidism and was on treatment. He had come to us with a diagnosis of T-Lymphoblastic lymphoma/leukemia based on a skin biopsy. His initial labs revealed Hb-7.8g/dl, TLC-19.6 x 10⁹/L, Platelets-79 x 10⁹/L and LDH-259U/L(125-220U/L). His skin biopsy, bone marrow biopsy and cervical biopsy were reviewed, which showed dense lymphoid infiltrate by monomorphic lymphoid cell population and were positive for CD3, Tdt, CD79 alpha and Mic-2, CD-20. CD-34, CD4, Cd8 were negative suggestive of T lymphoblastic lymphoma/leukemia. Peripheral blood sample showed 16% blasts which expressed positivity for CD19, CD7, CD38, CD123, Cd45, Cd79a and CD3 favouring a diagnosis of mixed phenotypic acute leukemia with myeloid/T-lymphoid phenotype. FISH for Bcr/Abl and MLL translocations were negative. CSF was uninvolved. We started him on modified BFM-90 protocol. His induction was complicated by Acinetobacter sepsis and septic shock and pancreatitis. He attained complete remission with no evidence of residual disease on bone marrow studies. Phase II of induction was complicated by *E.coli* GI sepsis. Consolidation with High dose methotrexate was complicated with sepsis-induced myocarditis. After one dose of methotrexate, he was switched to interim maintenance due to the poor general condition. He succumbed to septic shock during maintenance phase.

Mixed phenotype acute leukemia is an uncommon disease. The three cases had unusual extramedullary manifestations, which had even led to erroneous diagnosis in two of them. MPAL represents a

diagnostic and therapeutic dilemma. There are no randomized clinical trials to guide treatment decisions, however, results from various single institution series suggest that ALL like regimen are superior compared to AML like regimen, and that allogeneic stem cell transplant should be considered in first CR at least in adults²⁻⁵. Another aspect highlighted by these cases is that MPAL should always be suspected when a patient with acute leukemia has extramedullary disease.

References

1. Weinberg OK, Arber DA. Mixed-phenotype acute leukemia: historical review and a new definition. *Leukemia* 2010; 24(11):1844-51.
2. Xu XQ, Wang JM, Lu SQ, Chen L, Yang JM, Zhang WP, et al. Clinical and biological characteristics of adult biphenotypic acute leukemia in comparison with that of acute myeloid leukemia and acute lymphoblastic leukemia: a case series of a Chinese population. *Haematologica* 2009; 94(7):919-27.
3. Killick S, Matutes E, Powles R, Hamblin M, Swansbury J, Treleaven JG, et al. Outcome of biphenotype acute leukemia. *Haematologica* 1999; 84(8):699-706.
4. Rubnitz JE, Onciu M, Pounds S, Shurtleff S, Cao X, Raimondi SC, et al. Acute mixed lineage leukemia in children: the experience of St Jude Children's Research Hospital. *Blood* 2009; 113(21):5083-89.
5. Matutes E, Pickl WF, Veer MV, Morilla R, Swansbury J, Strobl H, et al. Mixed-phenotype acute leukemia: clinical and laboratory features and outcome in 100 patients defined according to the WHO 2008 classification. *Blood* 2011; 117(11):3163-71.