

EXHIBIT E

Case 726 -- A 61 year old male with pneumonia and leukocytosis

Hematopathology

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CLINICAL HISTORY

A 61-year old male with a past medical history of chronic obstructive pulmonary disorder (COPD) was recently admitted for left-sided pneumothorax. He underwent chest tube placement and pleurodesis and was discharged home. Three days later, he returned to the Emergency Room with shortness of breath, cough, and left-sided pleuritic chest pain. A CT scan of the chest showed left upper lobe lung consolidation consistent with pneumonia, a moderate left pleural effusion, and giant bullous emphysema.

Figure 1: Complete Blood Count (CBC) and Differential

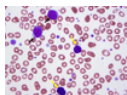
Patient Value	UPMC PUH/SHY Normal Range Male
WBC 12.5 x10E+9/L	[H] (3.8 - 10.6)
RBC 2.28 x10E+12/L	[L] (4.13 - 5.57)
Hgb 7.8 g/dl	[L] (12.9 - 16.9)
Hct 23.7 %	[L] (38.0 - 48.8)
MCV 104.0 fL	[H] (82.6 - 97.4)
MCH 34.3 pg	[H] (27.8 - 33.4)
MCHC 33.0 gm/dL	(32.7 - 35.5)
RDW 18.4 %	[H] (11.8 - 15.2)
PLT 284 x10E+9/L	(156 - 369)

Peripheral Blood Differential	ABS. No.	UPMC PUH/SHY Normal Range (ABS)
POLYS 19.0 %	(2.38)	(2.24 - 7.68)
BANDS 16.5 %	(2.06) [H]	(0.10 - 0.80)
LYMPHS 9.0 %	(1.12)	(0.80 - 3.65)
MONOS 26.0 %	(3.25) [H]	(0.30 - 0.90)
EOS 1.0 %	(0.12)	(0.00 - 0.40)
BLASTS 28.0 %	(3.50)	
META 0.5 %	(0.06)	
NRBC/100 WBC 1		

The patient's CBC and differential indicate a macrocytic anemia with an absolute monocytosis and 28% blasts.

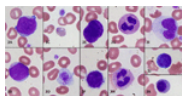
PERIPHERAL BLOOD

Figure 2: Peripheral Blood Smear, Wright-Giemsa stain, 400x



An intermediate-power view of the peripheral blood smear demonstrates red blood cells with 2+ anisocytosis including macrocytes, 1+ poikilocytosis including ovalocytes and tear drops, and 1+ polychromasia. The white blood cells show circulating blasts (black arrows), many large and giant platelets, and bare nuclei of immature megakaryocytic precursors (yellow arrows).

Figures 3A-K: Peripheral Blood Smear, Wright-Giemsa stain, 1000x



A-B: The blasts demonstrate a high nuclear:cytoplasmic ratio, fine nuclear chromatin, and prominent nucleoli. C, D, F: Hypogranular and giant platelet forms are seen. E: There are few immature megakaryocyte nuclei with characteristic "turtle-back" appearance. G-H: Some neutrophils show hypogranularity. Monocytes (I) and lymphocytes (J) are seen without significant abnormality, and there are few nucleated red blood cells (K).

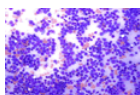
BONE MARROW

Figure 4: Bone Marrow Aspirate, Manual Differential Count

Bone Marrow Differential	Patient	Mean	Adult Normal Range
Blast	46.3 %	1.0	(0.0 - 2.0)
Promyelocyte	0.0 %	3.0	(2.0 - 4.0)
Myelocyte	2.0 %	12.0	(8.0 - 16.0)
Metamyelocyte	2.0 %	17.0	(10.0 - 25.0)
Band	2.3 %	12.0	(9.0 - 18.0)
PMN	2.3 %	9.0	(7.0 - 14.0)
Eos Myelo/Meta	0.3 %	2.0	(1.0 - 4.0)
Eos Band	0.7 %	1.0	(0.0 - 3.0)
Eos Seg	2.0 %	1.0	(1.0 - 2.0)
Basophil	0.3 %	0.0	(0.0 - 0.2)
Monocytes	1.7 %	1.0	(0.0 - 2.0)
Pronormoblasts	0.7 %	1.0	(0.0 - 1.0)
Normoblasts	35.0 %	24.0	(16.0 - 32.0)
Lymphocytes	3.7 %	16.0	(11.0 - 23.0)
Plasma Cells	0.7 %	2.0	(0.0 - 3.0)
Other	0.0 %		
Myeloid/Erythroid(ratio)	N/A	2.4	(1.5 - 3.3)
Tot. # of Cells counted	300		

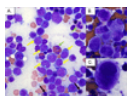
Manual differential count of the marrow aspirate indicates approximately 46% blasts.

Figure 5: Bone Marrow Aspirate, Wright-Giemsa stain, 400x



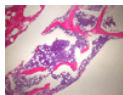
The marrow aspirate is hypercellular.

Figure 6: Bone Marrow Aspirate, Wright-Giemsa stain, 1000x



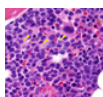
A: Higher-power view of the bone marrow aspirate demonstrates numerous blasts (yellow arrows) with the same morphology as that seen in the peripheral blood, along with maturing granulocytes (green arrows) and maturing erythroid cells (black arrows). B-C: There are dysplastic megakaryocytes including small monolobated megakaryocytes and hypolobated megakaryocytes.

Figure 7: Bone Marrow Biopsy, H&E, 40x



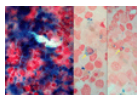
The bone marrow biopsy demonstrates hypercellularity for the patient's age (50-60%). The bony trabeculae appear unremarkable.

Figure 8: Bone Marrow Biopsy, H&E, 500x



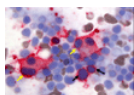
The marrow demonstrates scattered blasts (blue arrows) and dysplastic megakaryocytes including monolobated and hypolobated forms (yellow arrows).

Figure 9: Iron Stain, Bone Marrow Aspirate



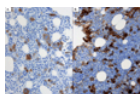
There are abundant iron stores (left), and rare ring sideroblasts (yellow arrows).

Figure 10: Immunocytochemical Stain for CD61, Bone Marrow Aspirate



Immunocytochemical stain for CD61 highlights megakaryocytes (yellow arrows) and few mononuclear cells morphologically compatible with blasts (black arrows).

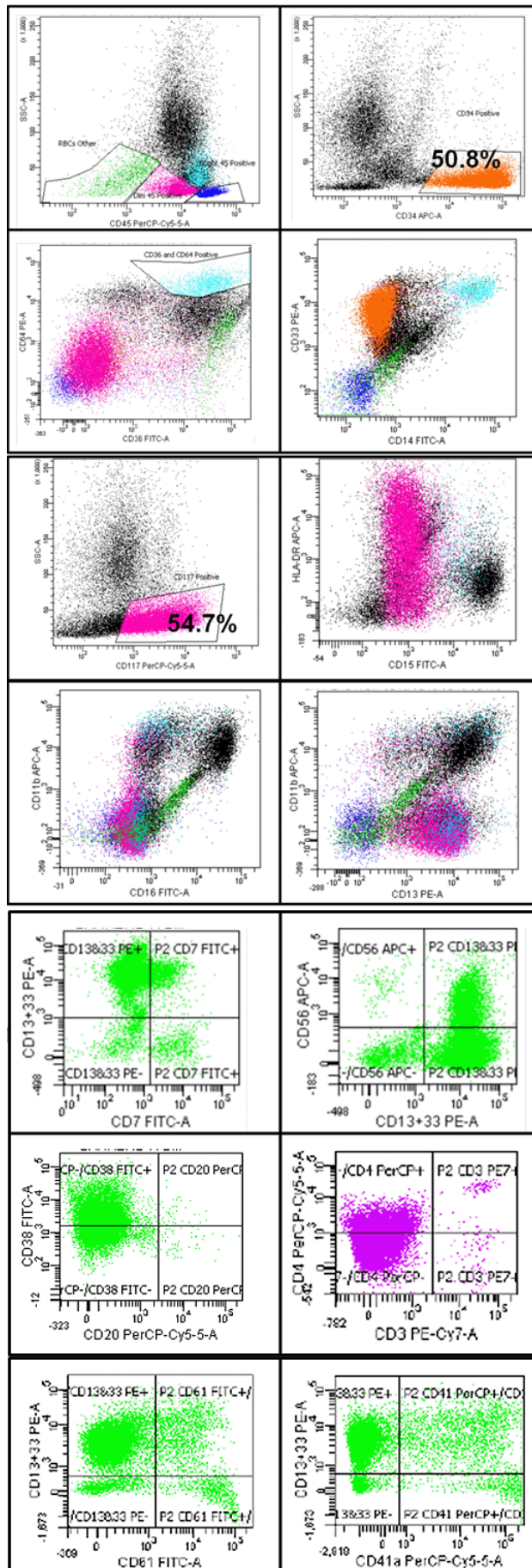
Figure 11: Immunohistochemical Stains, Bone Marrow Biopsy

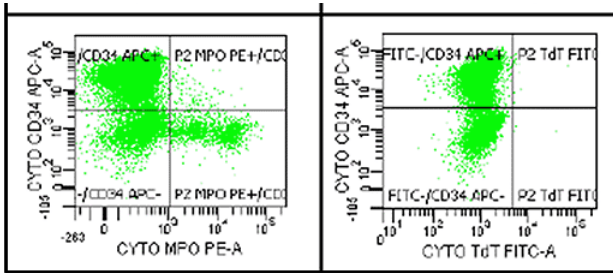


A: CD61 shows weak-to-moderately intense staining for megakaryocytes and shows weak staining of very few mononuclear cells. B: Factor VIII shows strong staining for megakaryocytes and moderately intense staining of few mononuclear cells morphologically compatible with blasts.

FLOW CYTOMETRIC IMMUNOPHENOTYPIC STUDIES

Figure 12: Flow Cytometric Immunophenotypic Studies, Bone Marrow Aspirate

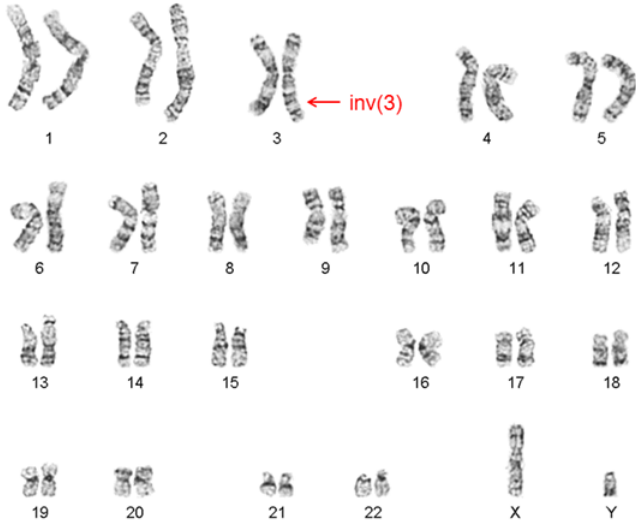




Flow cytometric studies performed on the aspirate showed a myeloblast population comprising 51% of the total analyzed cells with the following phenotype: CD34+, CD117+, CD45 dim+, CD13+, CD33+, CD13/CD33+, HLA-DR+, CD7 partial+, CD56 partial+, CD4 partial+, CD38 partial+, CD36 subset partial+, CD64-, CD14-, CD15-, CD16-, CD11b largely-, Tdt-, MPO-, CD41 largely-, and CD61 largely-. In addition there were few granulocytes, 5.2% CD14+ monocytes, few heterogeneous T cells, and few polyclonal B cells.

CYTOGENETIC STUDIES

Figure 13: Classical Chromosome Analysis



46,XY,inv(3)(q21q26)[20]

The patient's karyotype demonstrates a paracentric inversion of the long arm of one chromosome 3 in all 20 cells examined:

In addition, fluorescence in-situ hybridization (FISH) studies were negative for the BCR/ABL1 gene rearrangement in all 269 interphase cells examined.

MOLECULAR STUDIES

Molecular real-time polymerase chain reaction (PCR) was negative for the PML-RARalpha fusion transcript.

FINAL DIAGNOSIS