

Case 4

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Fellow, advanced hematopathology (Molecular)

Fox Chase Cancer Center

Case 4

A 76-year-old male with a history of colonic adenocarcinoma (Dx: 2000; s/p colectomy) presented with rapidly-enlarging soft tissue mass (7 x 4 x 2.5 cm) on right foot

Sept 2024: Purplish lesion on his right foot .

Dec 2024: Soft tissue mass (7 x 4 x 2.5 cm) at medial aspect of the first metatarsal phalangeal joint on MRI Right foot with and without contrast)

Jan 2025: PET/CT – Hyperintense subcutaneous lesion on right lower extremity (SUV 12.9).

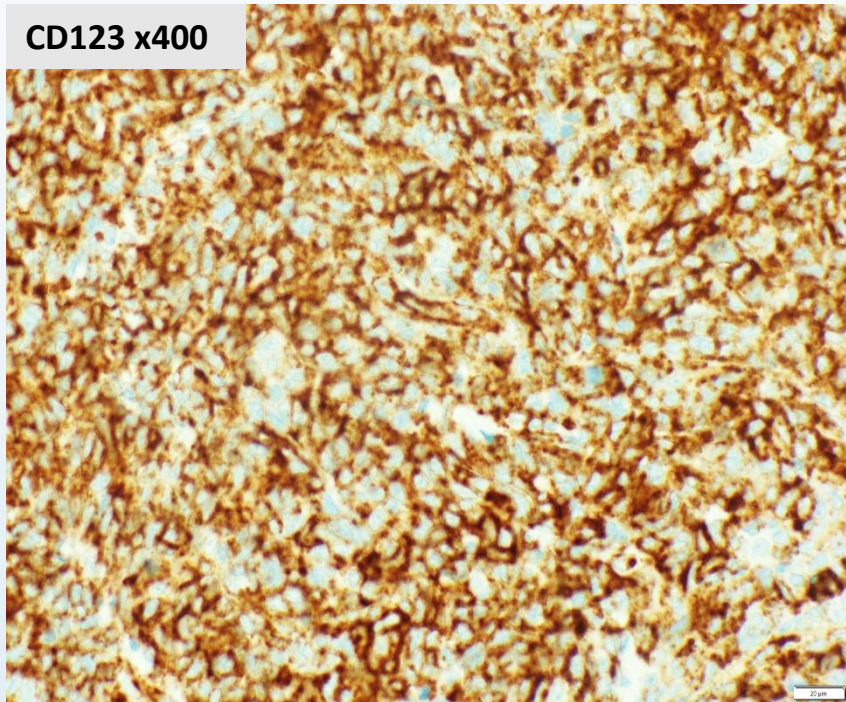
Digital Pathology (Whole Slide)

Biopsy of a large soft tissue mass at the first metatarsal-phalangeal joint

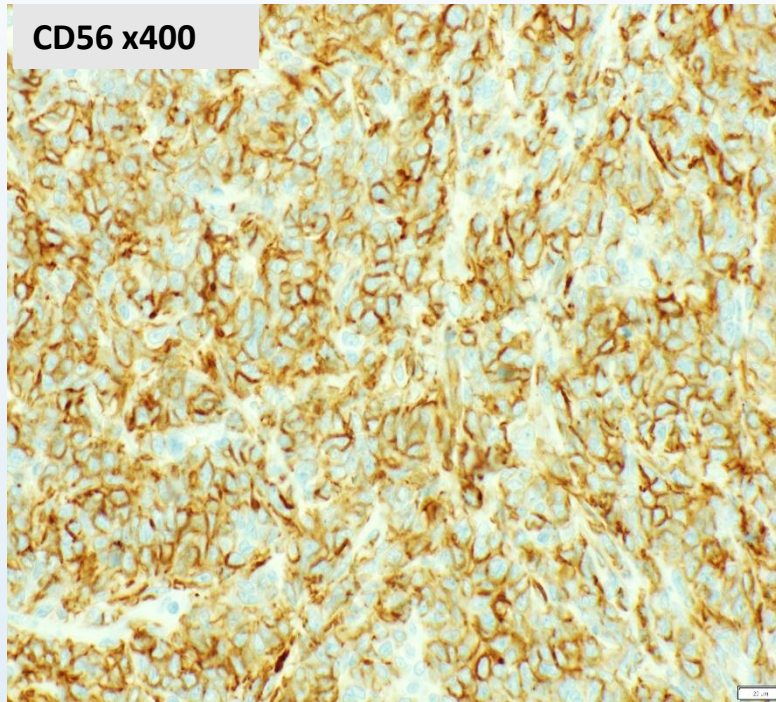
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Immunohistochemistry

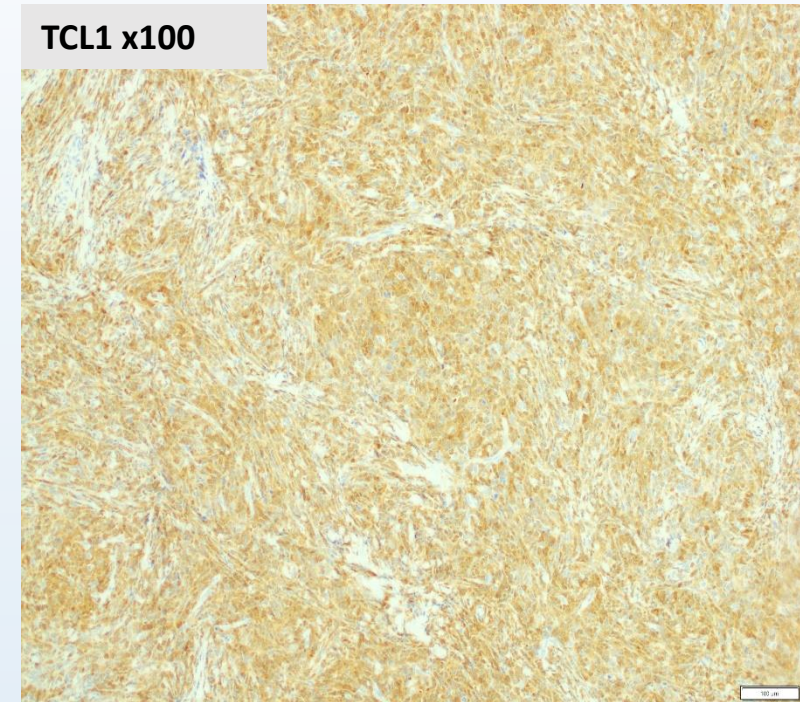
CD123 x400



CD56 x400



TCL1 x100



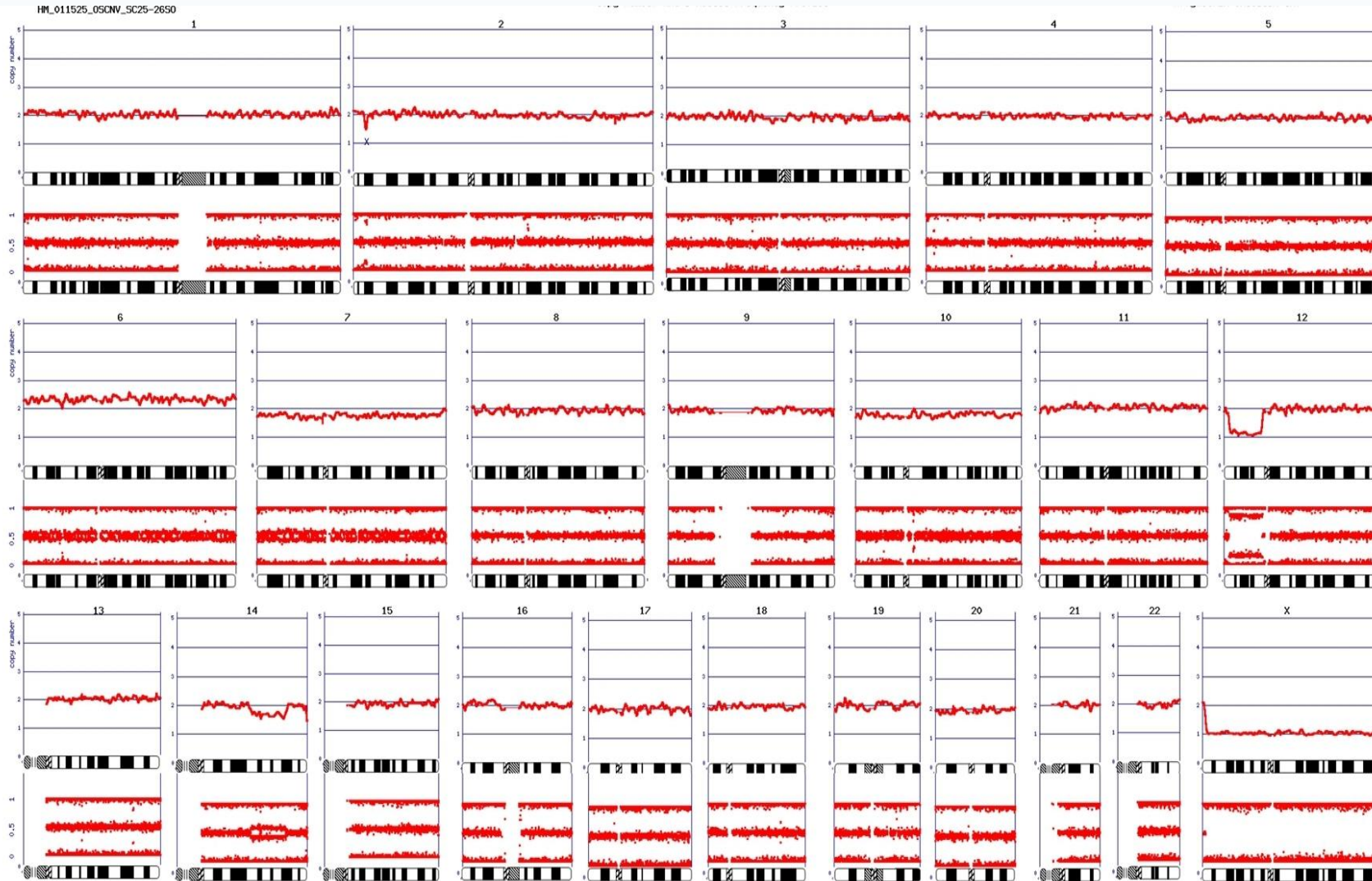
Summary of findings

Positive markers	Negative markers
CD45	CD10, CD19, CD20, CD21, CD22, CD23, CD30, CD79a (focal weak), MUM1 (focal/weak), cMYC, PAX5
BCL2	CD3, CD5 (focal/weak), CD7 (focal/weak), CD8, ALK1, SOX10
CD4	CD34, CD117, CD14, TdT, MPO, Lysozyme
CD56	CD163, CD303 (BDCA-2)
CD68	EBER by ISH
CD123	
TCL1	

Diagnosis

Blastic plasmacytoid dendritic cell neoplasm
(BPDCN)

Chromosomal Microarray Analysis (CMA)



Abnormal with losses of chromosomes or segments 7, 10, 12p and 14q and gain of 6 in mixed states. Loss of 12p is in about 80% of the cells whereas the other alterations are in about 30% of the cells.

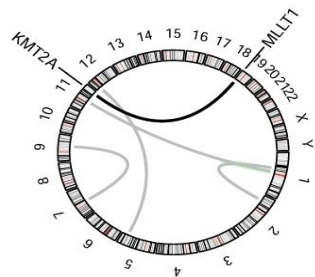
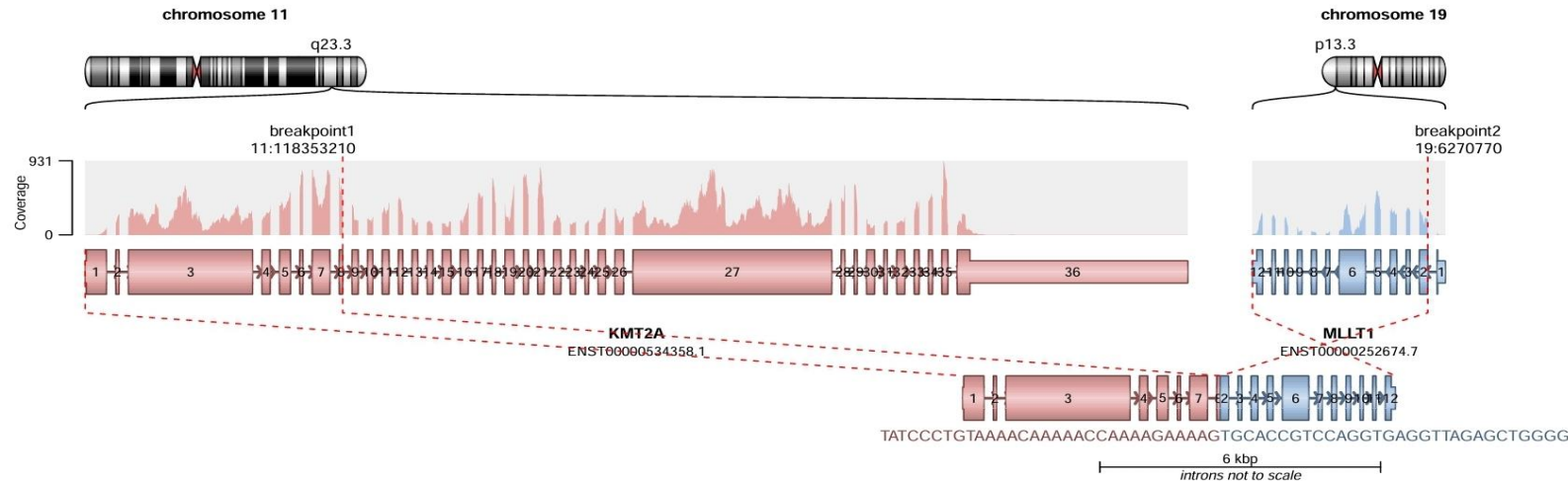
Molecular studies: Case 4

NGS (275 gene panel)

Gene	Protein Change	cDNA Change	Allele Freq	Significance
ASXL1	p.Leu823fs	c.2468delT	43.5	Tier 2
TET2	p.Lys751fs	c.2252_2255delAG AA	42.7 %	Tier 2
NRAS	p.Gln61Arg	c.182A>G	41.0 %	Tier 2

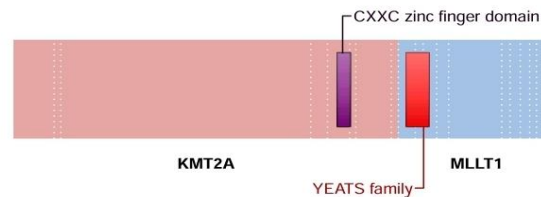
Targeted NGS RNA fusion analysis

KMT2A::MLLT1 (in-frame)
rsa(11;19)(q23.3;p13.3)



— translocation — deletion
— duplication — inversion

RETAINED PROTEIN DOMAINS
in-frame fusion



SUPPORTING READ COUNT

Split reads at breakpoint1 = 13
Split reads at breakpoint2 = 28
Discordant mates = 63

Diagnosis ???

Main Differential Diagnoses

Blastic plasmacytoid dendritic cell neoplasm (BPDCN)

Myeloid Sarcoma

Diagnostic Criteria

Expression of CD123 and one other pDC marker (TCL1 in our case) in addition to CD4 and/or CD56

Or

Expression of any three pDC markers and absent expression of all expected negative markers

Expected positive markers	Expected negative markers
CD123 (characteristic), TCL1 , CD303, TCF4, CD304	CD3, CD14, CD19, CD34, Lysozyme, MPO
CD4, CD56	
Additional positive markers	Additional negative markers
CD117, HLA-DR, CD13, CD33, CD36, CD43	CD1a, CD15, CD25, CD34, CD41, CD64,
CD45, CD2, CD5, CD7, CD8, CD79a, BCL2, CD22, TdT	CD113, MNDA
PDL1	

Molecular/Cytogenomic alterations

Resting, non-activated pDCs with aberrant NF- κ B pathway activation

TCF4 (previously E2-2) plays an obligatory role

Molecular alterations

- Monoallelic and biallelic 12p13/ETV6 deletions
- Recurrent mutations in RNA splicing genes ZRSR2, SRSF2, U2AF1, and SF3B1
 - Mutually exclusive Mutations in NRAS (27.3%), KRAS (9.1%), and ATM (21.2%)

Cytogenomic alterations

75% of BPDCNs have a complex karyotype

Copy-number losses (12p, 5q, 6q, 13q, 15q, and 9) are more common than gains

CDKN2A, CDKN2B, CDKN1B, RB1, and NR3C1

Clinical Trial > [Leuk Res.](#) 2018 Oct;73:86-94. doi: 10.1016/j.leukres.2018.09.006.

Epub 2018 Sep 17.

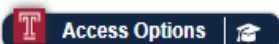
Genomic aberrations involving 12p/ETV6 are highly prevalent in blastic plasmacytoid dendritic cell neoplasms and might represent early clonal events



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Affiliations + expand

PMID: 30248580 DOI: [10.1016/j.leukres.2018.09.006](#)



Abstract

Background: Chromosomal aberrations at the ETV6 gene locus on 12p marrow samples involved by blastic plasmacytoid dendritic cell neoplas pathogenic role, incidence in cutaneous BPDCN lesions, and clinical sign assessed systematically.

Case Reports > [Cancer Genet.](#) 2015 Sep;208(9):464-7. doi: 10.1016/j.cancergen.2015.04.011.

Epub 2015 May 6.

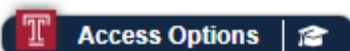
KMT2A (MLL)-MLLT1 rearrangement in blastic plasmacytoid dendritic cell neoplasm



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Affiliations + expand

PMID: 26164398 DOI: [10.1016/j.cancergen.2015.04.011](#)



Final Diagnosis

Blastic plasmacytoid dendritic cell neoplasm (BPDCN)

Thank you

Any questions/comments ?