

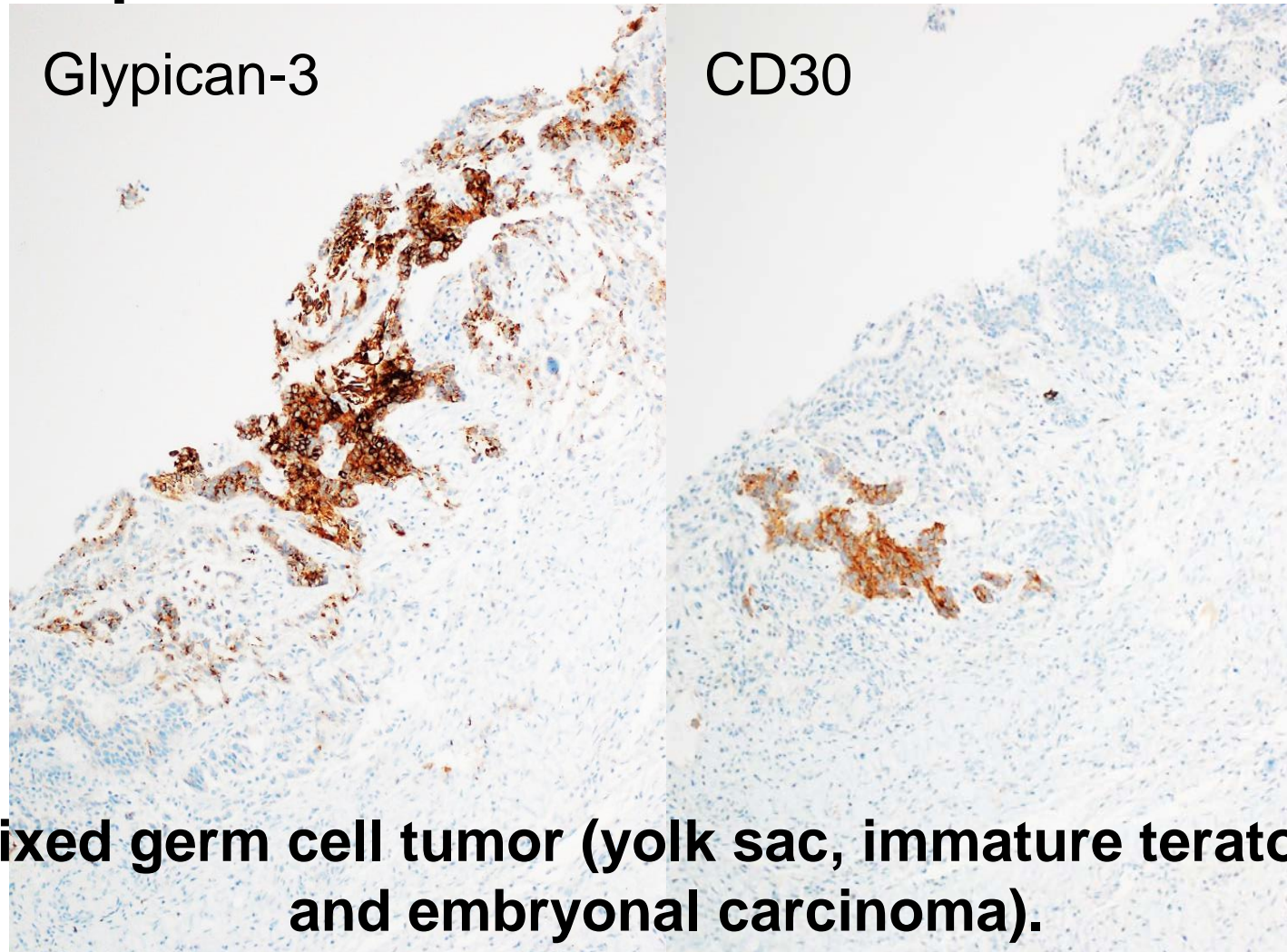
Case: SH2017-0244

Pawel Mroz, M.D., Ph.D.
Assistant Professor
Department of Laboratory Medicine and
Pathology



UNIVERSITY OF MINNESOTA
Driven to Discover®

14 year old male who in September of 2014 presented with a mediastinal mass.



Mixed germ cell tumor (yolk sac, immature teratoma and embryonal carcinoma).



UNIVERSITY OF MINNESOTA

Driven to Discover®

Cytogenetics



CBC:

AFP 93431 ng/ml

WBC 15.7

ANC 11.7;

ALC 1.6;

AMC 2.2;

Hb 10.5;

MCV 78.3;

PL 583,000.



UNIVERSITY OF MINNESOTA

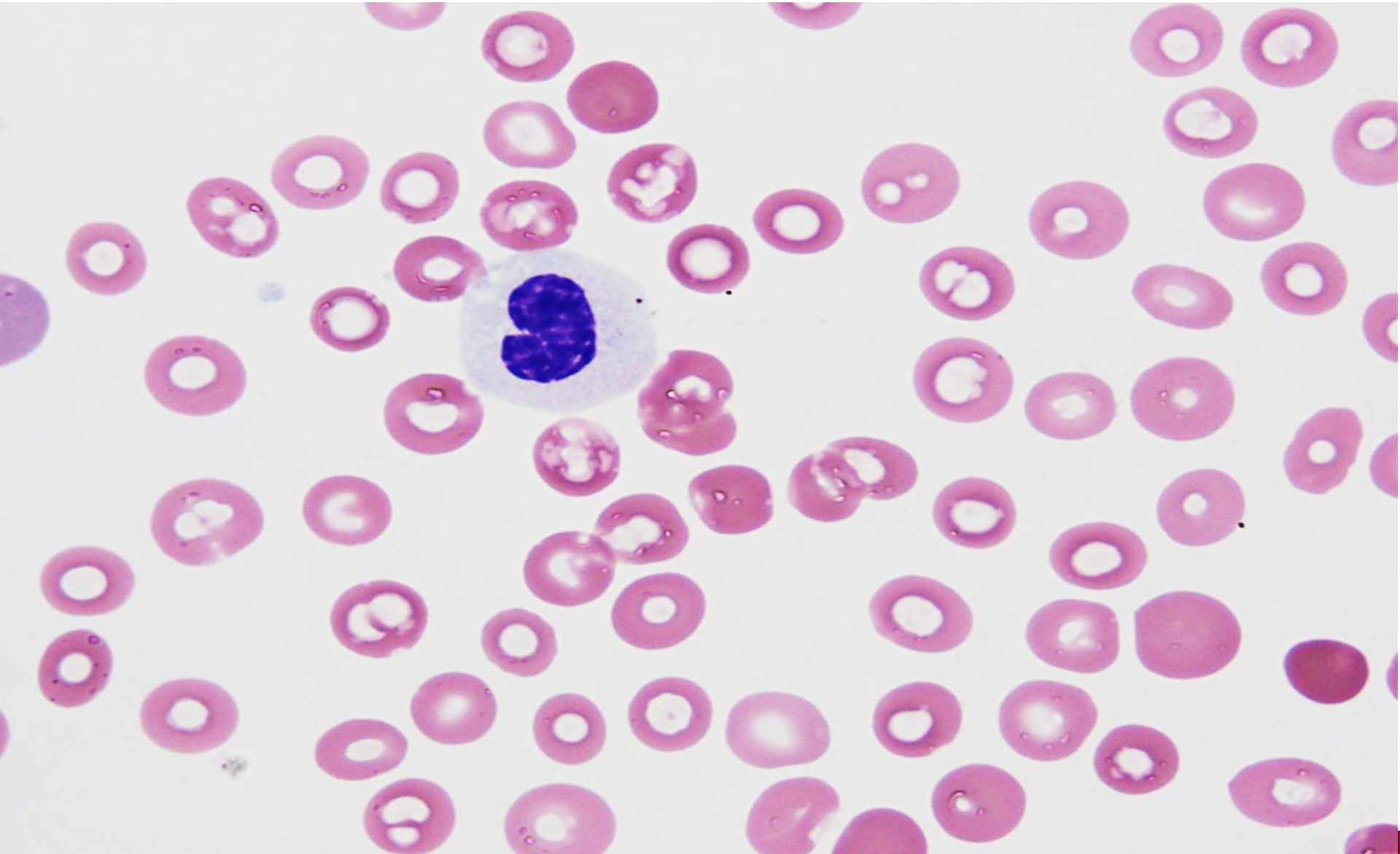
Driven to Discover®

Follow-up

- Between 09-12/2014 the patient received 5 cycles of cisplatin, etoposide and bleomycin.
- In 01/2015 imaging showed persistent mediastinal mass.
 - CBC: WBC 8.2 (normal ANC, ALC, and AMC); Hb 12.6; MCV 86; PL 269,000.
- In 02/2015 a thoracotomy with complete resection of mediastinal mass was performed:
 - Diagnosis: **treated malignant germ cell tumor with sarcomatous malignant transformation (malignant peripheral nerve sheath tumor).**
 - Persistent thrombocytopenia and neutropenia (ANC 0.9).
 - Patient received Neupogen with subsequent ANC>1.0 and no need for further doses.
 - BM biopsy was performed.

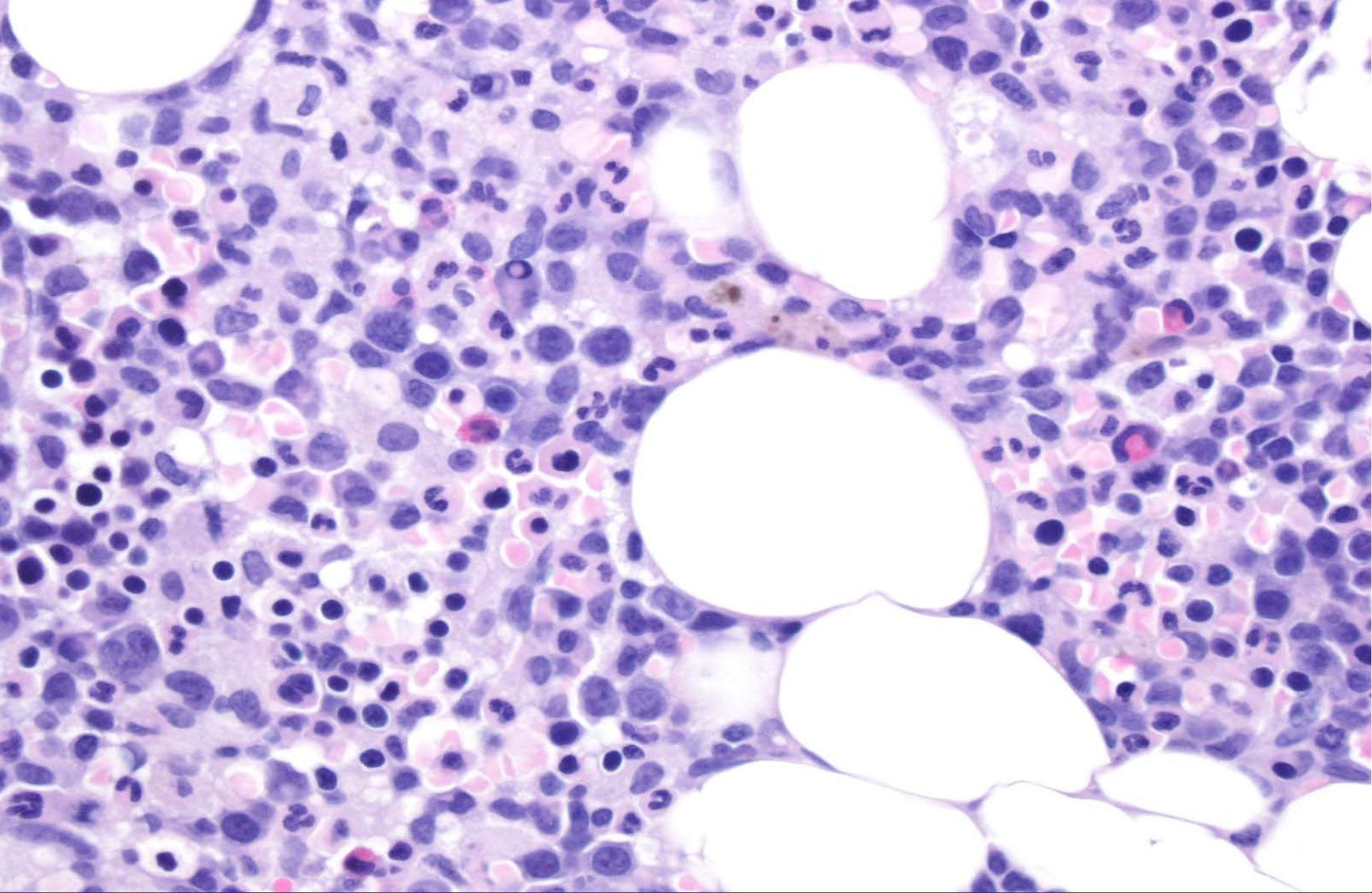


WBC 4.0 (ANC 1.6; ALC 1.4; AMC 0.8); Hb 8.6; MCV 86; plt 23,000.



UNIVERSITY OF MINNESOTA

Driven to Discover®



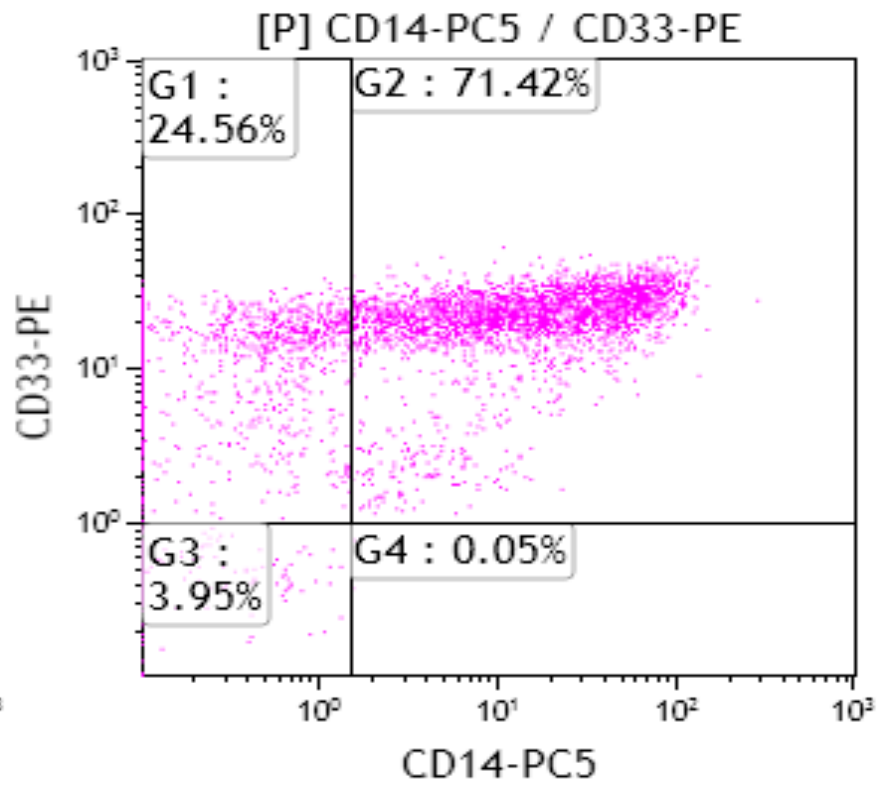
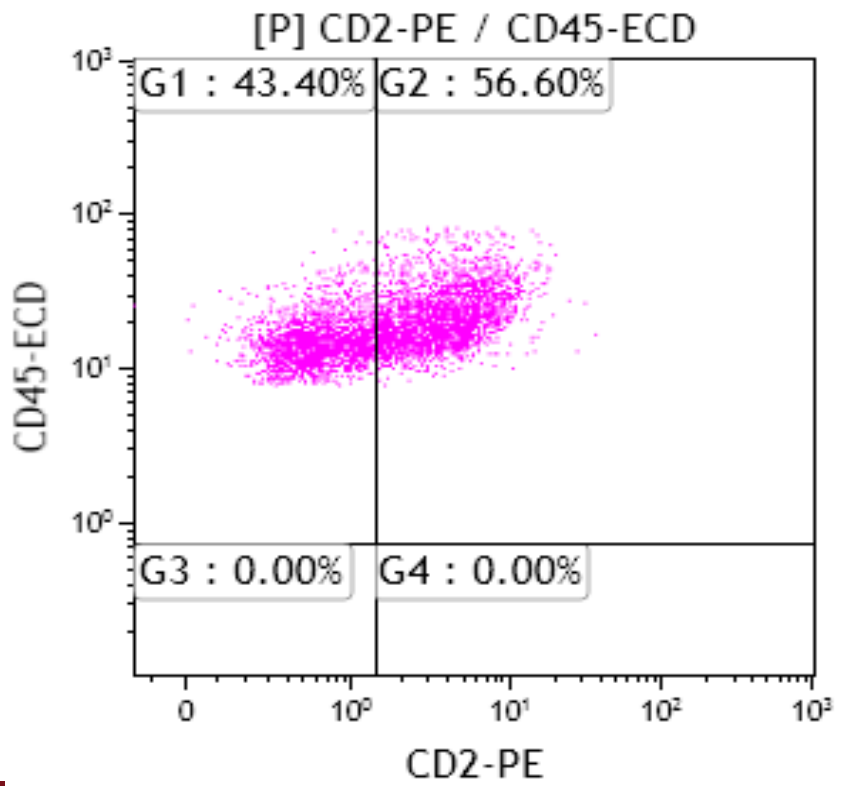
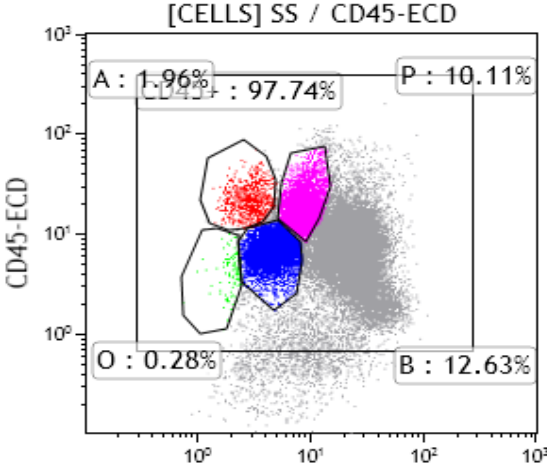
UNIVERSITY OF MINNESOTA
Driven to Discover®

BM stains

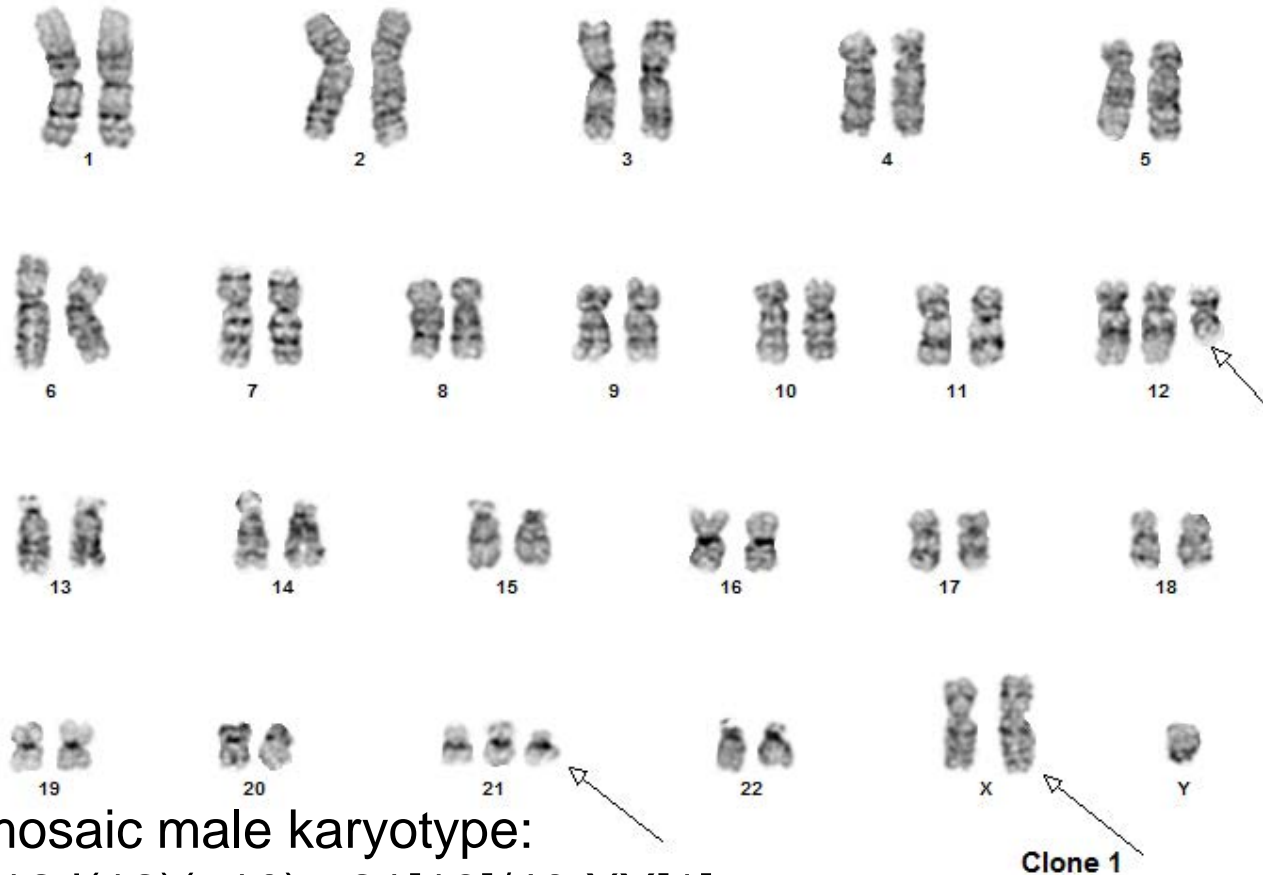
- An iron stain performed on marrow aspirate smear showed markedly increased storage and sideroblastic iron with about 5% ring sideroblasts.
- Cytochemical stains performed on marrow aspirate smears showed weakly myeloperoxidase positive blasts, negative for alpha naphthyl butyrate esterase.
- The immunohistochemical stains performed on particle clot section showed that CD34 and CD117 marked blasts comprising about 10-20% of all hematopoietic elements; CD61 marked megakaryocytes, CD68, CD163, and lysozyme highlighted the prominent reactive histiocytic hyperplasia.



Flow cytometry

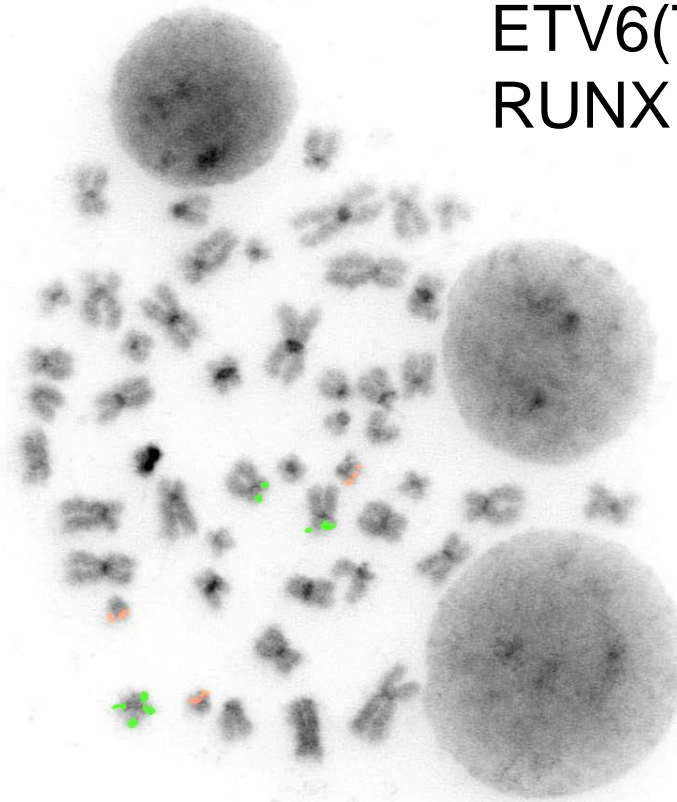


Cytogenetics



FISH

FISH showed evidence for isochromosome 12p and gains of the ETV6(TEL) and RUNX1(AML1) loci.



(nucish(MLLx2)[200],(ETV6x4,RUNX1x3)[177/200])



Proposed diagnosis

- MDS-EB-2, associated with a malignant germ cell tumor of the mediastinum.
- Histiocytic hyperplasia with cytophagocytosis in bone marrow, cause uncertain.

Panel diagnosis:

Myelodysplastic syndrome with excess blasts-2 and clonally-related mediastinal malignant germ cell tumor



Discussion

- Hematologic malignancies (HM) associated with mediastinal germ cell tumor (MGCT) are exceedingly rare with approximately 60 cases described to date.
- In most reported cases the HM is an AML frequently demonstrating megakaryocytic differentiation.
- Less commonly, malignant histiocytosis, MPN or MDS have been reported.
- The associated GCT is almost exclusively nonseminomatous and extragonadal.
- In rare cases HM was reported in association with CNS or testicular GCT.
- HM associated with GCT typically behave aggressively with median overall survival of only ~5 months.
- Allogenic SCT has been reported as the only curative approach in very rare cases.



Theories of origin

Both papers showed shared somatic mutations in PTEN and TP53 as well as a presence of isochromosome 12p in both GCT and AML samples.

Given that PTEN mutations and isochromosome 12p are exceedingly rare in AML and conversely, TP53 mutations are relatively rare in GCT the authors suggest that this evidence strongly supports that the tumors in this syndrome arise from the same founding clone that ultimately evolved into two different malignancies.



Acknowledgements

- Dr. Lina Shao,
- Dr. Diane Roulston,
- Dr. Charles Ross,
- Dr. Nathanael Bailey.



UNIVERSITY OF MINNESOTA

Driven to Discover®

Panel Diagnosis

- **Myelodysplastic syndrome with excess blasts-2 and clonally-related mediastinal malignant germ cell tumor.**