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Acute Myeloid Leukemia With *NUP98::NSD1* Fusion

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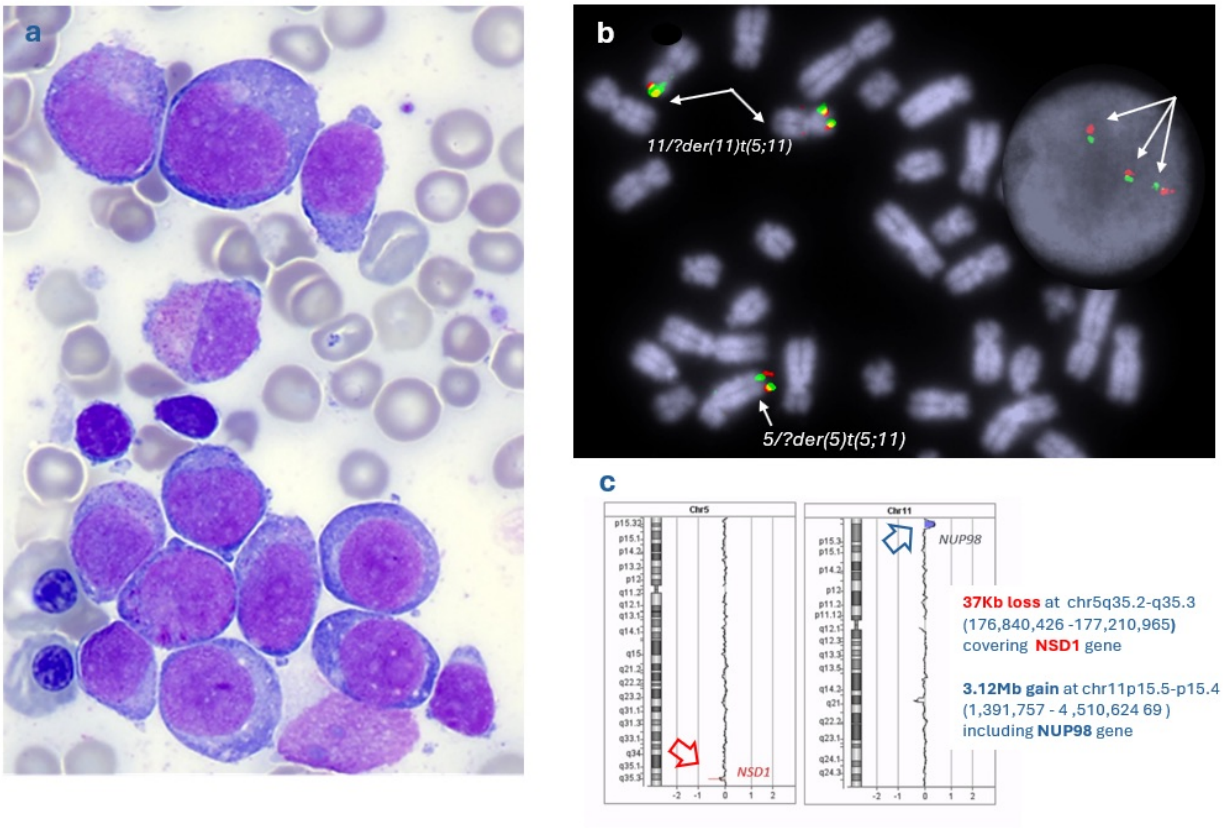

Figure 1: (a) Bone marrow aspirate showing large blasts with no Auer rods (May-Grünwald-Giemsa stain x 1000 magnification). (b) FISH showing an extra copy of *NUP98* gene on chromosome 5. (c) Molecular karyotyping (aCGH) revealing deletion of *NSD1* gene and gain of *NUP98* gene.

A 40-year-old male presented with pancytopenia. A complete blood count showed Hgb 56 g/L, WBC 2.65 x10^9/L, and platelet 35 x10^9/L with a neutrophil 0.48 x10^9/L. Bone marrow aspirate showed large blasts with basophilic cytoplasm and no Auer rods (Figure 1a). By flow cytometry these cells were positive for CD34, CD117, CD33, CD13, CD15, HLA-DR, cMPO and negative for CD19, CD20, CD5, CD7, CD14,

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cCD3, cCD79a. Targeted acute myeloid leukemia (AML) fluorescence in situ hybridization (FISH) showed gain of one extra copy of the *NUP98* gene mapped at B group chromosome, likely at 5q35 region (*NUP98* break apart probe (Cytocell), Figure 1b), confirmed by array comparative genomic hybridization (aCGH, Agilent 8x60K) along with concurrent *NSD1* loss indicating unbalanced t(5;11)(q35;p15.5) (Figure 1c). Myeloid next-generation sequencing (NGS) (Oncomine Myeloid Assay GX v2) revealed pathogenic variant in *WT1* p.Val354CysfsTer14 (VAF 60%) and *NUP98::NSD1* fusion. *FLT3*-ITD was positive (VAF 42%) by polymerase chain reaction (PCR). The patient was diagnosed with AML with *NUP98* rearrangement, specifically *NUP98::NSD1*. The patient was refractory to DA (daunorubicin-cytarabine)+ midostaurin, FLA-Ida (fludarabine, cytarabine, idarubicin), gilteritinib and venetoclax/azacitidine and sadly passed away.

AML with *NUP98* rearrangement is associated with adverse outcomes. *NUP98* fuses with over 30 partner genes [1]. *NUP98::NSD1* and *NUP98::KDM5A* are frequently-occurring *NUP98* fusions in AML. AML with *NUP98::NSD1* fusion is more frequently associated with myelomonocytic or monocytic/monoblastic morphology, *FLT3*-ITD and *WT1* mutations. *NUP98::NSD1* was an independent predictor for poor prognosis [2].

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References

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