INITIAL EVALUATION

TESTS

•BMA/Biopsy

• Serology/ virus PCR
• BM cytogenetics/FISH
• Flow cytometry for GPI linked CD55/CD59 or FLAER

History:
• Infection (10-20%): Influenza A, CMV, EBV, HHV-6, hepatitis (non A, B, C), HIV, parvovirus
• Leukemia (1-2%) ALL
• Drugs, toxins (v. few)
• PNH: hemolysis, hemoglobinuria, aplasia

Pancytopenia
• Hb < 10g/dL
• Platelets < 50 K/uL
• ANC < 1500/uL

Physical:
• Short stature, dysmorphic features,
• Skeletal abnormalities (thumbs radii),
• Skin; cafe au lait or hypopigmented patches

Family Hx:
• Cytopenias, transfusions
• Leukemias, MDS, other malignancies

Secondary AA 10-15%

NO

YES

Two lineages decreased
+
Hypoplastic BM
without infiltration or fibrosis
Idiopathic aplastic anemia (AA) 70%

Inherited BMF syndrome with pancytopenia/hypoplasia
15-20%
• Fanconi anemia (FA)
• Dyskeratosis congenita (DC)
• Shwachman Diamond syndrome (SDS)
• Congenital amegakaryocytic thrombocytopenia (CAMT)

severe AA (sAA)
• BM < 25% cellular or 25-50% if hematopoietic cells < 30%
+ 2 of:
• ANC < 500/uL
• Platelets < 20K/uL
• Reticulocytes < 20K/uL

very severe AA (vsAA)
as above but
• ANC < 200/uL

moderate AA (mAA)
hypoplastic BM and cytopenia not fulfilling above criteria

FA:
Often presents in 1st decade with thrombocytopenia -> pancytopenia
Note pigmentation defects, thumb abnormalities, renal and UT abnormalities

• DEB test
• Genetics: 13 genes *FANCA* (65%) and *FANCC* and G (12% ea) most common - almost all AR (*FANCB* X-linked)

DC:
Triad of leukoplakia, dystrophic nails and pigmented reticular rash (1st decade), followed by BMF (2nd and 3rd decades)

• Telomere length leukocyte subsets
• Genetics: 6 genes
XL: dyskerin *DKC1* (40%)
AR: *TERT* (2%), NOP10, NHP2
AD: - *TERC* (in AD-DC, AA, MDS, PNH, PF) (5%)
- *TERT* (in AA, AD-DC, PF)
- *TINF2* (11%)

SDS:
Pancreatic insufficiency with FTT and steathorrea
Short stature, protuberant abdomen, icthyotic rash, metaphyseal dysostosis
Neutropenia (20% pancytopenia) -> MDS, leukemia in 25%

• pancreatic isoamylase (> 3 yrs)
• serum trypsinogen (< 3 yrs)
• CXR, humeri, femurs
• Genetics: 1 gene
AR: *SBDS* >90%

CAMT:
Thrombocytopenia with absent megakaryocytes 0-5 yrs -> Pancytopenia

• Genetics:
AR: *MPL*

Abbreviations.
Hb, hemoglobin; ANC, absolute neutrophil count; CMV, cytomegalovirus; EBV, Epstein Barr virus; HHV-6, human herpes virus-6; HIV, human immunodeficiency virus; PNH, paroxysmal nocturnal hemoglobinuria; MDS, myelodysplastic syndrome; BMA, bone marrow aspirate; PCR, polymerase chain reaction; FISH, fluorescence in-situ hybridization; GPI, glycophosphatidyl inositol; FLAER, fluorescent aerolysin; AA aplastic anemia; UT, urinary tract; FTT, failure to thrive; DEB, diepoxybutane; FANCA, FANCB, FANCC, Fanconi anemia A B and C genes; DKC1, dyskerin gene; TERT, telomerase reverse transcriptase; NOP10, nucleolar protein 10; NHP2, nucleolar protein family A, member 2 (H/ACA small nucleolar RNPs); TERC, telomerase RNA component; TINF2, TERF1 (TRF1)-interacting nuclear factor 2; XL, X-linked inheritance; AR, autosomal recessive inheritance; AD, autosomal dominant inheritance; PF, pulmonary fibrosis; CXR, chest X-ray; SBDS, Shwachman Bodian Diamond syndrome gene; MPL, human homologue myeloproliferative leukemia virus gene. FA, Fanconi anemia; DC, dyskeratosis congenita; SDS, Shwachman-Diamond syndrome; CAMT, congenital amegakaryocytic thrombocytopenia.