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<th>Myeloid stem cell disorder</th>
<th>Definition &amp; diagnosis</th>
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| Aplastic anemia (AA)       | Peripheral blood pancytopenia w/ marrow hypopcellularity  
No clonal cytogenetic abnormality (hypocell acute leukemia, MDS)  
Marrow biopsy w/ aspirate necessary for diagnosis | Radiation, chemo, benzene, drugs (sulf a, NSAID), viruses (EBV), pregnancy, immune-mediated diseases (transfusion GVHD), PNH, inherited (fanconi’s anemia)  
Maybe autoimmune (neo-ag) | Marrow failure, chronic anemia, thrombocytopenic hemorrhage, infections  
Inherited: café au lait spots, short stature, thumb abnormalities, renal malformations (fanconi’s anemia)  
No adenopathy or splenomegaly | Supportive: abx prophylaxis  
Allo HSCT  
Immuno-suppression: ATG, ALG, steroids, cyclosporine  
Androgens (erythropoiesis), G-CSF, GM-CSF |
| Myelodysplastic syndrome (MDS) | Peripheral blood cytopenias w/ marrow cell dysplasia  
Hypercellular marrow (ineffective hematopoiesis)  
Smear: aniso, poikilo, macro, teardrop  
Marrow: auer rods, hypo & hyperseg pmn, megaloblastic, accelerated apoptosis  
FAB, IPSS classification | Benzene, chemo, radiation, AA, AML, auto HSCT for NHL (treatment-related MDS)  
Cytogenetic defect (30-70%)  
Younger patients often w/ familiar hematologic disorder or congenital defect in DNA repair (fanconi’s anemia) | Single cytopenias, bicytopenia or pancytopenia  
Adenopathy, splenomegaly more common than AA  
Most succumb to neutropenic infections or thrombocytopenic hemorrhages  
Incident increases w/ age  
May progress to AML | Allo HSCT only cure  
GM-CSF, G-CSF, Epo  
Immunosuppressive regimens, chemo (like AML) |
| Chronic myelogenous leukemia (CML) | Clonal stem cell disorder of all myeloid elements (B cells variably, T cells rarely)  
Smear: leukocytosis, thrombocytopenia (10%) or thrombocytosis (50%), normal granulocytes & RBC, left shift, basophilia  
Marrow: hypercellular w/ 20:1 myeloid-erythroid ratio, megakaryocytic hyperplasia  
Low LAP | Philadelphia chrom t(9:22) w/ enhanced TK activity, radiation | Half asymptomatic, fatigue, weight loss, ab fullness or pain, easy bruising or bleeding, hepatosplenomegaly  
Blast crisis (>30% blasts in blood or marrow, 2/3 myeloid & 1/3 lymphoid): fever, sweats, weight loss, bone pain  
Slightly more common in men, peaks 40-60 yrs  
May progress to AML or ALL | Chronic phase: observation, splenectomy, pheresis, chemo (bisulfan, hydroxyurea), interferon-alpha (may delay blast crisis), allo HSCT (GVLE) only cure, STI571 (inhibits TK)  
Accelerated, blast crisis: myeloid crisis resistant to AML therapy, lymphoid crisis better response to AML therapy |
| Chronic lymphocytic leukemia (ALL) | Clonal stem cell disorder of lymphocytic origin w/ lymphocytosis in peripheral blood and marrow | Philadelphia chrom t(9:22) w/ enhanced TK activity, radiation | Stage I: lymphocytosis, enlarged nodes  
Stage II: lymphocyt, spleen & liver +/- nodes  
Stage III: lymphocyt, anemia +/- above  
Stage IV: lymphocyt, thrombocytopenia +/- above 2:1 male/female ratio  
Half asymptomatic, fatigue, weight loss, ab fullness or pain, easy bruising or bleeding, hepatosplenomegaly  
Blast crisis (30% blasts in blood or marrow, 2/3 myeloid & 1/3 lymphoid): fever, sweats, weight loss, bone pain  
Slightly more common in men, peaks 40-60 yrs  
May progress to AML or ALL | Low-grade lymphoma therapy (aggressive to observation)  
Auto/allo HSCT to salvage |
| Polycythemia vera (PCV) | Erythrocytosis w/ low Epo  
Diagnosis of exclusion, RBC mass assay to distinguish from relative polycythemia, Marrow: hyperplasia of all 3 myeloid lineages | Cytogenetic clonal abnormalities (20%, bad prognosis) | Ruddy complexion, conjunctival plethora, left upper quad ab pain from splenomegaly, hyperviscosity (thromoses), hemorrhage, iron deficiency, pruritis  
Spent phase: myelofibrosis  
May progress to AML | Phlebotomy to maintain hematocrit < 45%  
Hydroxyurea  
Interferon-alpha  
Anagrelide for thrombocytosis |
| Essential thrombocythemia (ET) | Thrombocytosis  
Diagnosis of exclusion | Some cytogenetic clonal abnormalities | May be asymptomatic, thrombotic complications, hemorrhagic sequelae (qualitative platelet defects), splenomegaly (30-50%)  
Bimodal incidence (50-60, 30 yrs)  
May progress to AML (less than w/ PCV) | Observation if asymptomatic  
Hydroxyurea  
Interferon-alpha  
Anagrelide (non-myelosuppressive)  
Platelet pheresis |
| Myelofibrosis with agnogenic myeloid metaplasia (MMM) | Smear: leukaerythroblastosis, immature granulocytic precursors, erythroblasts, teardrop cells, large platelets  
Marrow biopsy necessary: collagen & reticulin fibers produced by fibroblasts | Some cytogenetic clonal abnormalities (bad prognosis) | Weight loss, fever, night sweats, fatigue, left upper quad ab pain, anemia, hepatosplenomegaly, portal hypertension, splenic infarct, pleural or pericardial effusions (extramedullary hematopoiesis of serosal surfaces)  
Variable WBC & platelet counts  
May progress to AML | Hydroxyurea (control of organomegaly, leukocytosis, thrombocytosis)  
Androgens  
Interferon-alpha  
Surgical splenectomy  
Auto & allo HSCT |
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| Acute myelogenous leukemia (AML) | Malignant transformation of a myeloblast w/ increased rate of self-renewal and limited ability to differentiate  
* Auer rods in blast cytoplasm | Radiation, chemo, benzene, smoking, chromosomal disorders (down’s, fanconi’s), chronic marrow disorders (MPD, MDS, AA, PNH, MM) | Marrow failure, infections, leukostasis (pulmonary & cerebral), hyperleukocytosis, myeloblastoma or EM leukemia (solid tumor of myeloblasts), leukemic infiltration of tissues, DIC, tumor lysis syndrome  
Higher incidence in elderly (poor prognosis) | Induction chemo w/ complete remission  
Post-remission: low dose maintenance, high dose consolidation, allo/auto HSCT  
Supportive                                                                 |
| Acute promyelocytic leukemia (APL) | Marrow: >30% myeloblasts, >20% abnormal hypergranular promyelocytes, *Auer rods*, faggot cells  
Cytochem: MPO+ | Cytogenetic abnormality  
*t(15;17)* w/ PML-RAR-alpha fusion | Leukopenia, coagulopathy, DIC  
Younger median age | All-transretinoic acid (ATRA, vitamin A therapy) followed by chemo (arsenic trioxide) and allo HSCT (only cure) |
| Acute lymphoblastic leukemia (ALL) | Malignant transformation of a lymphoblast w/ increased rate of self-renewal and limited ability to differentiate | Radiation, *viruses* (EBV & Burkitt’s, HTLV-1 & adult T cell leukemia/lymphoma), congenital (down’s, fanconi’s), abnormal chrom (1/3 w/ *Philadelphia chromosome*), CML | Hepatosplenomegaly more common than AML  
Higher incidence in kids (good prognosis)  
Good prognosis: t(12;21), t(8;21), t(15;17), inv(16), T cell ALL  
Poor prognosis: 11q23 translocation, Philadelphia chromosome | Induction chemo w/ complete remission  
Post-remission: intensive consolidation, intrathecal (CNS prophylaxis), prolonged low dose maintenance, allo HSCT (only cure) if high risk |