Figure 2. Diagnostic Work-up: Patient with suspected acquired or inherited bone marrow failure

Name:	
Age	
DOB:	
MRN:	
Clinical presentation:	

Specific parameter	**Comment**	**Result**
Infections, medications, toxins	BM viruses, chloramphenicol other antibiotics, benzene, recurrent infections.	
Detailed family history	Ask about early deaths, blood disorders (macrocytosis, chronic cytopenias), transfusions, cancer, recurrent infections, developmental anomalies.	
Comprehensive physical exam	Look for short stature, dysmorphic facial features, thumb abnormalities, cafe au lait, or depigmented skin lesions.	

Baseline laboratory test	**Date**	**Result/comment**
• CBC w/ differential • smear • reticulocyte count (% and absolute) • electrolytes • bun/cr • liver function tests • glucose • Hb electrophoresis (pre-transfusion) • consider detailed immunological w/u (T and B cells, Ig's, specific vaccine titers—NOT appropriate for most patients)		

Bone marrow aspirate/biopsy:	**Comment**	**Result**
Morphology/cellularity		
Cytogenetics	Genzyme http://www.genzymegenetics.com	
FISH for 5,7,9	Add trisomy 3q by FISH if suspicion of FA	
Flow cytometry for T, B and CD34	Hypoplastic acute leukemia	

Basic work-up BM hypoplastic:	**Comment**	**Result**
FA Testing/DEB test	Advisable to choose an expert lab	
HLA typing of immediate family (patient, parents, sibs)	Can ask for expedited testing	
Telomere length analysis	MUST order the **detailed procedure** (note-this needs to include lymphocyte subsets)– Repeat Diagnostics 604-985-2609 repeatdiagnostics.com	
PNH screen by flow	Blood for FACS assay of GPI-linked proteins	
Viral studies	HIV, parvovirus, EBV, CMV, HSV, VZV, Hepatitis A, B, C serology	
Nutritional studies	Red cell folate, vitamin B12	

Further work-up - If suspicion of inherited BMFS and in consultation with BMF expert

Test	Comment	Lab	Result
Plain film of hand	FA, DBA		
Skeletal survey	SDS		
U/S of pancreas	SDS		
U/S of renal system	FA, DBA		
Cardiac ECHO	FA, DBA		
Pancreatic isoamylase (>3 yrs) and serum trypsinogen (<3 yrs)	SDS: Isoamylase attains adult values by 3 yrs, while trypsinogen can increase in pts with SDS		
Red cell adenosine deaminase (ADA)	Important to obtain pre-transfusion	Stanford Bert Glader lab:	
Genetic testing for DC - step-wise approach:	Done if 3/5 lymphocyte telomere length <1st centile	Ambry Genetics 866-262-7943 http://www.ambrygen.com Note: please check expiration date printed on the blood collection tubes in Ambry specimen submission kit	
DKC1 xl 30%	1st set if male		
TINF2 ad 11%	1st		
TERC ad 6%	1st		
NOP10 ar rare <1%	2nd set if 1st all negative		
NHP2 ar rare <1%	2nd		
TERT ad or ar rare <1%	2nd		
MPL gene	Congenital Amegakaryocytic Thrombocytopenia (CAMT) often thrombocytopenic from 1st year of life	Prevention Genetics 715-387-0484 http://www.preventiongenetics.com	
Fanconi anemia complementation group testing and gene mutation identification	Only for patients known to have FA and not usually necessary		
SBDS	SBDS		

Patients with severe neutropenia, red cell aplasia or thrombocytopenia only		
ELA-2	SCN	GeneDx 301-519-2892
HAX-1 ar (Kostmann disease)	SCN; other uncommon genetic forms	GeneDx
Ribosomal protein genes	10 known DBA genes	
RUNX1	Thrombocytopenia, FH of AML	Prevention Genetics

Consults	Person	Date
BMF		
Social Work		
Stem Cell Transplant		

Abbreviations: DOB, date of birth; MRN, medical record number; BM, bone marrow; CBC, complete blood count; Hb, hemoglobin; Ig's, immunoglobulin subsets; FISH, fluoresence in-situ hybridization; FA, Fanconi anemia; DEB, diepoxybutane; HLA, human leukocyte antigen; PNH, paroxysmal nocturnal hemoglobinuria; HIV, human immunodeficiency virus; EBV, Epstein Barr virus; CMV, cytomegalovirus; HSV, Herpes simplex virus; VZV, varicella zoster virus; DBA, Diamond Blackfan anemia; SDS, Shwachman Diamond syndrome; ECHO, ultrasound; DC, Dyskeratosis congenita; SBDS, Shwachman Bodian Diamond syndrome gene; SCN, Severe congenital neutropenia; FH, family history; AML, acute myeloid leukemia; FH, family history; BMF, bone marrow failure, BMFS, bone marrow failure syndrome; Bun/cr, blood urea nitrogen/serum creatinine