Table 1. Diagnostic criteria and differential diagnoses of DBA syndrome

DIAGNOSTIC CRITERIA		
• **Pathogenic or likely pathogenic mutation in a DBA syndrome gene (Table 3),** **OR** • **Hematologic features consistent with DBA:** macrocytic anemia[1] with reticulocytopenia and BM erythroblastopenia; absence of dysplasia, dyserythropoiesis[2], and sideroblasts AND: exclusion of known differential diagnoses (below)		
TYPICAL FINDINGS (NOT MANDATORY FOR DIAGNOSIS) [3]		
• Age at onset less than 1 year • Elevated eADA activity (prior first transfusion; in non-transfused patients and/or parents) • Elevated HbF (reliably assessed in patients > 6 months of age) • Positive family history or unexplained history of anemia during infancy or childhood • Congenital abnormalities **(Table 4)** • Abnormal rRNA processing in patient cells [4]		
DIFFERENTIAL DIAGNOSES		
ACQUIRED	Transient erythroblastopenia of childhood	• Onset usually > 1 year of age • Normal MCV, eADA, HbF • Negative family history and no congenital abnormalities • Transient course: erythroid recovery in days to weeks
	Viruses: Specific to red cell lineage (Parvovirus B19) Non-specific (HIV, CMV, EBV and others)	• Positive PCR and/or serology • Normal eADA and HbF • Normal MCV (except Parvovirus B19) • Negative family history and no congenital abnormalities • Concomitant immune deficiency or chronic hemolysis
	Myelodysplastic syndrome [5], specifically with 5q deletion (acquired RPS14 haploinsufficiency)	• Typical BM findings (morphology, histology, karyotype, FISH, MDS-related somatic mutations) • Normal eADA
	Drugs Autoimmunity (SLE, acquired PRCA) Lymphoproliferative diseases Malignancy: CLL[5], LGL[5], acute leukemias and some solid tumors	• Typical BM and immunologic findings • Normal eADA • No congenital abnormalities • Features of malignancy
	Thymoma with concomitant PRCA[5]	• Typical imaging (chest x-ray, CT or MRI) • No congenital abnormalities • Mostly in adults, unlikely in children
GENETIC	IBMFS (specifically FA, SDS, DC)[6] Pearson syndrome Congenital sideroblastic anemia Congenital dyserythropoietic anemia	• Classical clinical presentation, laboratory findings • BM morphology consistent with respective condition • MCV and HbF can be elevated, eADA normal • Syndrome-specific diagnostic findings and genetics
	ADA2 deficiency	• Onset at any age, vasculopathy often absent • Low B cells and hypogammaglobulinemia • Normal eADA and HbF; MCV can be high • Low ADA2 enzyme activity and *ADA2* mutations • Typically, no congenital abnormalities
	Erythropoietin dysfunction	• Homozygous *EPO* R150Q mutation

[1] Additional cytopenia can be encountered (neutropenia more often than thrombocytopenia), transient thrombocytosis in infants.
[2] Except for cases with *GATA1* mutations.
[3] Highly suggestive of DBA syndrome; however not specific enough to make the diagnosis.
[4] Research test in specialized labs only; useful in cases with ambiguous or uninformative genetics.
[5] Typically presenting in adults.
[6] These IBMFS typically demonstrate multi-lineage cytopenia and often present with other disease-specific abnormalities affecting multiple organ systems. Such distinguishing features can help differentiate these conditions from DBA syndrome, which initially characteristically manifests with isolated erythroid hypoplasia.

Abbreviations: BM; bone marrow; eADA, erythrocyte adenosine deaminase; HbF, fetal hemoglobin; SLE, systemic lupus erythematosus; PRCA, pure red cell aplasia; CLL, chronic lymphocytic leukemia; LGL, large granular lymphocytic leukemia; CT, computer tomography; MRI, magnetic resonance imaging; IBMFS, inherited bone marrow failure syndromes; FA, Fanconi anemia; SDS, Shwachman Diamond syndrome; DC, dyskeratosis congenita.