Hemolytic Anemia Diagnostic Algorithm
Consider PNH

Consider physical agents including MAHA/HUS/aHUS/TTP

Work-up for autoimmune or alloimmune causes

Positive

suboptimal reticulocytosis, iron overload, or skeletal abnormalities

Negative

DAT and indirect Coombs

Anemia with reticulocytosis (jaundice, splenomegaly, ↑LDH, ↓haptoglobin)

chronically transfused patient

Family History and Blood Smear Review to assist with diagnosis

Hemoglobin Electrophoresis

RBC enzymopathies gene panel

Ektacytometry indicating RBC membrane disorder

Bone Marrow Studies

Normal except erythroid hyperplasia

binuclear or multinuclear erythroblasts

CDA gene panel

Normal

Abnormal

Abnormal

Globin gene and HHA/CDA panel or subpanels depending on family history and smear review

Globin gene sequencing and deletion/duplication analysis

RBC enzyme activity

Normal

Ektacytometry (osmotic fragility also an option, although less sensitive)