Hemolytic Anemia Diagnostic Algorithm

Erythrocyte Diagnostic Laboratory
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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)

Family History and Blood Smear Review to assist with diagnosis

Chronically transfused patient

Hemoglobin Electrophoresis

Normal

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

Normal except erythroid hyperplasia

Bone Marrow Studies

RBC enzyme activity

Normal

Abnormal

Ektacytometry indicating RBC membrane disorder

RBC membrane disorders gene panel, especially if splenectomy is contemplated

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

Globin gene sequencing and deletion/duplication analysis

Globin gene panel

No

Normal

Abnormal

RBC enzymopathies gene panel

Yes

Consider PNH

Yes

CDA gene panel