Case scenario

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On year old admitted with pallor. o/e no bleeding manifestations,severe pallor,tinge of jaundice. No significant lymphnode enlargement .p/a spleen 5 cm,liver span 8 cm,and firm in consistency. Answer the following.

What is the probable diagnosis?

Arguments for your dx and closet differential dx.

How will you confirm the dx?

How will you manage?

What are the complication?

Discussion: in view of pallor ,jaundice,hsm a hemolytic process is most likely. Absence of bleeding, Lymph node enlargement(at least two cell line involvement) makes a dx leukaemia unlikely. Pallor in one yr old make us think about congenital problem like hemolytic anemias, acquired process like infection(malaria),less common possibilities like leukemia,histiocytosis . in this child with the narrated scenario it is most likely to be a hemolytic anemia(shape/ hemoglobinopathy/enzyme)

1 yr,severe pallor, jaundice ,hsm,nobleeding,no lymphnode **Pallor** –rbc production is affected **Jaundice**- there is destruction of rbc **Hepatomegaly**- firm –infiltrative/metabolic process, Soft spleen -in infections **Splenomegaly**-reticuloendothelial response to hemolysis **Lack of bleeding** – a process that do not interfere with production/destruction of platelets/clotting factors	
Hereditary spherocytosis-family history,newborn jaundice,anemia transfusion,cholecystectomy for adults Thalassemia major- anemia in second half of ist yr, recurrent transfusion,typical facies,hsm Sickle cell anemia- anemia,bacterial infection dactylitis,sequestartions Malaria- fever,travel to other states,migrant population near by Disseminated tuberculosis,contact with open case,malnutrition mod,to severe,age less than 1 yr	

Markers of Extravascular Hemolysis
1. Increased unconjugated bilirubin.
2. Increased lactic acid dehydrogenase in serum.
3. Decreased plasma haptoglobin
4. Increased fecal and urinary urobilinogen

Markers of Intravascular Hemolysis
1. Increased unconjugated bilirubin.
2. Increased lactic acid dehydrogenase in serum.

3. Hemoglobinuria
4.. Hemosiderinuria

Increased Erythropoiesis
• Reticulocytosis: Frequently up to 10–20%;
Peripheral smear- Sickle cells, spherocytes

Hereditary spherocytosis	
Hb –low **Reticulocytosis** **Indirect bilirubin increased** **Ps**-The spherocytes are smaller in diameter and appear hyperchromic on the blood film as a result of the high hb concentration. The central pallor is less conspicuous than in normal cells. Spherocytes may be the predominant cells or may be relatively sparse, depending on the severity of the disease, but they usually account for >15-20% of the cells The presence of spherocytes in the blood can be confirmed with an osmotic fragility test. The RBCs are incubated in progressive dilutions of an iso-osmotic buffered salt solution. - **Osmotic fragility** -Exposure to hypotonic saline causes the RBCs to swell, and the spherocytes lyse more readily than biconcave cells in hypotonic solutions. This feature is accentuated by depriving the cells of glucose overnight at 37°C, known as the *incubated osmotic fragility test.* Unfortunately, this test is not specific for hereditary spherocytosis, and results may be abnormal in immune and other hemolytic anemias **eocin-5-maleimide test** a specific test **mutation analysis**: β-spectrin and ankyrin genes	

Thalassemia major	
severe anemia, reticulocytopenia, numerous nucleated erythrocytes, and microcytosis with almost no normal-appearing erythrocytes on the peripheral smear The unconjugated serum bilirubin level is usually elevated, but other chemistries may be normal at an early stage Bone marrow hyperplasia can be seen on radiographs Hb electrophpresis at isoelectric ph Genetic mutation analysis –indian mutations- 619 bp deletion •• IVS 1-5 (G-C) •• IVS 1-1 (G-T) •• FS 8/9 (+G) •• FS 41/42 (-CTTT).	

Sickle cell	
The most commonly used procedures for newborn diagnosis include thin layer/isoelectric focusing and high-performance liquid chromatography (HPLC). A 2-step system is recommended, with all patients who have initially abnormal screens being retested during the first clinical visit and after 6 mo of age to determine the final hemoglobin phenotype In addition, a complete blood cell count (CBC) and hemoglobin analysis are recommended on both parents to confirm the diagnosis and to provide an opportunity for genetic counseling.	h

NEWBORN SCREENING RESULTS: SICKLE CELL DISEASE[*]	POSSIBLE HEMOGLOBIN PHENOTYPE[†]	BASELINE HEMOGLOBIN RANGE	EXPERTISE IN HEMATOLOGY CARE REQUIRED
FS	SCD-SS	6-11 g/dL	Yes
	SCD-S β^0 thal	6-10 g/dL	Yes
	SCD-S β^+ thal	9-12 g/dL	Yes

In newborn screening programs, the hemoglobin with the greatest quantity is reported first followed by the other hemoglobins in decreasing quantity. In newborns with a hemoglobin analysis result of FS, the pattern supports Hb SS, hereditary persistent fetal hemoglobin, or Hb S β-thalassemia zero. In a newborn with a hemoglobin analysis of FSA, the pattern is supportive of diagnosis Hb S β-thalassemia+. The diagnosis of Hb S β-thalassemia+ is confirmed if at least 50% of the hemoglobin is Hb S, HbA is present, and the amount of Hb A_2 is elevated (typically >3.5%), although Hb A_2 is not elevated in the newborn period. In newborns with a hemoglobin analysis of FSC, the pattern supports a diagnosis of Hb SC. In newborns with a hemoglobin analysis of FAS, the pattern supports a diagnosis of Hb AS (sickle cell trait).

Management

Hereditary spherocytosis	If Hb >10 g/dL and reticulocyte count <10%: none If severe anemia, poor growth, aplastic crises, and age <2 yr: transfusion Folic acid, 1 mg qd Splenectomy- For patients with more severe anemia and reticulocytosis or those with hypoplastic or aplastic crises, poor growth, or cardiomegaly, splenectomy is recommended after age 5-6 yr to avoid the heightened risk of postsplenectomy sepsis in younger children. Vaccines (conjugated and/or capsular) for encapsulated organisms, such as pneumococcus, meningococcus, and *Haemophilus influenzae* type b, should be administered before splenectomy, and prophylactic oral penicillin V (age <5 yr, 125 mg twice daily; age 5 yr through adulthood, 250 mg twice daily) should be administered thereafter

Thalassemia major	**Blood transfusion**. A transfusion program generally requires monthly transfusions, with the pretransfusion hemoglobin level between 9.5 and 10.5 g/dL. Excessive iron stores from transfusion cause many of the complications of β-thalassemia major. Excessive iron stores can be prevented by the use of **deferoxamine (Desferal**) or deferasirox (Exjade). Deferoxamine chelates iron and some other divalent cations, allowing their excretion in the urine and the stool. Deferoxamine is given subcutaneously over 10-12 hr, 5-6 days a week **The oral iron chelator deferasirox** (Exjade) is commercially available in the United States. Although the optimal dose of deferasirox is well defined, some patients have a less-than-expected response to the maximum approved doses (30 mg/kg/day). **Hematopoietic stem cell** transplantation has cured many children

Sickle cell	**Infection**- Because of a marked incidence of bacterial sepsis and meningitis and fatal outcome under 5 years of age, the following management is recommended.

	All children with sickle cell disease should receive oral penicillin prophylaxis starting by 3–4 months of age: • 125 mg bid (,3 years) • 250 mg bid (3 years and older **Treatment of specific complications** **Transfusion therapy**: Transfusion therapy is used to manage acute and chronic complications of sickle cell disease **Induction of fetal hemoglobin** **Hematopoietic stem cell transplantation** (HSCT): Currently HSCT (including umbilical cord blood) is the only curative therapy.

Complications

Complications develop as a result of:

• Chronic anemia (in patients who are undertransfused or in untransfused thalassemia intermedia patients)

• Iron overload – Due to repeated red cell transfusions in β-thalassemia major. In patients not treated with chelation therapy, cardiac disease from iron loading typically develops in late teens and early 20s. Iron overload also develops in β-thalassemia intermedia due to increased absorption of dietary iron.

• Endocrine disturbances (e.g., growth retardation, pituitary failure with impaired gonadotropins, hypogonadism, insulin-dependent diabetes mellitus, adrenal insufficiency, hypothyroidism, hypoparathyroidism)

• Cirrhosis of the liver and liver failure (exacerbated if concomitant hepatitis B or C infection is present)

• Cardiac failure due to myocardial iron overload (often associated with arrhythmias and pericarditis may occur)

• Osteopenia and osteoporosis are common and the risk is directly proportional to age (the prevalence of osteoporosis is about 60% in patients 20 years and older). The causes of this include medullary expansion, deficiency of estrogen and testosterone, nutritional deficiency (including calcium, vitamin D and zinc) and chelator toxicity. Genetic factors likely also contribute

• Pulmonary hypertension (tricuspid regurgitant jet velocity greater than 2.5 m/s) occurs in both β-thalassemia major and β-thalassemia intermedia. Splenectomy may exacerbate this risk, particularly in patients who are not regularly transfused