World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 7.409

HEREDITARY SPHEROCYTOSIS: A CASE STUDY

***H. Omar, Y. Moumin, K. Ouafi, A. Belmekki and J. El Bakkouri**

Hematology Laboratory, Cheikh Khalifa University Hospital, Casablanca Mohammed VI Faculty of Health Sciences, Casablanca.

***Corresponding Author: H. Omar**
Hematology Laboratory, Cheikh Khalifa University Hospital, Casablanca Mohammed VI Faculty of Health Sciences, Casablanca.

Article Received on 15/11/2024 **Article Revised on 04/12/2024** **Article Accepted on 25/12/2024**

ABSTRACT
Hereditary spherocytosis (HS) is an autosomal dominant genetic hemolytic disease, characterized by reduced deformability of red blood cells, leading to their premature destruction. Clinical manifestations vary according to the severity of the disease and the type of genetic mutation, and commonly include hemolytic anemia, splenomegaly, and elevated indirect hyperbilirubinemia. Gallstones are also frequently observed in affected patients. We report the case of a 19-year-old female patient with moderate regenerative anemia, splenomegaly, and a family history of hemolytic anemia. Complementary tests revealed gallstones, spherocytes on the blood smear, elevated indirect hyperbilirubinemia, and marked reticulocytosis. The diagnosis was confirmed by increased red blood cell fragility and the exclusion of other causes of hemolytic anemia. The standard treatment for moderate and severe forms remains splenectomy, although management is often symptomatic. This case highlights the importance of early diagnosis and personalized management to prevent complications associated with hereditary spherocytosis.

KEYWORDS: Hereditary spherocytosis, routine laboratory tests in the diagnosis of Hereditary spherocytosis.

INTRODUCTION
Hereditary spherocytosis (HS) is a commonly encountered inherited hemolytic disorder, primarily inherited in an autosomal dominant manner. HS is a familial anomaly involving red blood cell (RBC) membrane proteins, associated with reduced deformability, increased fragility, and progressive destruction of spherical cells. The clinical manifestations in HS patients show evident heterogeneity.[1]

Hereditary spherocytosis (HS) is the most frequent cause of congenital hemolytic anemia, with a prevalence of approximately 1/2000 or 1/5000 in Europe, and 2043 cases reported over the past 36 years (1978 to 2013) in China. There are no factual data on the prevalence in Morocco.[2][3]

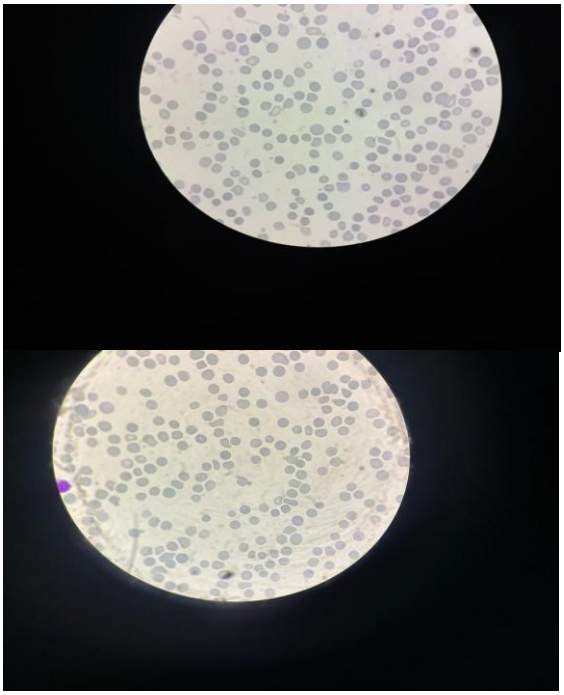
Clinical manifestations vary depending on the severity of the disease and the type of genetic mutation. Most patients with hereditary spherocytosis have a positive family history. This disease should be suspected in any young individual presenting with mild to moderate anemia, splenomegaly, and elevated indirect hyperbilirubinemia. Patients may also present with asymptomatic gallstones of unknown etiology.[4]

We present a case of hereditary spherocytosis, focusing on the role of routine laboratory tests in the diagnosis of this disease.

CASE REPORT
The patient was a 19-year-old female.

MEDICAL HISTORY
- Personal: Chronic moderate normocytic normochromic regenerative anemia and splenomegaly.
- Family: Hemolytic anemia in her father and brother of unclear etiology. The patient had been monitored for 3 months for moderate regenerative anemia, and was referred to hematology for better management. Given the anemia, splenomegaly, and family history, the hematologist ordered additional tests:
- Ultrasound revealed splenomegaly (16 cm) and gallstones, but no hepatomegaly.

Immunohematology
- **CBC**: Hb 10.7 g/dl, MCV 90 fl, MCHC 34 g/dl, Platelets 253,000/mm³, WBC 9,550/mm³, Reticulocytes 419,050/mm³
- **Blood smear**: Numerous spherocytes



X100

- **Red cell fragility test**: Initial hemolysis 5.5%, final hemolysis 4.5%
- **PT**: 100%, aPTT (patient/control) ratio 1
- **Direct Coombs test**: Negative
- **Hemoglobin Electrophoresis**: HbA 96%, HbA2 2.6%

Biochemistry

- Bilirubin >100 µmol/L with predominance of indirect bilirubin
- Folate: 2.50 ng/ml (reference: 3.1–20.5 ng/ml)
- Vitamin B12: 329 pg/ml (reference: 187–893 pg/ml)

DISCUSSION

Hereditary spherocytosis is one of the most frequent causes of erythrocyte membrane disorders, accounting for more than 70% of cases of hereditary hemolytic anemia.[5]

Hereditary spherocytosis is suspected in cases of mild to moderately regenerative anemia, splenomegaly, and jaundice (indirect hyperbilirubinemia) in a young patient with a family history of hemolytic anemia, with a sex ratio of 1/2.[6][7] In our case, the patient exhibited this clinical triad along with a positive family history.

Gallstones are present in approximately half of the cases of hereditary spherocytosis.[8] Our patient had gallstones on abdominal ultrasound.

The hemolysis workup revealed elevated indirect hyperbilirubinemia, increased LDH, and decreased haptoglobin, along with a red blood cell fragility test showing decreased red blood cell resistance in the case of HS.[9][10] This was true in our patient, with bilirubin >100 µmol/L and a decrease in the red blood cell fragility test (5.5% initial hemolysis, 4.5% final hemolysis).

Differential diagnosis of HS includes autoimmune hemolytic anemia (AIHA), glucose-6-phosphate dehydrogenase (G6PD) deficiency, pyruvate kinase (PK) deficiency, and hemoglobinopathies (thalassemia and sickle cell disease). These conditions should be ruled out by a negative direct Coombs test, normal G6PD and PK levels, and normal hemoglobin electrophoresis before diagnosing HS.[11][12] This was confirmed by the complementary test results in our case.

The diagnosis is confirmed by reticulocytosis and red blood cell morphology, particularly the presence of spherocytes on the peripheral blood smear, in the context of a family history and clinical signs suggestive of the disease.[13][14] In our case, the reticulocyte count was 12.66% (419,660 cells/mm³) and numerous spherocytes were present on the blood smear.

Splenectomy is considered the standard surgical treatment for moderate to severe forms of hereditary spherocytosis.[15] This option may be proposed for our case.

CONCLUSION

This case of hereditary spherocytosis underscores the importance of early diagnosis in a young patient presenting with moderate hemolytic anemia, splenomegaly, and a family history of hemolytic anemia. The results of complementary tests, including the presence of spherocytes and reduced red blood cell resistance, confirmed the diagnosis. Gallstones, frequently associated with this condition, were also observed. Splenectomy remains the treatment of choice for moderate to severe forms. Early and regular management is essential to prevent long-term complications.

REFERENCES

1. Wu Y, Liao L, Lin F. The diagnostic protocol for hereditary spherocytosis—2021 update. *J Clin Lab Anal*, 2021 Dec; 35(12): e24034. doi:10.1002/jcla.24034, Epub 2021 Oct 24.
2. Merguerian MD, Gallagher PG. Hereditary Spherocytosis.
3. King MJ, Zanella A. Hereditary red blood cell membrane disorders and laboratory diagnostic testing. *Int J Lab Hematol*, 2013; 35(3): 237-243. https: //doi.org/10.1111/ijlh.12070
4. Zamora EA, Schaefer CA. Hereditary Spherocytosis. 2023 Jul 4. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing, 2023 Jan;. PMID: 30969619.
5. Shim YJ, Jung HL, Shin HY, Kang HJ, Choi JY, Hah JO, Lee JM, Lim YT, Yang EJ, Baek HJ, Choi HS, Yoo KH, Park JE, Kim S, Kim JY, Park ES, Im HJ, Chueh HW, Kim SK, Lee JH, Yoo ES, Park HJ, Lee JA, Park M, Kang HS, Park JK, Lee NH, Park SK,

Lee YH, Lee SW, Choi EJ, Kong SG; Red Blood Cell Disorder Working Party of the Korean Society of Hematology. Epidemiological Study of Hereditary Hemolytic Anemia in the Korean Pediatric Population during 1997-2016: A Nationwide Retrospective Cohort Study. *J Korean Med Sci*, 2020 Aug 24; 35(33): e279. doi: 10.3346/jkms.2020.35.e279. PMID: 32830468; PMCID: PMC7445306.

6. Ge Y, Li J, Han Y, Xie H, Shangguan S, Jiang Q, Chen X, Liu R. [Analysis of the characteristics of SPTB gene variants among 16 children with Hereditary spherocytosis]. *Zhonghua Yi Xue Yi Chuan Xue Za Zhi*, 2023 Mar 10; 40(3): 269-275. Chinese. doi:10.3760/cma.j.cn511374-20221019-00698. PMID: 36854399.
7. Bai L, Zheng L, Li B, Huang H, Shi X, Yi Y. Clinical and genetic diagnosis for 26 patients with hereditary spherocytosis. *Zhong Nan Da Xue Xue Bao Yi Xue Ban*, 2023 Apr 28; 48(4): 565-574. English, Chinese. doi: 10.11817/j.issn.1672-7347.2023.220390. PMID: 37385619.
8. King MJ, Zanella A. Hereditary red blood cell membrane disorders and laboratory diagnostic testing. *Int J Lab Hematol*, 2013, 35(3): 237-243. https: //doi.org/10.1111/ijlh.12070.
9. Barcellini W, Bianchi P, Fermo E, Imperiali FG, Marcello AP, Vercellati C, Zaninoni A, Zanella A. Hereditary red blood cell membrane defects: diagnostic and clinical aspects. *Blood Transfus*, 2011 Jul; 9(3): 274-277. doi: 10.2450/2011.0086-10. Epub 2011 Jan 13. PMID: 21251470; PMCID: PMC3136593.
10. Kim Y, Park J, Kim M. Diagnostic approaches to hereditary hemolytic anemia in the genetic era. *Blood Res*. 2017, 52(2): 84-94. https://doi.org/10.5045/br.2017.52.2.84.
11. King MJ, Zanella A. Hereditary red blood cell membrane disorders and laboratory diagnostic testing. *Int J Lab Hematol*, 2013, 35(3): 237-243. https: //doi.org/10.1111/ijlh.12070.
12. Agarwal AM, McMurty V, Clayton AL, Bolia A, Reading NS, Mani C, Patel JL, Rets A. Clinical utility of targeted next-generation sequencing panel in routine diagnosis of hereditary hemolytic anemia: A national reference laboratory experience. *Eur J Haematol*. 2023 Jun; 110(6): 688-695. doi: 10.1111/ejh.13951. Epub 2023 Mar 8. PMID: 36825813.
13. Kalfa TA, Begtrup AH. EPB42-Related Hereditary Spherocytosis. 2014 Mar 13 [updated 2022 Apr 7]. In: Adam MP, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle, 1993–2023. PMID: 24624460.
14. Manciu S, Matei E, Trandafir B. Hereditary Spherocytosis - Diagnosis, Surgical Treatment, and Outcomes. A Literature Review. *Chirurgia (Bucur)*, 2017 Mar-Apr; 112(2): 110-116. doi: 10.21614/chirurgia.112.2.110. PMID: 28463670.
15. Manciu S, Matei E, Trandafir B. Hereditary Spherocytosis - Diagnosis, Surgical Treatment, and Outcomes. A Literature Review. *Chirurgia (Bucur)*, 2017 Mar-Apr; 112(2): 110-116. doi: 10.21614/chirurgia.112.2.110. PMID: 28463670.