



## Case Report

# Clinical pathology aspect on diagnosis cholelithiasis in $\beta$ -Thalassemia patient: A case report

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## ABSTRACT

**Background:** Thalassemia is categorized based on the abnormal globin chain and is divided into primary, intermediate, and minor subtypes based on the chain abnormality, respectively.

**Case presentation:** An Indonesian adolescent, 18 years old, complained of abdominal pain for 1-day. Medical history patient showed thalassemia for 13 years, routine control and received transfusions. Physical examination: Anemic conjunctiva (+/+), epigastric tenderness (+). Laboratory tests: Hb of 4.2 g/dL, MCV of 59.8 fL, and MCH of 19.6 pg. Peripheral blood smears showed microcytic hypochromic, target cells, and teardrop cells. Increased albumin: creatinine ratio  $\geq 300$  mg/gr. Hb Electrophoresis showed increased HbF and HbA2 fractions. Abdominal Ultrasound showed cholelithiasis. The patient performed laparoscopic cholecystectomy and was successful.

**Discussion:** Cholelithiasis is often found in thalassemia intermedia complications. Regular ultrasound examination in  $\beta$ -Thalassemia is used to detect cholelithiasis.

**Conclusion:** Clinical pathology analysis supports the diagnosis of cholelithiasis in the  $\beta$ -Thalassemia patient.

## 1. Introduction

Thalassemia is a heterogeneous grouping of genetic disorders that result from a decreased synthesis of alpha or beta chains of hemoglobin (Hb) [1,2]. It was reported that the number of cases of thalassemia was 4.4 : 10,000 live births [3]. Complications of thalassemia included hepatomegaly, splenomegaly, pulmonary hypertension, and anemia due to ineffective hemolysis and erythropoiesis [4]. One of the most common complications in thalassemia cases is cholelithiasis which is reported in 10–57% of thalassemia patients [5]. The aimed to report an Indonesian adolescent with  $\beta$ -thalassemia and cholelithiasis. We report based on SCARE 2020 guidelines [6].

## 2. Case presentation

An Indonesian adolescent, 18 years old, complained of abdominal pain for 1-day, intermittent pain, can't defecate for 7 days, can't fart, and low intake of food. The patient consumed microleak but couldn't defecate. Medical history showed the patient was diagnosed with thalassemia 13 years ago and had routine medical checkups and

transfusions. Physical examination showed pale conjunctiva (+/+), splenomegaly, and abdominal tenderness. Hematology laboratory investigation showed Hb (4.2 g/dL), RBC ( $2.14 \times 10^6/\mu\text{L}$ ), Hct (12.8%), MCV (59.8 fl), MCH (19.6 pg), and MCHC (32.8 g/L). Peripheral blood smear examination revealed hypochromic macrocytic anemia, anisopoikilocytosis, and leukocytosis with immature granulocytes (Fig. 1).

The patient also underwent a clinical chemical laboratory investigation, which showed BUN of 5 mg/dL, AST of 67 IU/L, ALT of IU/L, Na of 135 mmol/L, Direct bilirubin of 0.35 mg/dL, and triglyceride of 211 mg/dL. Urinalysis laboratory showed protein (+1), bilirubin (+1), albumin/creatinine ( $\geq 300$  mg/GCR), and protein/creatinine (0.3 g/GCR). The hemoglobin electrophoresis results showed a decrease in the HbA fraction and an increase in the HbF, HbG, and HbA2 fractions (Fig. 2). Radiological examination showed abdominal X-ray showed splenomegaly, and abdominal Ultrasound showed cholelithiasis with sludge in bile.

The patient performed laparoscopic cholecystectomy and was successful. The patient and family are recommended to do a blood examination once a month or if the patient has signs of anemia such as paleness when outpatient. If Hb shows a decrease, PRC will be carried

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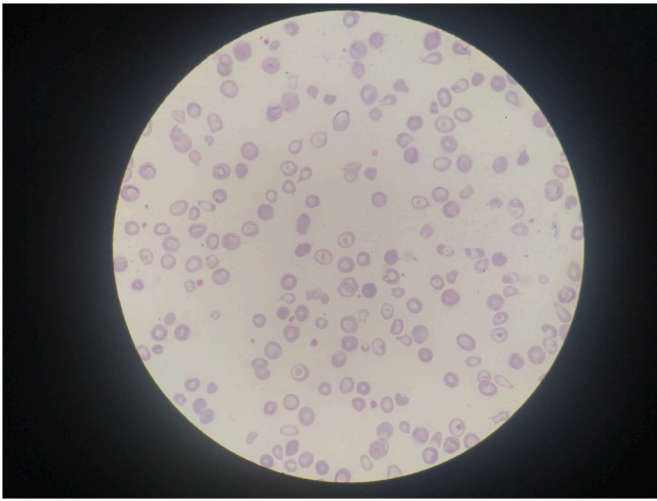
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**Fig. 1.** The microscopic picture of 1000 $\times$  magnification of the patient's peripheral blood smear showed an image of erythrocytes with the formation of target cells and teardrop cells.

out again.

### 3. Discussion

The mechanism of anemia in patients with  $\beta$ -thalassemia occurs due to the loss of beta chains and excess alpha chains that make them unstable and precipitate, causing damage to red blood cell membranes. In addition, anemia in  $\beta$ -thalassemia patients is due to the short erythrocyte life span due to hemolysis and premature death of erythroid precursors in the bone marrow [7,8]. No treatment can cure thalassemia intermedia. Blood transfusion every 2–4 weeks is the only therapy for anemia in thalassemia patients. This continuous transfusion can result in iron overload in many organs, such as the heart, liver, kidneys, endocrine organs and others. The accumulation of free iron (ferrous iron/ $\text{Fe}^{2+}$ ) can cause a Fenton reaction that forms free radicals, causing oxidative stress, which will oxidize cell lipid membranes (lipid peroxidation) and nucleic acid modification, causing cell death, tissue damage and ultimately organ damage [9–11].

Complications of cholelithiasis are more common in thalassemia

intermedia than in thalassemia major due to the ineffectiveness of erythropoiesis and the occurrence of peripheral hemolysis [4,12,13]. Gallstones in hemolytic anemia are often referred to as stones with black pigment. The content of the black pigment is a cross-linked network polymer bilirubin. Moreover, about 40–80% have a radiopaque appearance. Approximately 55–63% of patients with thalassemia intermedia suffer from gallstones. In patients with  $\beta$ -thalassemia, an ultrasound examination should be performed to detect gallstones [5,14,15].

The prevalence of cholelithiasis is higher in thalassemia intermedia compared to thalassemia major. Bilirubin production is increased due to the destruction of red blood cells during blood transfusion and partly because of ineffective erythropoiesis. The high transfusion regimen can prevent residual ineffective erythropoiesis resulting in decreased bilirubin production. Ineffective erythropoiesis and peripheral hemolysis, resulting in increased bilirubin production, are why the prevalence of cholelithiasis is higher in thalassemia intermedia compared to primary thalassemia patients [4,5,16].

The limitation of the case is the lack of a complete iron profile examination which includes ferritin and Prussian blue bone marrow aspirants staining [2].

### 4. Conclusion

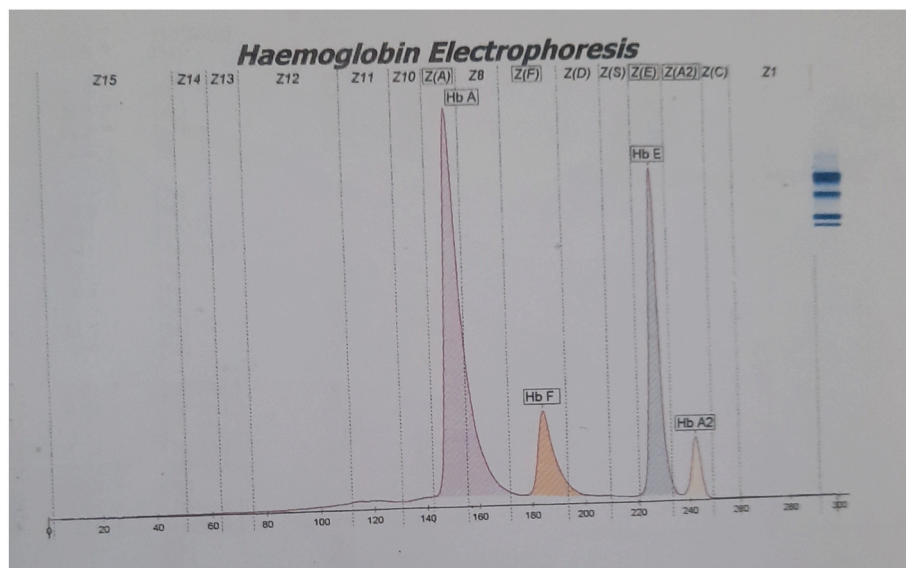
Complications of cholelithiasis are more common in thalassemia intermedia than in thalassemia major. In patients with  $\beta$ -thalassemia, an ultrasound examination should be performed to detect the presence of gallstones. Urinalysis examination is critical to determine the complications of albuminuria in thalassemia patients. When outpatient, the patient and family are recommended to do a blood examination once a month or if the patient has signs of anemia such as paleness.

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Not applicable.

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**Fig. 2.** Hemoglobin electrophoresis showed decreased Hb A fraction, increased Hb F, Hb E and Hb A2 fractions.

## Author contribution

All authors contributed toward data analysis, drafting and revising the paper, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

## Trial registry number

1. Name of the registry:-
2. Unique Identifying number or registration ID:-
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):-

## Guarantor

Muhamad Robi'ul Fuadi is the person in charge of the publication of our manuscript.

## Consent

Written informed consent was obtained from the patient's parent or guardian for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

## Declaration of competing interest

Muhammad Bintang Maulana and Muhamad Robi'ul Fuadi declare that they have no conflict of interest.

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