Case report

Massive pleural effusion as a presentation of extramedullary hematopoiesis among patients with non transfusion dependent beta-thalassemia

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Abstract:

Thalassemia is one of the most common hemoglobinopathies. Beta-thalassemia results from a decreased or absent production of the beta-globin chain of hemoglobin. Extramedullary hematopoiesis (EMH) is one of the complications of beta-thalassemia, primarily seen among non transfusion dependent patients. EMH predominately occurs in the spleen, liver and lymph nodes but has been reported in almost all organs. Despite this, EMH is rare regarding presented with serous effusions. We present a case report of EMH occurring in the pleura with pleural effusion in a patient with beta thalassemia together with discussion of the diagnostic approaches and treatment implications.

Keywords : ● *Thalassemia* ● *Extramedullary hematopoiesis* ● *Pleural effusion*

J Hematol Transfus Med. 2024;34:133-8.

Received 11 February 2024 Corrected 13 February 2024 Accepted 31 May 2024

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รายงานผู้ป่วย

ภาวะน้ำในเยื่อหุ้มปอดปริมาณมากเนื่องจากการสร้างเม็ดเลือดนอกไขกระดูกในผู้ป่วยเบต้าธาลัสซีเมียชนิดไม่พึ่งพาเลือด

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หน่วยโลหิตวิทยา ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

บทคัดย่อ

ธาลัสซีเมียเป็นโรคทางพันธุกรรมที่ทำให้เกิดความผิดปกติของฮีโมโกลบินที่พบบ่อยที่สุด เบต้าธาลัสซีเมียเกิดจากการสร้างสายเบต้าโกลบินของฮีโมโกลบินลดลงหรือไม่สร้างเลย การสร้างเม็ดเลือดนอกไขกระดูก (extramedullary hematopoiesis, EMH) เป็นภาวะแทรกซ้อนของโรคเบต้าธาลัสซีเมียอย่างหนึ่งซึ่งพบในผู้ป่วยธาลัสซีเมียชนิดไม่พึ่งพาเลือดเป็นหลัก ภาวะ EMH พบได้บ่อยที่ ม้าม ตับ ต่อมน้ำเหลือง แต่ก็มีรายงานพบได้เกือบทุกอวัยวะ อย่างไรก็ตาม EMH พบได้น้อยมากที่มาด้วยน้ำในเยื่อหุ้มอวัยวะภายใน (serous effusion) ผู้นิพนธ์ได้รายงานผู้ป่วยเบต้าธาลัสซีเมียที่มาด้วย EMH ซึ่งเกิดขึ้นที่เยื่อหุ้มปอดและมีน้ำในเยื่อหุ้มปอด รวมทั้งได้อภิปรายเกี่ยวกับการวินิจฉัยและการประยุกต์การรักษา

คำสำคัญ : ● *ธาลัสซีเมีย* ● *การสร้างเม็ดเลือดนอกไขกระดูก* ● *น้ำในเยื่อหุ้มปอด*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2567;34:133-8.

Introductions

Thalassemia is one of the most common hemoglobinopathies with around 5% of world's population expected to have some degree and type of thalassemia[1]. Beta-thalassemia results from a deficient production of the beta-globin chain of hemoglobin (Hb). Beta-thalassemia is classified in minor, intermediate and major, defined by their severity of clinical and laboratory findings. Extramedullary hematopoiesis (EMH) is one of the complications of beta-thalassemia, primarily seen in intermedia subtype or patients with nontransfusion-dependent thalassemia (NTDT)[1-3]. EMH is the proliferation of hematopoietic tissue outside the bone marrow as a compensatory response to longstanding hypoxia. It predominately occurs in the spleen, liver and lymph nodes but has been reported in almost all organs[1,3,4]. Despite this, EMH is rare regarding presenting serous effusions[5].

EMH tends to be microscopic and asymptomatic but may become large enough to cause organomegaly or a tumor-like mass, which can be detected by roentgenography or computed tomography[1-3]. Intrathoracic EMH may manifest as a mass, especially in the posterior mediastinum but rarely in the anterior mediastinum. Other cases of intrathoracic EMH may manifest as a diffuse interstitial pulmonary process in conjunction with dyspnea[1]. We present a case of beta-thalassemia with a massive pleural effusion resulting from pleural-based intrathoracic EMH with discussion of the diagnostic approaches, and treatment implications.

Report of case

Patient Data: A 38-year-old male with beta-thalassemia/HbE disease (NTDT), unknown beta-gene mutation, received a diagnosis at the age of 10. The patient had never received a blood transfusion, and his baseline Hb level was 7.5 to 8 g/dL. Current medication was folic 5 mg once daily.

Chief complaint: Progressive dyspnea for one month.

Present illness:

One month before visiting the hospital, the patient developed dyspnea, particularly during exertion and coughing. He could lie down normally, and he had whitish nonpurulent sputum. He presented no fever, sore throat, nasal discharge or weight loss.

Two weeks before visiting the hospital, the patient developed more severe dyspnea. While staying inactive, the patient felt tired. The patient also reported chest pain on the right side while breathing.

The patient denied any history of COVID-19 and reported a history of recent COVID-19 vaccinations one year ago before developing dyspneic symptoms. He denied a history of cancer as well as immune-deficiency disease. The patient denied a history of consuming alcohol, smoking, using herbal medicine or illicit drug, and he practiced protected sexual activity.

Physical examination:

Vital signs: BT 37.0°C, PR 110/min, RR 26/min, BP 106/67 mmHg, SpO_2 98% (room air)

GA: A male with good consciousness, no thalassemic face

Skin: No rash, no skin nodules

HEENT: Moderately pale, no jaundice

Lymph nodes: No lymph node enlargement

CVS: Systolic ejection murmurs grade III all valvular area, regular pulse

Lungs: Decreased breath sound, dullness on percussion, and reduced vocal resonance at right lower lung filed, no trachea shift, no subcutaneous emphysema

Abdomen: Soft, no distension, no tenderness, spleen can be palpated 8 cm below LCM, liver span 12 cm

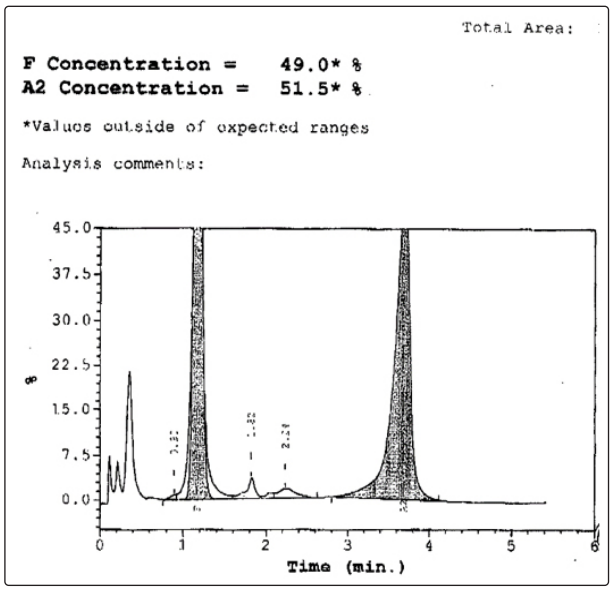
Extremities: No edema, no clubbing fingers

Neurological system: Motor, sensory and deep tendon reflex were grossly intact

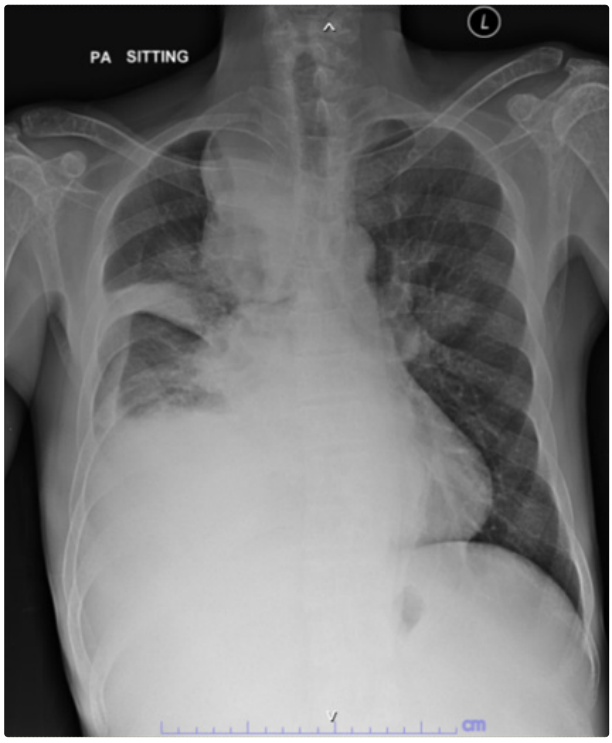
Laboratory data:

CBC: Hb 7.5 g/dL, Hct 21.5%, MCV 63 fL, MCH 20.8 pg, MCHC 33.2 g/dL, RDW 32.3%, WBC 4,520/μL (neutrophil 45.3%, lymphocyte 51.6%), platelet count 153,000/μL

Hb typing: (Figure 1)



Chest film: (Figure 2)



CT chest included upper abdomen with contrast:

- Multiple heterogeneous enhancing masses in both paravertebral regions and anterior ribs up to 12.5 cm, without significantly enlarged mediastinal nor hilar nodes.

- Large amount of right pleural effusion with mild thin enhancement of the pleura, no pleural nodule.

- Marked hepatosplenomegaly

Pleural fluid profile: Appearance: cloudy and serosanguinous, glucose 105 mg/dL, total protein 3.3 g/dL, albumin 1.9 g/dL, LDH 136 U/L (Light's criteria: protein ratio 0.68, LDH ratio 0.58, interpretation as exudative profile), WBC 714 cells/μL (PMN 9%, Monocyte 91%), RBC 78,000 cells/μL, PCR for tuberculosis/nontuberculous mycobacteria (TB/NTM): negative, culture for bacteria and TB: negative, cytology: negative for malignancy, few mesothelial cells and scattered mononuclear inflammatory cells among dilute bloody background.

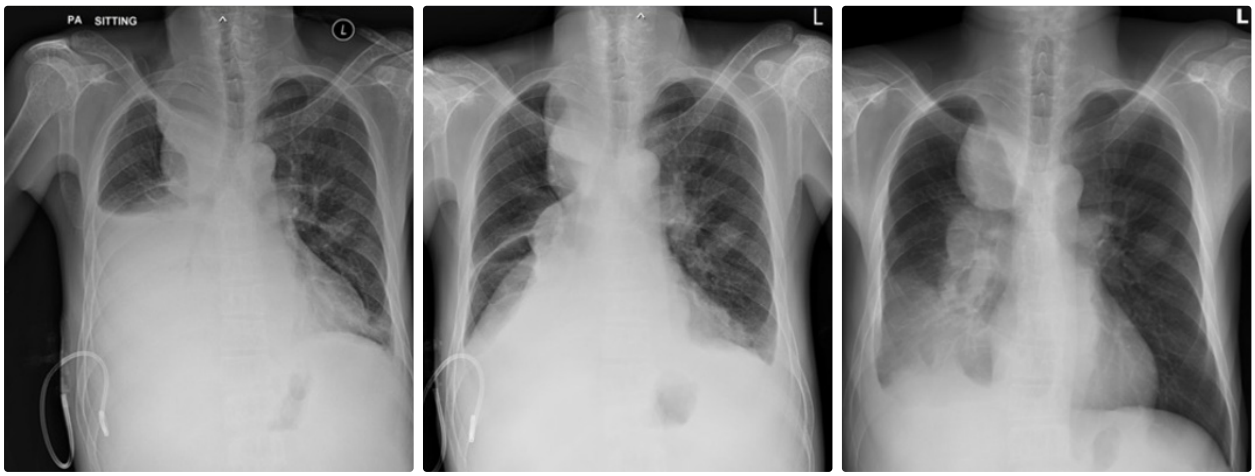
Clinical chemistry: BUN 11 mg/dL (6 to 20), creatinine 0.57 mg/dL (0.6 to 1.1), total protein 4.8 g/dL (6.6 to 8.7), albumin 2.5 g/dL (3.5 to 5.2), globulin 2.3 g/dL (3.1 to 3.5), total bilirubin 1.77 mg/dL (0.0 to 1.2), direct bilirubin 0.68 mg/dL (< 0.3), AST (SGOT) 21 U/L (0 to 40), ALT (SGPT) 25 U/L (0 to 41), alkaline phosphatase (ALP) 56 U/L (40 to 129), ferritin 1,996 ng/mL (300 to 400) and LDH 233 U/L (140 to 220).

Diagnosis and treatment:

The diagnosis of this patient was beta-thalassemia/HbE disease (NTDT) with EMH with right massive pleural effusion. The cause for pleural effusion was likely from EMH which are commonly found among patients with thalassemia intermedia or NTDT and other causes of pleural effusion such as TB and malignancy were excluded.

After diagnosis, treatment consisted of regular blood transfusion aimed for hemoglobin (Hb) target of 9-10 g/dL to decrease further EMH as well as iron chelation therapy. Thoracentesis and percutaneous catheter drainage (PCD) for pleural effusion were also required. A radiotherapist was consulted to perform radiation therapy at the right pleura (dose 2 Gy for 6 fractions). After radiotherapy, pleural effusion was decreased and his symptoms improved. However, his chest film showed recurrent right pleural effusion. The thoracic surgeon was also consulted for additional video-assisted thoracic surgery (VATS) with talc pleurodesis (Figure 3). After the treatment, the patient's condition was monitored on a monthly basis for one year. The symptoms of dyspnea disappeared, and he was able to return to work, to live his daily live as usual and he regularly received blood transfusions with no recurrence of pleural effusion.

Chest films show progression after treatment: (Figure 3)



S/P PCD Rt basal chest S/P Radiation S/P Tale pleurodesis Rt lung

Discussion

EMH is hematopoiesis occurs in organs other than bone marrow that constitutes a compensatory response to ineffective production of hematologic cells in various conditions including thalassemia[1-4]. Therefore, the prevalence of EMH is higher in NTDT than transfusion dependent thalassemia (TDT)[1-3]. EMH can develop in many organs, most commonly the spleen and liver, but rarely included in the list of possible causes of pleural effusion[5-8].

Most cases of EMH-related pleural effusion are reported among patients with NTDT. These patients presented unilateral pleural effusion, started blood transfusions after the age of 15 years and mean Hb level was 9.02 ±0.82 g/dL (6.5 to 8.1 g/dL)[7].

Pleural fluid profile in EMH usually showed clear gross appearance and exudative profile. It usually indicated quite low white blood cell count with lymphocyte predominance, glucose more than 60 mg/dL, low protein, high lactate dehydrogenase (LDH) and pH tended to be alkaline. Cytologic fluid analysis was negative for malignancy, while fluid cultures and staining were negative for bacteria and TB. Mesothelial cells can be present in pleural fluid, while myeloid elements were absent[7]. This patient received a diagnosis of beta thalassemia/HbE disease, NTDT, with massive right pleural effusion. The pleural fluid profile was exudative with lymphocyte predominance. Moreover, fluid culture and staining were negative, cytologic fluid analysis for malignancy was negative and the patient had few mesothelial cells. Overall, pleural fluid profile in this case report was consistent with the related study except the cloudy and serosanguinous appearance that might have occurred from traumatic tapping.

Regarding management, only thoracentesis could not control the effusion as fluid that accumulated rapidly. Repeated thoracentesis and pleurodesis were required[7]. Regular blood transfusion, hydroxyurea and radiotherapy were also used in EMH-related pleural effusion[7,8]. Treatments for this patient included blood transfusion, thoracocentesis and PCD, concurrent with radiotherapy and pleurodesis. After the treatment, the patient still received regular blood transfusion and he had no recurrent pleural effusion during follow-up.

Conclusion

EMH-related pleural effusion is a rare form of EMH that usually involves unilateral pleural effusion. The pleural fluid shows a lymphocyte predominance exudative profile with is negative for malignancy and culture. The treatment of EMH-related pleural effusion requires multidisciplinary approach including blood transfusion, thoracentesis, radiotherapy and pleurodesis.

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