DE GRUYTER
OPEN

DOI: 10.1515/dch-2015-0003

Clinical case of Aplastic Crisis associated with Extramedullary Hematopoiesis in an adult with Hereditary Spherocytosis and Parvovirus B19 Infection

Andreea Jercan*, Rusu Munteanu Gina, Camelia Dobrea, Daniel Coriu, Aurelia Tatic
Center of Hematology and Bone Marrow Transplant, Fundeni Clinical Institute, Bucharest, Romania

Abstract:

Hereditary spherocytosis is an inherited hemolytic anemia due to red cell membrane defects, characterised by chronic hemolysis with different severity degrees, splenomegaly and microspherocytosis on the peripheral blood film.

Among the possible complications in these patients are aplastic crisis and extramedullary hematopoiesis.

In this article we present the case of a 42 years old man with hereditary spherocytosis diagnosed during childhood (average haemoglobin (Hb) value of 11-12 g/dl), which presented with worsening anemia, fever, chills, bone and muscle pain. The evolution was with accentuation of anemia (Hb 4.2 g/dl), decease of reticulocyte number (Ret 0,8%) and bilirubin (indirect bilirubin 2.7 g/dl). ParvovirusB19 DNA was 100.000.000 copies/ml. A computer tomography (CT)scan was performed and showed extramedullary hematopoiesis areas situated paravertebraly in the inferior thorax and hepatosplenomegaly.The infectious episode was self-limited and improved with substitution treatment.

Key Words:
Spherocytosis, aplastic crisis, extramedullary hematopoiesis, Parvovirus B19 infection.

***Corresponding author**: Jercan Andreea, Department of Hematology, Fundeni Clinical Institute, Sos. Fundeni nr. 258, sector 2, Bucharest, Romania, phone:+40761612450, e-mail:je.andreea@gmail.com*

Introduction

Hereditary spherocitosis is an inherited hemolytic anemia characterized by a red cell membrane defect, increased number of reticulocytes, increased MCHC (mean corpuscular hemoglobin concentration) index, presence of microspherocites on the peripheral blood smear, intermittent jaundice, splenomegaly and abnormal osmotic fragility test.[1]

Among it's complications there are worsening anemia, wich can be secondary to the accentuation of hemolysis due to unspecific viral infections (low Hb, high Ret,highbilirubin (Br)), aplastic crysis in Parvovirus B19 infection (low Hb(suddenly), low Ret, low Br) and folatedepletion secondary to accelerated hematopoiesis. Other complications can be cholelithiasis and extramedullary hematopoiesis.

Parvovirus B19 infection is global, it is more common in childhood and is transmitted respiratory. In temperate areas, the infection usually occurs in spring and in small outbreaks every few years.[2]

In general, Parvovirus B19 infection is asymptomatic. The most common presentation of the infection is infectious erythema ("fifth disease"), a childhood exanthema characterized by "slapped cheeks".[2]

It has two phases, initially with flu-like symptoms (viraemia phase), followed by, when the immune complexes are formed, the rash (rarely seen in adults) and the arthropathy (arthralgia and even arthritis, mimicking rheumatoid arthritis, that resolves in a few weeks).[2]

Case Presentation

A 42 years old male, with mild hereditary spherocytosis, diagnosed during childhood, with a family history of hereditary spherocytosis (daughter), presents to the territorial hospital in March 2013 for fever, chills, vomiting, myalgia. Lab tests showed anemia (Hb 7.1 g/dl), indirect bilirubin 6,7 mg/dl, heterogenous splenomegaly (ultrasonography) and hepatocytolisis.

He was sent to our Clinic for diagnosis and treatment, with an average general status, pallor, jaundice, splenomegaly and flu-like symptoms. The lab tests show worsening anemia (Hb 6.1 g/dl, Ht 16.8%, Ret 3.8%, MCV(mean corpuscular volume) 83 fl, MCH (mean corpuscular hemoglobin) 30,3pg, MCHC (mean corpuscular hemoglobin concentration) 36.6 g/dl), L (leukococytes) 8600/mmc, PLT (platelets) 164000/mmc, with microspherocytes on the peripheral blood smear. The indirect bilirubin was lower (from 6.7 to 5.2 mg/dl) and the hepatocytolisis persisted.

We performed a viral screening test for HBV (hepatitis B virus), HCV (hepatitis C virus), HIV (human immunodeficiency virus), EBV (Epstein–Barr virus) and CMV (cytomegalovirus), and it was negative.

Abdomino-pelvine ultrasound: homogeneous hepatomegaly (18.4 cm), heterogeneous splenomegaly (20 cm) with hiperechoicsubcapsular area in the upper 1/3 (52/45 mm), gallbladder without stones.

The chest radiography ***(Fig. 1)*** sowed no infection, but instead highlighted the polycyclic appearance of the pulmonary hilum, that required superior imaging.

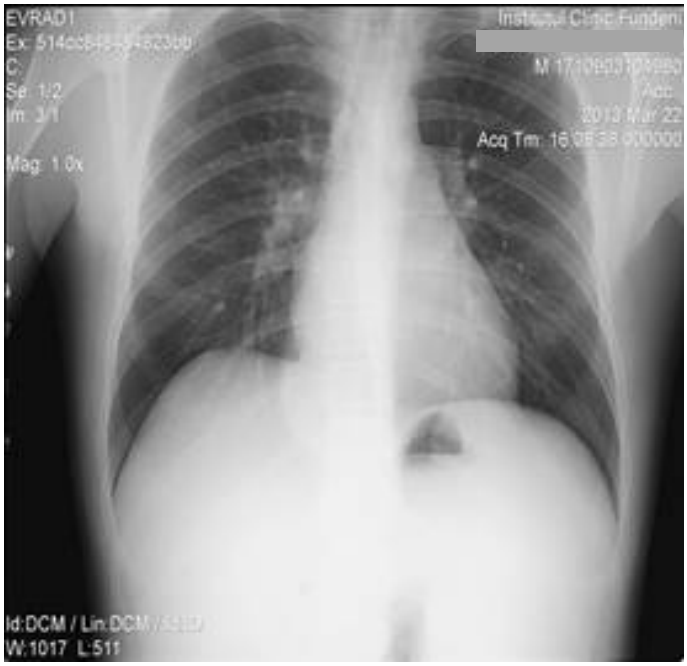


Fig.1 Chest radiography: polyciclyc pulmonary hilum (Dr. RusuMunteanu Gina, Fundeni Clinical Institute)

Radiographic appearance and the patient's symptoms (worsening back pain), imposed performing a CT scan ***(Fig. 2 and 3)***, which described a dense mass of tissue disposed paravertebraly in the lower thorax, with maximum size of 44/23 mm (to the right). These lesions were interpreted asextramedullary hematopoiesis areas.

Given the hepatomegaly and the heterogenous splenomegaly, we performed an abdominal-pelvic CT scan that showed homogenous hepatomegaly (22 cm), without dilated biliary tree and important polilobated splenomegaly (23 cm).

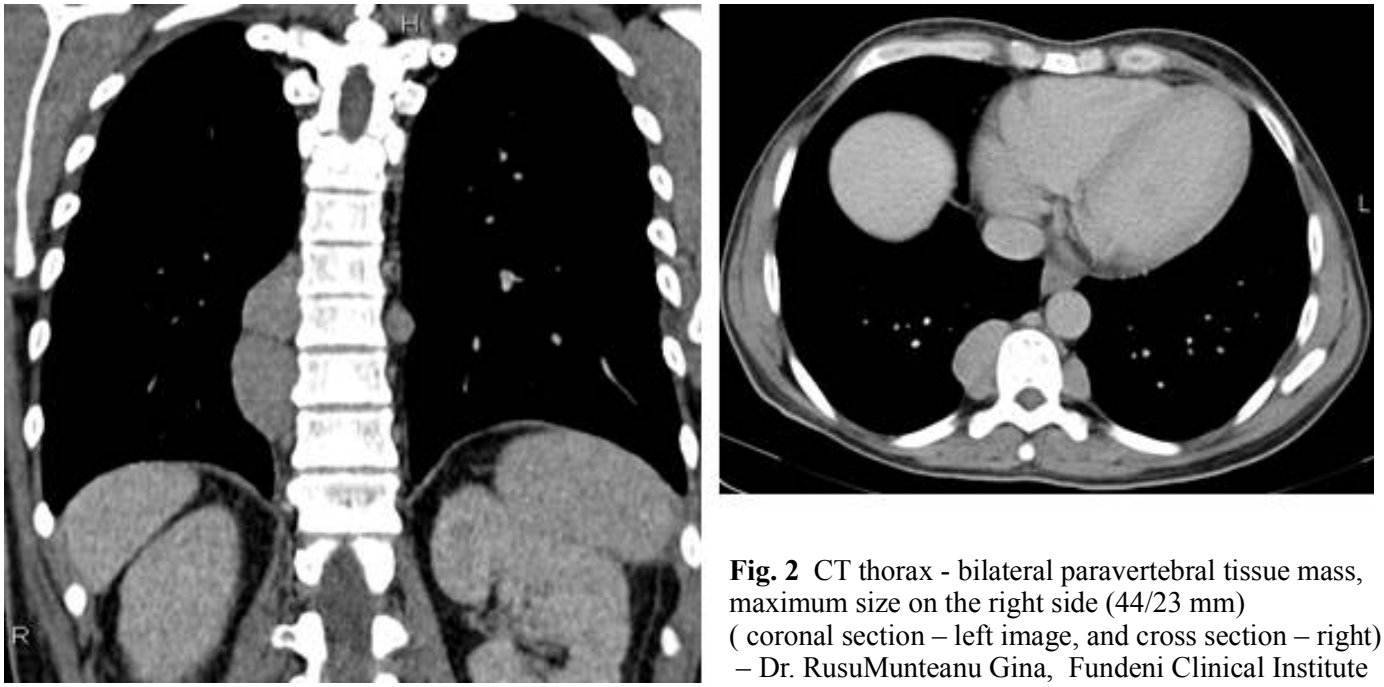


Fig. 2 CT thorax - bilateral paravertebral tissue mass, maximum size on the right side (44/23 mm)
(coronal section – left image, and cross section – right)
– Dr. RusuMunteanu Gina, Fundeni Clinical Institute

The evolution was with decreasing jaundice (indirect bilirubin reached 2.7 mg/dl), impaired general status, increased anemia (Hb reached 4.2 g/dl) and marked decrease in reticulocytes (0.8%)

Considering the severe and sudden anemia associated with decreased reticulocyte count and bilirubin, we rised the

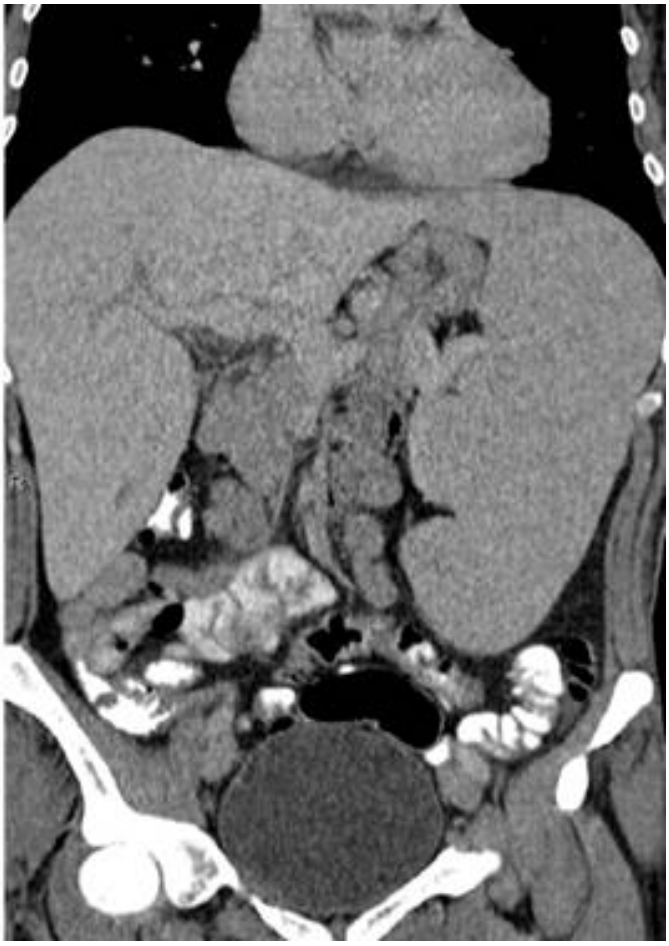
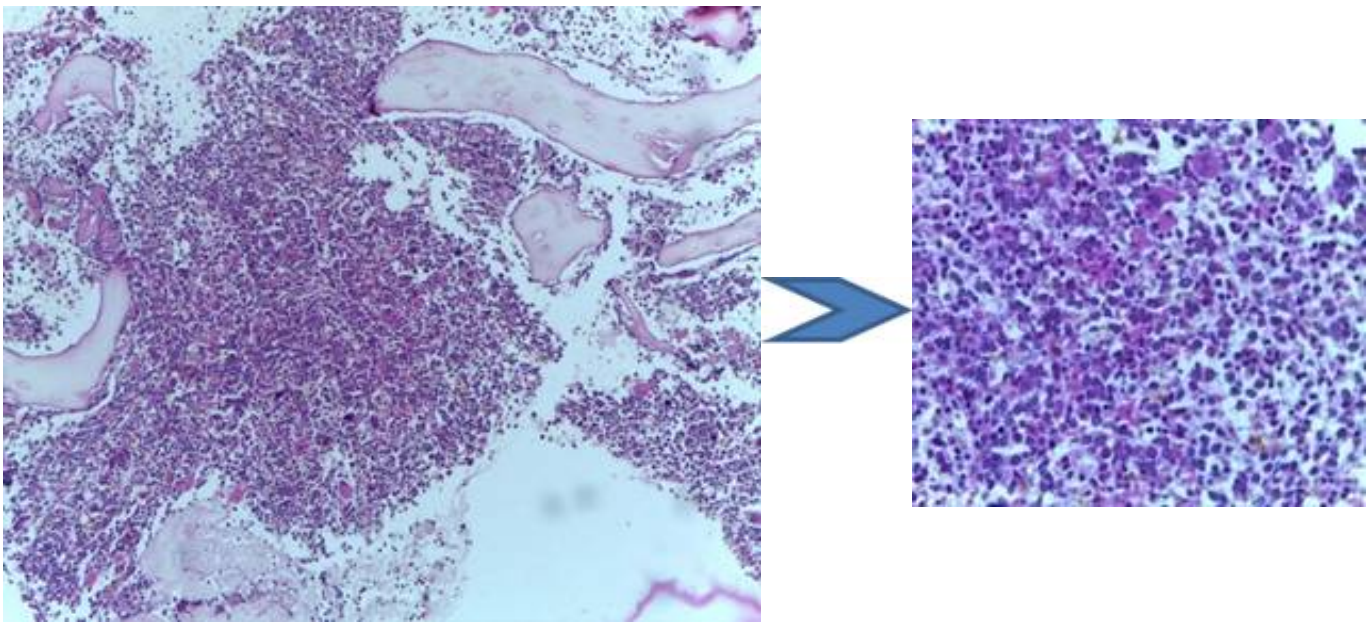


Fig. 3 Abd-pelvicCT scan, coronal section – hepatosplenomegaly, polilobated spleen (Dr. RusuMunteanu Gina, Fundeni Clinical Institute)

suspicion of aplastic crisis, so we performed a bone marrow analysis (9 days after the onset of the symptoms), which, however, showedhypercellularity with increased percentage of erythroblastic series – megaloblastoid appearance. **(Fig. 4)**
Parvovirus B19 DNA was 100.000.000 copies/ml – 8 days after the onset of the symptoms.

Fig. 4 Bone marrow biopsy–Hypercelulary marrow, macromegaloblastosis (Dr. CameliaDobrea, Fundeni Clinical Institute)



We established the diagnosis of aplastic crisis secondary to Parvovirus B19 infection in an adult with Hereditary Spherocitosis and localized paravertebral extramedullary hematopoiesis.

We treated with blood transfusions, folic acid and liver protectors (considering the associated hepatocytolisis).

The response to the conservatory treatment was with the improvement of the anemia, two weeks after the onset, the hemoglobin reached 9.4 g/dl and Ret 10%.

He was evaluated 3 months after the infectious episode, and the hemoglobin was 10 g/dl. The hepatocytolisis resolved, Parvovirus B19 was undetectable and the CT scan showed a slight regression of the hepatosplenomegaly and persistent extramedullary hematopoiesis areas.

Discussion

Parvovirus B19 infection in adults.

The acute Parvovirus B19 infection usually occurs in children who develop the classical symptoms of "slapped cheeks". In our case, the patient avoided the infectious contact during childhood, so he didn't develop immunity against the virus, which led to acute infection at age 42, complicated with transient aplastic crisis.[2]

Transient aplastic crisis

Accentuated anemia associated with decreased reticulocyte count (secondary to erythropoietic-maturationarrest) andlowerindirect bilirubin (reduced number of red blood cells that can be destroyed) is typical in aplastic crisis.

Transient aplastic crisis is usually a unique life event, suggesting the induction of a lasting immune response. Although self-limited, the aplastic crises can cause severe, occasionally fatal anemia, which can precipitate congestive heart failure or stroke. The bone marrow is characterized by the absence of erythroid maturation and the presence of gigantic pronormoblasts (pathognomonic cells resulted from the cytopathic effect of Parvovirus B19). Leukocytes and platelets may decrease slightly during the aplastic crisis, especially in patients with functional spleen. Parvovirus B19 may precipitate hemophagocytic syndrome usually with a favorable evolution.[2]

Our patient developed transient aplastic crisis (Hb 4 g/dl, indirect bilirubin 2.7 mg/dl, Ret 0.8 %) self-limited with supportive treatment (red blood cells transfusion, folic acid).

Extramedullary hematopoiesis

Extramedullary hematopoiesis lesions represent a rare complication in patients with hereditary spherocytosis. In children, it can cause growth deficiency, bone marrow expansion and skeletal deformities. It seems that chronic stimulation by high levels of erythropoietin, secondary to ineffective hematopoiesis, is the cause for the extramedullary hematopoiesis. There are some cases reported of extramedullary hematopoiesis in adults without splenectomy. There are cases of extramedullary hematopoiesis in the mediastinum3-7, pelvic area8 and of massive hemothorax due to intrathoracicextra-medullary hematopoiesis[9].

Our patient shows paravertebral extramedullary hematopoiesis lesions that persisted at the 3 months reevaluation after the acute infectious episode.

Splenectomy indication

We take into discussion the opportunity of splenectomy. Our patient has mild anemia, without transfusion requirement, but with important splenomegaly and persistent extramedullary hematopoiesis lesions.

There are no published data on the optimal moment of splenectomy in hereditary spherocitosis. All important texts specify that the splenectomy indication depends on the clinical judgment and the severity of the symptoms (effects of anemia, transfusion requirement, cholelithiasis).[1]

Most patients with hereditary spherocitosis have mild-medium splenomegaly, with no clinical significance. Spleen size is no indication for splenectomy. There are no clinical evidence that in this case spleen rupture is more common than in the general population.[10]

Splenectomy is very effective in reducing haemolysis, causing a significant prolongation of red blood cells life span. Complications (anemia and cholelithiasis) are greatly reduced in severe forms and even abolished in mild forms, but with the increased risk of infections with encapsulated microorganisms (especially Streptoccocus).[10]

There is a published case of extramedullary hematopoiesis in a patient with hereditary spherocitosis with regression of the lesion following splenectomy.[8]

Conclusion: Parvovirus B19 infection could be a cause for aggravation of the anemia in patients with hereditary hemolytic anemias.

Conflict of interest: Authors state no conflict of interest

REFERENCES:

1. P. H. B. Bolton-Maggs, R. F. Stevens, N. J. Dodd, G. Lamont, P. Tittensor and M. J. King, "Guidelines for the diagnosis and management of hereditary spherocytosis", British Journal of Haematology, 126: 455–474, 2004.

2. N. S. Young, K. Brown "Mecanism of disease Parvovirus B19", NEJM, 350:586-97, 2004.

3. H. Mulder, J.T.Schlangen,A.E.vanVoorthuisen, "Extramedullary hematopoiesis in the posterior

mediastinum", RadiolClin (Basel), 44(6):550-6, 1975.
4. J.J. Petit, C. Estany,"Mediastinalextramedullary erythropoiesis in hereditary spherocytosis.",Clin Lab Haematol., 9(3):327-32, 1987.
5. Y. Bastion, B. Coiffier, P. Felman, D. Assouline, J.D. Tigaud, D. Espinouse,P. A. Bryon, "Massive mediastinalextramedullary hematopoiesis in hereditary spherocytosis: a case report.", Am J Hematol.,35(4):263-5, 1990 Dec.
6. A. Pulsoni, G. Ferrazza, F. Malagnino, L. Maurillo, E. Pescarmona, A. Picardi, E.A. Rendina, S. Amadori, "Mediastinalextramedullary hematopoiesis as first manifestation of hereditary spherocytosis." Ann Hematol., 65(4):196-8, 1992 Oct.
7. N. Xiros, T. Economopoulos, E. Papageorgiou, G. Mantzios, S. Raptis, "Massive hemothorax due to intrathoracicextramedullary hematopoiesis in a patient with hereditary spherocytosis.", Ann Hematol., 80(1):38-40, 2001 Jan.
8. C. D. Sutton, G. Garcea, L.J. Marshall, T.D. Lloyd, C. De Alwis, M.H. Lewis, "Pelvic extramedullaryhaematopoiesis associated with hereditary spherocytosis.",Eur J Haematol., 70(5):326-9, 2003 May.
9. E. Granjo, R. Bauerle, R. Sampaio, P. Manata, N. Torres, A. Quintanilha, "Extramedullary hematopoiesis in hereditary spherocytosis deficient in ankyrin: a case report.", Int J Hematol., 76(2):153-6, 2002 Aug.
10. P. Bolton-Maggs, J. Langer, A. Iolascon, P. Tittensor, M. J. King, "Guidelines for the Diagnosis and Management of Hereditary Spherocytosis"; The British Committee for Standards in Haematology, September 2011