Haematologica 2000; 85:1211-1213
case of the month

Stem Cell Disorders

Isolated spleen agenesis: a rare cause of thrombocytosis mimicking essential thrombocythemia

VALÉRIE CHANET,* OLIVIER TOURNILHAC,* VALÉRIE DIEU-BELLAMY,° NATHALIE BOIRET,° PHILIPPE SPITZ,° OLIVIER BAUD,* CLAUDE DARCHA,# PHILIPPE TRAVADE*, HENRI LAURICHESSE*

**Fédération des Maladies Infectieuses, Médecine interne et Hématologie Adultes ,°Laboratoire Central d'Hématologie, #Laboratoire d'Anatomie Pathologique; °Service de Radiologie, Hôpital Hôtel Dieu, Clermont-Ferrand, France*

ABSTRACT

Thrombocytosis is a common feature of myeloproliferative disorders but may also result from various conditions including chronic iron deficiency, hemorrhage, chronic inflammation and splenectomy. We report two cases of secondary thrombocytosis caused by isolated and congenital asplenia, mimicking essential thrombocythemia. These two adult cases of spleen agenesis were unexpected. We conclude that in thrombocytosis without clinical evidence of splenomegaly, attentive screening of blood in search of Howell-Jolly bodies and abdominal ultrasonography should always be performed not only to detect mild spleen enlargement but also to make sure of the presence of this organ.

Key words: asplenia, thrombocytosis, essential thrombocythemia

Thrombocytosis, a frequent blood cell anomaly, is a consequence of chronic iron deficiency, hemorrhage, chronic inflammation and splenectomy. Thrombocytosis can also result from blood cell dyscrasias reflecting hematologic malignancies including myeloproliferative disorders: essential thrombocythemia (ET), chronic myelocytic leukemia, polycythemia vera, and agnogenic myeloid metaplasia. In the absence of specific cytogenetic or molecular markers, the diagnosis of ET is supported by the lack of other causes of thrombocytosis. We report two cases of sustained and isolated thrombocytosis mimicking ET but due to an apparently constitutional absence of spleen.

Case Reports

Case #1

A 56-year old woman was referred in 1986 for diagnosis and treatment of generalized eczema with mild eosinophilia. She had a history of hysterectomy and ovariectomy for myofibroma, and extra-membranous glomerulonephritis 11 years earlier. Her full blood count was as follows: hemoglobin, 129 g/L; hematocrit, 42.6%, mean cell volume, 86 fL; white blood cells, 11.7x10^9/L; neutrophils, 52%; eosinophils, 8%; lymphocytes, 34%; monocytes, 9%; platelets, 890.0x10^9/L. Clinical examination was normal except skin involvement. Erythrocyte sedimentation rate, fibrinogen and serum iron concentration were in the normal ranges. Leukocytosis, eosinophilia and eczema disappeared but sustained thrombocytosis persisted. Bone marrow trephine biopsy was normal, showing a normal number of megakaryocytes of normal size and no myelofibrosis. There were Howell-Jolly bodies (H-JB) on the blood smear (0.5% of erythrocytes). The spleen was not visible by abdominal ultrasonography and tomodensitometry. No functioning splenic tissue was detected by scintigraphy using ^{99m}Tc-labeled red cells (Figure 1). No treatment was given. She developed diabetes mellitus and lymph node sarcoidosis respectively 8 and 10 years later. She had erysipela 12 years later complicating a leg ulcer. She was then given pneumococcal 23 valent and *Haemophilus influenzae* b vaccines. No hemorrhage or thrombotic manifestations occurred during 14 years of follow-up. Her platelet count still oscillates between 600.0 and 900.0×10^9/L.

Case #2

A 56-year old man was referred in 1997 because of a myocardial infarction. He had a history of tobacco intoxication and dyslipidemia. His full blood count was as follows: hemoglobin, 144 g/L; hematocrit, 43.6%, mean cell volume, 95 fL, white blood cells, 7.9×10^9/L; neutrophils, 41%; eosinophils, 1%; lymphocytes, 49%; monocytes, 9%; platelets, 513.0×10^9/L. There were Howell-Jolly bodies (H-JB) on his blood smear (0.7% of erythrocytes). Ten years earlier (date of the oldest blood count available) the platelet count oscillated between 500.0 and

Correspondence: Olivier Tournilhac, M.D., Fédération des Maladies Infectieuses, Médecine interne et Hématologie Adultes, Hôpital Hotel Dieu, Bd Leon Malfreyt, BP69, 63003 Clermont-Ferrand, France. Phone: international +33-04-73750075 – Fax: international +33-04-73750067 — E mail: otournilhac@chu-clermontferrand.fr

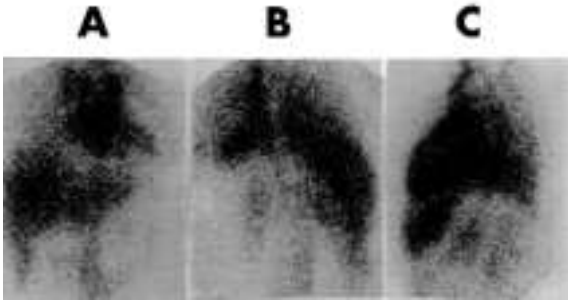

Figure 1. Case #1: ^{99}mTc-labeled red cell scintigraphy showing absence of functioning splenic tissue in an anterior view (A), posterior view (B), left lateral view (C).

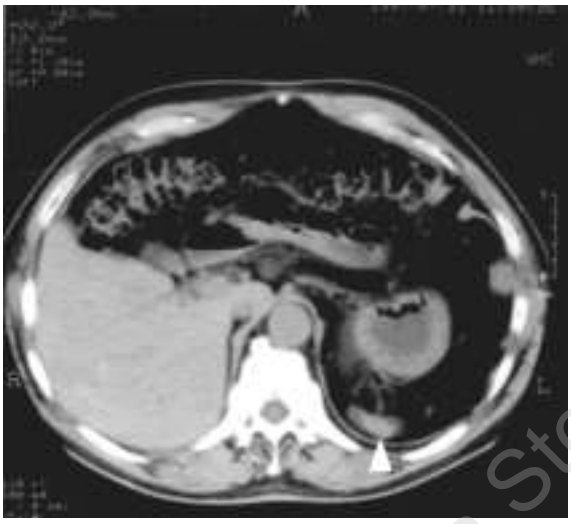

Figure 2. Case #2: Abdominal tomodensitometry: presence of a small vestigial spleen (arrow) in the sub-mesosolic posterior compartment.

800.0×10^9/L. Erythrocyte sedimentation rate, fibrinogen, C reactive protein, serum ferritin, iron concentration and transferrin were in the normal ranges. Bone marrow trephine biopsy was normal with a normal number of megakaryocytes of normal size and no myelofibrosis. Cytogenetic analysis of blood displayed 14 normal mitoses. Reverse transcriptase polymerase chain reaction analysis of blood revealed no BCR-ABL mRNA transcripts. The spleen was not visible by abdominal ultrasonography. Tomodensitometry showed a small homogenous structure, consistent with a vestigial spleen whose diameter was 2 cm, located in the submesosolic posterior compartment (Figure 2). Low-dose aspirin, pneumococcal 23 valent and *Haemophilus influenzae* b vaccines were given. No hemorrhage, thrombotic manifestations or infections occurred during 3 years of follow-up.

Discussion

We describe two cases of spleen agenesis revealed in adults by thrombocytosis with H-JB on blood smear, in one case immediately after a myocardial infarction, and in the other case during the investigation of a transient eczema. Morphologic examination (and functional analysis in one case) showed the absence of a spleen or presence of a vestigial organ. Neither case had associated malformation. One case had no history of infection while the other did. Apart from the myocardial infarction, which may have been associated with other important risk factors (tobacco use and dyslipidemia), neither case had a history of thrombosis or bleeding. In both cases asplenia was the sole explanation of thrombocytosis, since no iron deficiency, inflammatory state or myeloproliferative disease was evident. The question of the origin of these asplenias was under discussion. The patients had no history of splenectomy or abdominal radiation therapy. The possibility of functional hyposplenia was assessed but we found no bowel disorder such as celiac disease nor condition leading to spleen infarction such as myeloproliferative disorder.[1] So the diagnosis of secondary thrombocytosis caused by isolated splenic agenesis was made. Congenital absence of spleen has been reported mostly in association with malformations known as Ivemark' syndrome.[2] This congenital and generally sporadic disorder is rare (incidence of 1 in 10,000 to 20,000 live births), with variable penetrance and possible familial cases.[3] Heart defects, anomalous systemic or pulmonary venous connections and abdominal heterotaxia are described. Severe bacterial infections have been reported.[4] The overall survival rate does not exceed 20% at one year.[5] Familial or sporadic cases of spleen agenesis have also been reported in children without cardiac anomalies mostly revealed by overwhelming infection.[4,6] Such a condition has also been reported in two adults. Rose described a 37-year old woman with asplenia, isolated thrombocytosis and no history of infection.[7] Germing described a 60-year old female with isolated asplenia detected following an overwhelming pneumoccocal infection.[8] In both cases the absence of spleen was suggested by the presence of H-JB and was confirmed by ultrasound or tomodensitometry and scintigraphy and no associated malformations were reported.[7,8] Although it is well known that functional hyposplenia or splenectomy can induce thrombocytosis, little is known of the effects of isolated congenital asplenia. This condition seems to be rare in adults, but our observations suggest that this possibility should be considered when making an etiologic diagnosis of thrombocytosis. Neither of our cases fulfilled the crite-

ria for ET but, in the absence of recurrent causes of secondary thrombocytosis, a diagnosis of ET would probably have been made. Furthermore, in order to prevent vascular complications[9] hydroxyurea would have been given, at least to case #2, because of the antecedent myocardial infarction. Thus, in order to avoid a mistaken diagnosis of ET, in the absence of clinically evident spleen enlargement, attentive screening of peripheral blood cells in search of H-JB and abdominal ultrasound including an evaluation of spleen size should be systematic. Tomodensitometry or scintigraphy should then be performed if the spleen is not detected by ultrasound.

Since isolated spleen agenesis seems to be compatible with long survival, important questions remain concerning treatment. An increased risk of late thrombotic events, especially heart infarction, has been reported in splenectomized patients,[10,11] but this question is not still resolved. Some authors recommend the use of antiaggregant therapy;[12] this policy could also be used in patients with spleen agenesis. Life-threatening infections can occur after splenectomy or functional hyposplenia and may reveal spleen agenesis even in adults after many years of silence.[4,6,8] Prophylactic management in these patients, including immunization and antibiotics, remains a concern for physicians. Penicillin prophylaxis has been extensively used, especially post-splenectomy and in functional hyposplenia related to sickle cell disease, but the optimal duration of treatment needs to be more clearly assessed. Pneumococcal immunization is strongly recommended[13] and case control and immunologic studies consistently provide evidence for revaccination every 3 to 5 years.[14] Likewise *Haemophilus influenzae* b (Hib) vaccine can also be recommended in asplenic patients.[15]

Contributions and Acknowledgments

VC and OT were the principal investigators and participated equally in making the diagnoses, giving clinical care, conceiving and writing the paper. VD and PS performed case imaging. NB and CD performed cytological and histologic examinations respectively. OB gave clinical care and technical support to the work. PT and HL were responsible for direct supervision and critical revising of the final version of the manuscript.

Disclosures

Conflict of interest: none.

Redundant publications: no substantial overlapping with previous papers.

Manuscript processing

Manuscript received April 12, 2000; accepted August 11, 2000.

References

1. Marsh GW, Lewis SM, Szur L. The use of ^{51}Cr-labelled heat-damaged red cells to study splenic function. II. Splenic atrophy in thrombocythaemia. Br J Haematol 1966; 12:167-71.
2. Phoon CK, Neill CA. Asplenia syndrome: insight into embryology through an analysis of cardiac and extracardiac anomalies. Am J Cardiol 1994; 73:581-7.
3. Cesko I, Hajdu J, Toth T, Marton T, Papp C, Papp Z. Ivemark syndrome with asplenia in siblings. J Pediatr 1997; 130:822-4.
4. Waldman JD, Rosenthal A, Smith AL, Shurin S, Nadas AS. Sepsis and congenital asplenia. J Pediatr 1977; 90:555-9.
5. Phoon CK, Neill CA. Asplenia syndrome--risk factors for early unfavorable outcome. Am J Cardiol 1994; 73:1235-7.
6. Feder HM Jr, Pearson HA. Assessment of splenic function in familial asplenia. N Engl J Med 1999; 341:210-2.
7. Rose C, Quesnel B, Facon T, Fenaux P, Jouet JP, Bauters F. Congenital asplenia, a differential diagnosis of essential thrombocythemia. Presse Med 1993; 22:1748.
8. Germing U, Perings C, Steiner S, Peters AJ, Heintzen MP, Aul C. Congenital asplenia detected in a 60 year old patient with septicemia. Eur J Med Res 1999; 4: 283-5.
9. Cortelazzo S, Finazzi G, Ruggeri M, et al. Hydroxyurea for patients with essential thrombocythaemia and a high risk of thrombosis. N Engl J Med 1995; 332: 1132-6.
10. Boxer MA, Braun J, Ellman L. Thromboembolic risk of postsplenectomy thrombocytosis. Arch Surg 1978; 113:808-9.
11. Linet MS, Nyren O, Gridley G, et al. Causes of death among patients surviving at least one year following splenectomy. Am J Surg 1996; 172:320-3.
12. Ellison EC, Fabri PJ. Complications of splenectomy. Etiology, prevention, and management. Surg Clin North Am 1983; 63:1313-30.
13. Prevention of Pneumococcal Disease. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep. 1997; 46(RR-8):1-24.
14. Butler JC, Shapiro ED, Carlone GM. Pneumococcal vaccines: history, current status, and future directions. Am J Med 1999; 107:69S-76S
15. Germing U, Gaigounidis A, Schneider W. Improved prophylaxis against overwhelming postsplenectomy infections. Eur J Haematol 1997; 59:329-30.