

**DIGITAL ISCHEMIA DUE TO SYSTEMIC SCLEROSIS
ASSOCIATED WITH ESSENTIAL THROMBOCYTHEMIA: A
CASE REPORT**

Faida Ajili¹, Hajer Ben Mansour², H  la Ghedira², Sami Zriba²,
Leila Metoui¹, Imen Gharsallah¹, Nadia Ben Abdelhafidh¹,
Bassem Louzir¹, Fehmi M'sadak², Salah Othmani¹

¹Department of Internal Medicine, Military Hospital of Tunis, 1008 Montfleury,
Tunisia

²Department of Clinical Hematology, Military Hospital of Tunis, 1008 Montfleury,
Tunisia

Source of Support:

Nil

Competing Interests:

None

Corresponding author: Dr Faida Ajili

faida1977@yahoo.fr

Our Dermatol Online. 2013; 4(4): 508-510

Date of submission: 14.08.2013 / acceptance: 17.09.2013

Abstract

Digital ulcers (DU) are a well-known problem in patients with systemic sclerosis. It is an underestimated complication of the disease causing pain and morbidity. Essential thrombocytosis is another cause of DU. The association of these two diseases increases the risk of ischemic complications and impairment of hand function which are frequently observed in patients with digital ulcers.

This report deals with a 68-year-old patient with rare association of Essential thrombocytosis, Systemic sclerosis and Raynaud's phenomenon that was refractory to medical treatment of Systemic sclerosis (iloprost, calcium channel blockers) and improved with hydrea^{  }.

Key words: systemic sclerosis; digital ulcers; essential thrombocythemia

Cite this article:

Faida Ajili, Hajer Ben Mansour, H  la Ghedira, Sami Zriba, Leila Metoui, Imen Gharsallah, Nadia Ben Abdelhafidh, Bassem Louzir, Fehmi M'sadak, Salah Othmani: Digital ischemia due to Systemic Sclerosis associated to Essential Thrombocythemia: A case report. *Our Dermatol Online*. 2013; 4(4): 508-510.

Introduction

Systemic sclerosis (SSc) is a non-organic specific autoimmune disease that is characterized by fibrosis and excessive laying down of collagen in the skin, gastrointestinal tract and the lungs with an activation of immune system with production of autotibodies and extensive vascular damage. Raynaud's phenomenon (RP) and digital ulcers (DU) represent two faces of the same coin in SSc vasculopathy [1]. Essential thrombocytosis (ET) is another cause of DU. It is a slowly progressive disorder characterized by long asymptomatic periods punctuated by thrombotic or hemorrhagic events [2]. The association of these two diseases increases the risk of ischemic complications and impairment of hand function which are frequently observed in patients with digital ulcers.

We report a rare case of a 68-year-old woman with ET, Systemic sclerosis (SSc) and Raynaud's phenomenon (RP) that was refractory to medical treatment of SSc (iloprost, calcium channel blockers) and improved with hydrea^{  }.

Case Report

A 68- year-old woman with no significant past medical

history, was presented with a 2-week history of pain and bilateral bluish discoloration of the finger tips and toes. The pain was associated with numbness and tingling with decreased sensation to his fingers and toes and was exacerbated by cold. The patient also reported epigastric pain, post prandial vomiting, heartburn and dysphagia. Physical examination showed proximal skin sclerosis, thin skin, less hair, bilateral and symmetrical sclerodactily and pulp ulcers of 10 fingers (Fig. 1) and the big toes.

In blood count, Hb was normal on 13.2 g / dl, WBC 12600 elements /mm³ and platelet count of 634000 elements /mm³. The chest radiography had demonstrated interstitial syndrome, and the X-rays of hands showed resorption of phalangeal tufts of several fingers. The pressure of the lower esophageal sphincter and its peristalsis were reduced in esophageal manometry. Then, the diagnosis of Sytemic sclerosis was confirmed and initial treatment consisted of calcium channel blockers and colchicine. The clinical outcome was marked by the worsening of RP and the extent of digital ulcers.

On the other hand, the thrombocytosis was compounded.

A bone marrow biopsy was done and concluded at a megakaryocytic lineage hyperplasia, and presence of JAK2 mutation in molecular biology which is compatible with the diagnosis of essential thrombocythemia (ET). The patient



Figure 1. Pulp ulcers of fingers in our patient.

Discussion

Acute digital ischemia may be caused by several entities including collagen vascular diseases [3], Raynaud's disease [4], Buerger's disease [5], peripheral atherosclerosis [6], heparin-induced thrombocytopenia with thrombosis syndrome [7], consumption coagulopathy [8] and many others. Although rare, hematologic disorders, however, have to be considered in the differential diagnosis of acute digital ischemia. Essential thrombocytosis is one of them.

It is a slowly progressive disorder characterized by long asymptomatic periods punctuated by thrombotic or hemorrhagic events [9]. The disease usually affects middle-aged to elderly individuals, with an average age at diagnosis of 50 – 60 years [10]. It, however, may also affect children and young adults. The major risk factors for thrombosis are (age older than 60 years and previous thrombotic episode), whereas the advent of thrombosis appears to be unrelated to either the platelet count or hemostasis tests [11].

The most common symptoms in ET at presentation are due to disturbances of the microcirculation, particularly fingers, toes, and central nervous system manifestations including headache, dizziness, and visual and acoustic symptoms [2]. The term erythromelalgia, specific to the myeloproliferative disorders, refers to the occlusion of the microcirculation by platelets and is characterized by redness, congestion, and painful burning sensations of the extremities. Symptoms are characteristically relieved by cold or elevation of the extremity.

In systemic sclerosis, the origin of the ulcers is thought to be multifactorial, including microangiopathy, macrovasculopathy, microtrauma, bacterial infection, fibrosis, and calcinosis. Chronic microangiopathy seems to play an important role in the pathogenesis with endothelial cell damage being most probably the initiating factor [12]. Early diagnosis help to manage this disorder, which is treatable, but not curable. Therapy involves physical therapy as well as the targeting of blood vessel mechanics and fibrosis by colchicine, nifedipine, calcium

started a treatment based on hydroxyurea (Hydréa®) with a good clinical evolution of RP after failure of illoprost. On follow-up, she was symptom-free with no evidence of ischemic changes (Fig. 2) and her platelet count was of 219000 elements /mm³.



Figure 2. Improvement of the ischemic lesions with hydreia.

channel blockers and illoprost [13].

The patient described in this case report was atypical, because she was free of all the aforementioned thrombosis risk factors. We thought initially that her painful acrocyanosis, which progressed to digital gangrene, was probably due to Raynaud's disease related to the SSc rather than to classic essential thrombocythemia, because her extremities were neither warm nor congested. Also, her symptoms were exacerbated by cold and were not relieved by aspirin.

In fact, our patient was managed on admission with aspirin (to reverse the platelet-mediated thrombotic effect) and nifedipine (to reverse the vascular spasm). However, the patient's pain increased, so, we initiate the hydroxyurea with a good clinical course, then we think that DU is in fact due to both: SSc and ET and this makes the originality of our case.

In ET, the high-risk patient population (age >60 years, previous thrombotic episode), however, deserves in fact therapeutic intervention. Cytoreductive therapy with hydroxyurea [14], as our patient, or anagrelide [15] have been effective in preventing additional thrombotic episodes in this population.

When drugs measures fail to limit ischemic phenomena, and there is apparent danger of imminent gangrene, treatment includes urgent therapeutic platelet apheresis which lowers the platelet count, followed by periarterial sympathectomy which provides a valuable adjunctive treatment option in the setting of a normal platelet count to increase the nutritional collateral flow [14].

Discussion

In SSc, the repetitive vasospasm of RP and the structural changes of the digital vessels are the leading contributory causes of the incipient development of ischemic digital ulcers. The association of SSc and ET increases the gravity of DU. The management of RP and DU in this particular case, requires a multimodal approach using a combination of pharmacological and local treatments.

It deserves cytoreductive therapy with hydroxyurea in order to minimize the risk of ischemic digital ulcers and thrombotic episode especially after the non efficiency of the classic treatment of RP.

REFERENCES

1. Lawrence A, Khanna D, Misra R, Aggarwal A: Increased expression of basic fibroblast growth factor in skin of patients with systemic sclerosis. *Dermatol Online J.* 2006;12:2.
2. Levine SP: Thrombocytosis. In: Greer JP, Foerster J, Lukens JN, Rodgers GM, Paraskevas F, Glader B, eds. *Wintrobe's clinical hematology*. 11th ed. Philadelphia: Lippincott Williams & Wilkins, 2003:1591–601.
3. Herrick AL, Oogarah PK, Freemont AJ, Marcuson R, Haeney M, Jayson MI: Vasculitis in patients with systemic sclerosis and severe digital ischaemia requiring amputation. *Ann Rheum Dis.* 1994;53:323–6.
4. Cooke JP, Marshall JM: Mechanisms of Raynaud's disease. *Vasc Med.* 2005;10:293–307.
5. Shionoya S: Buerger's disease: diagnosis and management. *Cardiovasc Surg.* 1993;1:207–14.
6. Longo GM, Friedman AC, Hollins RR, Buresh CJ, Baxter BT: Distal radial artery lesion as a source of digital emboli. *J Vasc Surg.* 1998;28:710–4.
7. Chang JC: Review: postoperative thrombocytopenia: with etiologic, diagnostic, and therapeutic consideration. *Am J Med Sci.* 1996;311:96–105.
8. Davis MP, Byrd J, Lior T, Rooke TW: Symmetrical peripheral gangrene due to disseminated intravascular coagulation. *Arch Dermatol.* 2001;137:139–40.
9. Sanchez S, Ewton A: Essential thrombocythemia: a review of diagnostic and pathologic features. *Arch Pathol Lab Med.* 2006;130:1144–50.
10. Kutti J, Ridell B: Epidemiology of the myeloproliferative disorders: essential thrombocythaemia, polycythaemia vera and idiopathic myelofibrosis. *Pathol Biol (Paris).* 2001;49:164–6.
11. Regev A, Stark P, Blickstein D, Lahav M: Thrombotic complications in essential thrombocythemia with relatively low platelet counts. *Am J Hematol.* 1997;56:168–72.
12. Alix Naert, Petra De Haes: Successful Treatment with Bosentan of Lower Extremity Ulcers in a Scleroderma Patient. *Case Rep Med.* 2013;2013:690591.
13. Hausteufel UF: Systemic sclerosis-scleroderma. *Dermatol Online J.* 2002;8:3.
14. Cortelazzo S, Finazzi G, Ruggeri M, Vestri O, Galli M, Rodeghiero F, et al: Hydroxyurea for patients with essential thrombocythemia and a high risk of thrombosis. *N Engl J Med.* 1995;332:1132–6.
15. Fruchtman SM, Pettitt RM, Gilbert HS, Fiddler G, Lyne A: Anagrelide: analysis of long-term efficacy, safety and leukemogenic potential in myeloproliferative disorders. *Leuk Res.* 2005;29:481–91.