Letter to the Editor

Raynaud´s phenomenon

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Sir,

Female patient 35 years old in treatment due to systemic sclerosis since1 year ago treated with azathioprine 50 mg/day, felodipine 5 mg/day who came to the emergency room due to her fingertips discoloration and pain. During her examination her fingertips was affected predominantly on her right hand with cyanosis (Figs. 1-3), digital scars on fingertips (Fig. 4).

The diagnosis of secondary Raynaud´s phenomenon associated with her systemic disease. The rest of the examination showed acrosclerosys.

She began 4 days ago with pain and fingertips discoloration associated to the weather cold in the winter, the clinical diagnosis of secondary Raynaud´s phenomenon associated to her systemic disease.

The secondary Raynaud´s phenomenon can be the first clinical manifestation of collagen diseases or present themselves during them. From 2015 to 2017, were studied in the Dermatology and Rheumatology departments a total of 90 patients of these 26 (28.8%) had Raynaud's phenomenon in systemic sclerosis 12 (46.15%), dermatomyositis 6 (23.07%), SLE 5 (19.23%) were studied in the Dermatology and Rheumatology departments.), mixed connective tissue disease2 (7.69%), rheumatoid arthritis 1 (3.84%). In our cases the most frequent association of the secondary Raynaud´s phenomenon was with systemic sclerosis.

On 1862 the French physician Maurice Raynaud described in his thesis an entity characterized by local asphyxia and symmetric gangrene that affected extremities, caused by an overactive neurological reflex [1-3]. Since then, the term Raynaud´s phenomenon (RF) has been used to name these vasospastic episodes, which manifest themselves with cyanosis or pallor in fingers and toes [1,2,4,5].

The Raynaud phenomenon manifests as transient and reversible episodes of peripheral ischemia, which affect fingers and toes in exaggerated vasoconstriction of peripheral arterioles and arteries. Triggers such as cold (the most common), emotional stress and medications, such as beta-blockers, ergot derivates, chemotherapeutic drugs, cyclosporine, bromocriptine, interferon alfa, beta amphetamines, cocaine, nicotine exposure, among other triggers like smoking, vibration or spontaneously [3-7]. It has a general distribution and affects approximately 3 to 5% of the global population with a shift in prevalence toward colder climates [2,3].

It is thought this phenomenon is an abnormal and exaggerated endothelial vascular response to a stimulus (neurogenic, neural, hormonal, vasodilators and vasoconstrictors), generated by an endothelial damage within the microvasculature [4]. The endothelial cells release diverse substances, including endothelin 1 (ET-1), which has a vasoconstrictor effect, regulated by the nitric oxide vasodilator action product of cyclic guanosine monophosphate (cGMP) increments. Within the Raynaud´s phenomenon patient, the cGMP is diminished whenever imbalance between the vasoconstriction and vasodilation exists [4].

When this condition occurs in disease absence, it is known as primary/idiopathic Raynaud´s phenomenon (PRP) or Raynaud disease (80% of cases) [5]. Whereas patients with secondary Raynaud phenomenon (SRP) may occur in association with autoimmune conditions (up to 80 to 95% of the cases) as rheumatoid arthritis (20% of the

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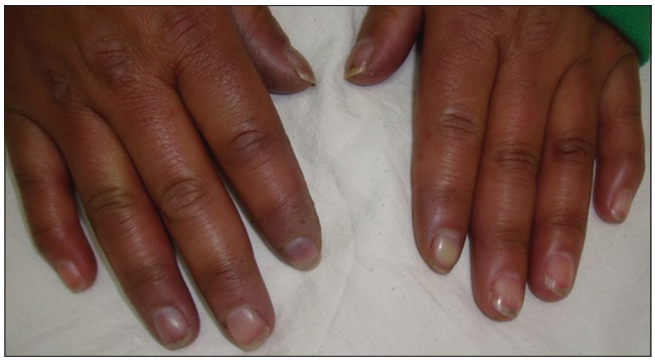

Figure 1: Dorsal face of the hands with cyanosis.

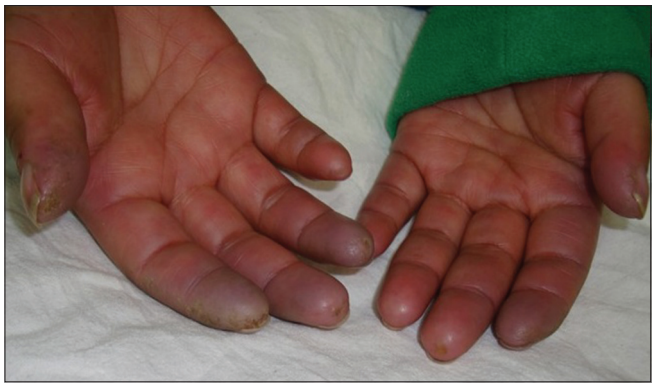

Figure 2: Palmar face of the hands with cyanosis and scars on fingertips.

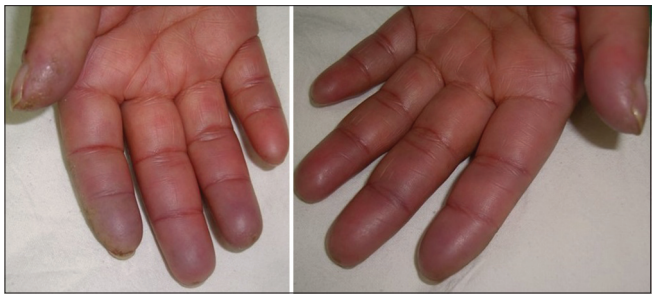

Figure 3: Close up the Raynaud´s phenomenon

cases) scleroderma (90%), systemic erythematous lupus (10-45%), Sjögren syndrome (30%) [2], mixed connective tissue disease, dermatomyositis, arteries diseases [3,4,6,7]. It has been reported in association with neoplasms, including solid tumors and hematologic diseases such as polycythemia vera, essential thrombocytosis leukemias, lymphomas, myeloid metaplasia, Multiple myeloma and cryoglobulinemias, due to the blood viscosity increase [5,7]. Other causes had been described such as endocrinopathies (hypothyroidism, carcinoid syndrome, pheochromocytoma) and arterial disease (Arteriosclerosis, Peripheral embolism, Horton´s vasculitis, thromboangiitis obliterans, Prinz-metal's angina) [7] (Table 1).

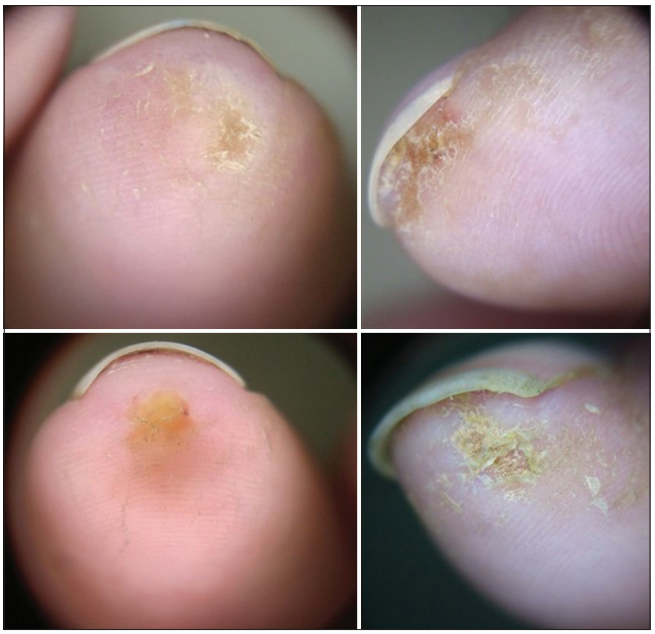

Figure 4: Digital scars on fingertips.

Major risk factors of PRP include female gender, family history of PRP, migraine, smoking and estrogen replacement therapy. The set middle age is 14 years old and only 27% of the cases begins after 40 years old [5]. Clinically, it is characterized by the coloration change of skin on the hands, feet, nose, nipples or ears. It has a "triphasic color pattern": Initially pallor, due the constricted blood-flow and ischemia; Then becoming cyanosis, a sign of tissue hypoxia due the presence of deoxyhemoglobin; and lastly turning red, secondary to the reflex vasodilation (reactive hyperemia) [2,4-6]. This phenomenon most be differentiated from acrocyanosis. This last one characterized by hand and feet continuous cyanosis, exacerbated by low temperatures [5].

The risk of autoimmune disease in patients with Raynaud disease is approximately 6% to 12%. After two years follow-up, if the patient does not present clinical or laboratories signs suggestive of systemic disease the risk dramatically decrease [5]. Complications of primary Raynaud phenomenon are extremely rare. In patients older than 30 years old presenting intensive cyanotic episodes, painful, asymmetric or associated with ischemic cutaneous lesions, in presence with clinical evidence of connective tissue disease, it is suggestive of secondary Raynaud phenomenon [5]. The SRP tends to be asymmetric the attacks are prolonged and Up to 50% of patients with scleroderma may have multiple, bilateral, painful and disabling digital ulcers that heal slowly and tend to relapse [6,7].

Table 1: Raynaud×s disease and secondary phenomenon

	Raynaud disease	Secondary Raynaud×s phenomenon
Prevalence (%)	3.5 – 4	0,4
Women: men	20:1	4:1
Set age (years)	< 15-20	> 25-30
Family history (%)	25	NO
Systemic disease association	NO	Yes
Ulcers/necrosis	Rare	Frequent
Symmetric	Yes	NO
Capillaroscopy	Normal	Capillary dilatations, zones without capillaries, hemorrhages zones
Autoantibodies	Negative or low titles	Frequent
		Causes
		Autoimmune diseases
		Systemic scleroderma, mixed connective tissue disease, systemic erythematous lupus (10-45%), Sjogren syndrome (30%) (8), dermatomyositis, rheumatoid arthritis
		Drugs and toxics
		Ergot derivates, betablockers, chemotherapeutic drugs, cyclosporine, bromocriptine, interferon alfa, beta amphetamines, cocaine, nicotine exposure
		Endocrinopathies
		Hypothyroidism, carcinoid syndrome, Pheochromocytoma
		Arterial Diseases
		Arteriosclerosis, Peripheral embolism, Horton × s vasculitis, thromboangeitis obliterans, Prinz-metal's angina
		Hematologic diseases neoplams
		Polycythemia vera, essential thrombocytosis, leukemias, lymphomas, myeloid metaplasia, multiple myeloma, cryoglobulinemias, solid neoplasms

The diagnosis is made in base different criteria: cold sensibility history, presence of pallor on finger or cyanosis episodes after cold exposition. This may be further corroborated by pictures of hands during the attack. Note that It is not necessary to confirm the diagnosis by provocative tests [2,5].

The evaluation of RF patients must include clinic history, complete physical examination and complementary studies including: hemogram with erythrocyte sedimentation, general biochemistry, thyroid hormones, antinuclear antibodies and specific antibodies, rheumatoid factor and capillaroscopy [2,4,5]. The latter one having a negative predict value of 93% under normal conditions. Additionally, patients with Raynaud disease associated with abnormal capillary patterns increase risk of transition to an autoimmune condition of 47% [4].

The objective of Raynaud phenomenon treatment is reducing vasoconstriction and alleviation of patient symptoms. The treatment is classified in general (no pharmacological) measures and pharmacological measures [4]. General measures such as cold protection, tobacco and vasoconstrictor pharmacy avoidance, and prevention of vibration/stress, are usually enough to control Raynaud disease [4,6]. Only in secondary cases and/or in association with digital ulcers pharmacologic treatment is necessary [4,5-7].

Calcium antagonists (nifedipine, amlodipine, nicardipine) are first-line drugs whenever general measures fail. This treatment presents slight effects on primary Raynaud phenomenon, but moderate benefits regarding secondary forms of scleroderma, decreasing the frequency and intensity of the episodes [2,5,6].

When calcium channel blockers are not effective, therapy with phosphodiesterase 5 inhibitors such as, sildenafil and vardenafils may be substituted; if there is severe vascular involvement (digital ulcers or critical ischemia), infusions of prostaglandin analogs may be used [5,6]. The interdigital and palmar injections of botulinum toxin A improve clinical, especially alleviating pain in patients with Raynaud's phenomenon and digital ulcers [6].

Surgical treatment is reserved for patients with poor response to pharmacological treatment with severe ischemia or active digital ulcers, and are reduced to debridement of necrotic or infected tissue, open thoracoscopic and digital surgical sympathectomy,

electrical stimulation of bone marrow and vascular reconstruction [2].

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles.

REFERENCES

1. Salazar-López R. Historia del tratamiento de la vasculitis. Rev Colomb Cir Plást Reconstr. 2017;23:75-8.
2. Joven B, Carreira P. Síndrome de Raynaud: etiología y manejo. Reumatol Clin. 2008;4:59-66.
3. Maverakis E, Patel F, Kronenberg D, Chung L, Fiorentino D, Allanore Y, et al. International consensus criteria for the diagnosis of Raynaud´s phenomenon. J Autoinmmun. 2014;48-49:60-5.
4. Guerrero-García A. Fenómeno de Raynaud. Biociencias. 2017;12:93-9.
5. Wigley F. Raynaud´s Phenomenon. N Eng J Med. 2002;347:1001-4.
6. Cervigón-González I, Sánchez-Neila N, Montes-García S, Palomo Arellano A. Algoritmo terapéutico del fenómeno de Raynaud y de las ulceraciones digitales isquémicas de la esclerodermia sistémica. PIEL (Barc). 2016;32:1.
7. Conde-Baena P, Vargas-Hitos J, Sabio J, Navarrete-Navarrete N, Zamora-Pasadas M, Jiménez-Alonzo J. Varón de 62 años con fenómeno de Raynaud. Actual Med. 2015;100:98-100.

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