Conversion to Paradoxical Finding on Technetium-99m-labeled RBC Scintigraphy after Treatment for Secondary Raynaud's Phenomenon

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Abstract An 18-year-old woman reported that after exposure to cold temperatures her fingers appeared blue and her hands and feet felt cold. Secondary Raynaud's phenomenon (RP) associated with peripheral vascular disease was suspected. Technetium (Tc)-99m-labeled RBC hand scintigraphy after cold change showed decreased blood pool activity in her fingers. The patient's symptoms improved after she received sarpogrelate HCL (200 mg/day) and nifedipine (40 mg/day). Follow-up scintigraphy performed 7 months after the patient started treatment showed paradoxically increased blood pool activity in her fingers after cold challenge. To the best of our knowledge, this is the first case report of a patient with secondary RP showing paradoxical change on scintigraphy after she received medication that improved her symptoms.

Keywords Raynaud's phenomenon · Tc-99 m RBC scintigraphy · Paradoxical reaction

Introduction

Raynaud's phenomenon (RP) is characterized by episodic vasospasm and ischemia of the extremities in response to stress or exposure to cold [1]. There have been several studies of RP using perfusion scintigraphy [2–6]. After cold challenge, patients with RP show two types of findings on perfusion scintigraphy [4, 5]: (1) decreased perfusion or blood pool activity or (2) increased perfusion or blood pool activity [4]. The latter is called paradoxical reaction of RP. To date, little is known about the mechanism involved in the paradoxical reaction of RP. We report a patient with secondary RP showing scintigraphic change to paradoxical reaction after receiving medication that relieved her symptoms.

Case Report

An 18-year-old woman was seen for complaints that her fingers turned blue and her hands and feet felt cold after exposure to cold temperatures. The symptom had worsened over the previous month. Her past medical history was unremarkable. Laboratory testing for autoimmune disorders of connective tissue, including antibody tests such as antinuclear antibody, anti-double-stranded DNA, and complements such as C3 and C4, was uninformative except for an elevated level of total hemolytic complement (CH 50; 63.2 U/ml, reference value 23–46 U/ml). CH50 is known to be elevated in various inflammatory diseases.

The patient underwent computed tomography angiography; the findings were suggested occlusive lesions involving interosseous arteries. She was diagnosed with peripheral occlusive artery disease, although she did not have risk factors of

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Before medication (A-B)

Fig. 1 Tc-99m-labeled RBC scintigraphy of the hands before (a, b) and after starting medication (c, d) in a patient with secondary Raynaud's phenomenon. The fingers of the hand that underwent cold challenge showed decreased blood pool activity (Fig. 1a, b). After 7 months of

medication, the fingers of the hand that underwent cold challenge showed paradoxically increased blood pool activity (asterisks in Fig. 1c and d) compared with the fingers of the hand not undergoing cold challenge. *F/P ratio* finger-to-palm ratio

peripheral artery disease such as smoking, diabetes mellitus, dyslipidemia, hypertension, stroke or family history of vascular disease.

Technetium (Tc)-99m-labeled RBC hand scintigraphy after cold challenge was performed before treatment (Fig. 1a, b, palmar view). The patient's left hand was immersed in cold water (4 °C) for 60 s, and then pyrophosphate was injected intravenously to the right foot. After 20 min, Tc-99m pertechnetate (TcO₄) was injected intravenously. A blood pool scan was obtained 10 min later (Fig. 1a). The following week, the same procedure was performed for with the right hand (Fig. 1b). The fingers of the hand that underwent cold showed decreased blood pool activity compared with the unchallenged hand (Fig. 1a, b). Finger-to-palm ratio was calculated by the method of Galuska et al. [7].

The patient was diagnosed with secondary RP. She was informed about avoiding trigger factors such as cold exposure, emotional stress, nicotine, caffeine. She was also given cilostazol 100 mg/day (Pletal, a quinolone derivative). Because of headaches, the patient's medication was changed to sarpogrelate HCL 100 mg/day (Anplag, a serotonin 2A and 2B antagonist) 2 weeks later, and after an additional 2 weeks, the dose was increased to 200 mg/day. Headache disappeared after changing prescription.

After 3 months of medication, the patient's symptoms (color change and feeling coldness in her extremities) were relieved. However, 1 month later (in September, autumn), symptoms recurred and she was given nifedipine CR at 40 mg/day (calcium channel blocker) in addition to the sarpogrelate. After 1 month of medication, her symptoms were much relieved. Seven months after starting treatment, the patient underwent follow-up scintigraphy using same protocol (Fig. 1c, d). The fingers of the hand undergoing cold challenge showed paradoxically increased blood pool activity (asterisks in Fig. 1c and d) compared with the hand not undergoing cold challenge.

Discussion

The pathophysiology of RP is poorly understood. RP may be primary (idiopathic) or secondary to an underlying condition—including collagen-vascular, hematological, or occlusive arterial disease—or induced by medication [1, 8].

Most people with primary RP respond well to avoidance of precipitating factors and medication [1]. Patients with secondary RP require treatment of the underlying disorder. Although there are no guidelines on the medical treatment of RP, there

are several medications that can be used on a case-by-case basis [1]. Nifedipine, a calcium channel blocker, promotes relaxation of vascular smooth muscle cells, which leads to vasodilation [1]. Other drugs, such as topical nitrates, prostaglandins, phosphodiesterase type 5 inhibitors, antioxidants, angiotensin-receptor antagonists, and angiotensin-converting-enzyme inhibitors also have been used [1].

To date, little is known about the mechanism involved in the paradoxical reaction of RP. Lim et al. [5] has suggested that when the structure of a vessel is changed, leading to diminished perfusion of the fingers even at room temperature, paradoxical vessel dilatation after exposure to cold might occur. However, this explanation may not account for our patient, because her symptoms had been relieved by medication at the time of the scintigraphy that showed paradoxical perfusion after cold challenge. Follow-up evaluation using computed tomography angiography or serum level of CH50 was not performed. The cause and mechanism of the paradoxical increase in perfusion after exposure to cold in patients with RP are still unknown. Further study is needed.

Conclusions

To the best of our knowledge, this is the first report of a patient with secondary RP that has shown an alteration in scintigraphic findings to a paradoxical pattern after successful treatment using medication. To understand this paradoxical reaction, additional

studies of treated patients with RP using follow-up perfusion scintigraphy are needed.

Conflicts of interest None.

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