European Journal of Case Reports in Internal Medicine

Erythromelalgia Caused by Polycythemia Vera Combined with Primary Aldosteronism

Morika Suzuki[1], Takashi Watari[2]

[1]Department of General Internal Medicine, National Hospital Organization Sendai Medical Center, Miyagi, Japan

[2]Postgraduate Clinical Training Centre, Shimane University Hospital, Shimane, Japan

Doi: 10.12890/2020_001852 - European Journal of Case Reports in Internal Medicine - © EFIM 2020

Received: 29/06/2020
Accepted: 13/07/2020
Published: 13/08/2020

How to cite this article: Suzuki M, Watari T. Erythromelalgia caused by polycythemia vera combined with primary aldosteronism. *EJCRIM* 2020;**7**: doi:10.12890/2020_001852.

Conflicts of Interests: The Authors declare that there are no competing interests.

ABSTRACT

A 61-year-old woman with a history of primary aldosteronism caused by unilateral hyperplasia of the adrenal gland presented with a 2-week history of redness and severe pain in the right thumb and thenar regions. She had initially visited a dermatologist and was diagnosed with cellulitis and treated with cefditoren pivoxil for 5 days, but there was no improvement. The pain worsened and was accompanied by a burning sensation. The dermatologist prescribed famciclovir for 5 days owing to suspicion of herpes zoster. The patient was then referred to our department because her symptoms persisted. Physical examination showed no abnormalities other than the redness in the right thumb and thenar regions and spontaneous moderate pain present throughout the right thumb. Investigations revealed normal blood chemistry and coagulation factor levels, except for elevated haemoglobin (18.2 g/dl). Further investigations revealed an erythropoietin level of 2.3 IU/ml and Janus kinase 2 mutation. Hence, we diagnosed the patient with erythromelalgia caused by polycythemia vera. In this report, we discuss the treatment of polycythemia causing erythromelalgia, and the aetiology of primary aldosteronism and polycythemia vera.

LEARNING POINTS

- Polycythemia can cause erythromelalgia, which should be treated with aspirin.
- Primary aldosteronism causes secondary erythropoiesis through activation of the renin-aldosterone system, but the mechanism is not clear.
- Erythropoiesis may be promoted by concurrent primary aldosteronism and polycythemia vera, resulting in secondary erythromelalgia.

KEYWORDS

Erythromelalgia, polycythemia vera, primary aldosteronism

INTRODUCTION

Erythromelalgia (EM) causes redness and pain in the upper and lower extremities. Secondary EM is caused by myeloproliferative disease, including polycythemia vera, and secondary aldosteronism associated with underlying causes such as drug use, infection and collagen disease. Primary aldosteronism (PA) is an endocrine disorder which causes secondary polycythemia, but its mechanism is still unclear. Here, we report a rare case that was complicated by polycythemia vera during PA treatment and developed into secondary EM. The molecular pathology is discussed.

European Journal of Case Reports in Internal Medicine

CASE DESCRIPTION

A 61-year-old woman presented with redness and severe pain in the right thumb and thenar regions that had persisted for over 2 weeks. She had a history of primary aldosteronism caused by unilateral hyperplasia of the adrenal gland diagnosed 3 years previously. Adrenal venous sampling showed excessive aldosterone production on the right side. However, imaging studies showed no obvious mass lesions, and the diagnosis of PA due to adrenal microadenoma was made. Her blood pressure was well controlled by spironolactone without surgical treatment until a month before presentation. She had initially visited a dermatologist and the redness and severe pain in her hand was diagnosed as cellulitis and treated with cefditoren pivoxil for 5 days, but there was no improvement. The pain worsened and was accompanied by a burning sensation. The dermatologist prescribed famciclovir for 5 days owing to suspicions of herpes zoster. The patient was then referred to our department because her symptoms persisted.

Upon review, she denied any symptoms, apart from the pain in her hand. Her vital signs were normal, except for a blood pressure of 151/105 mmHg. Physical examination showed no abnormalities other than the redness in the right thumb and thenar regions and spontaneous moderate pain throughout the right thumb with no ulceration (*Fig. 1*).

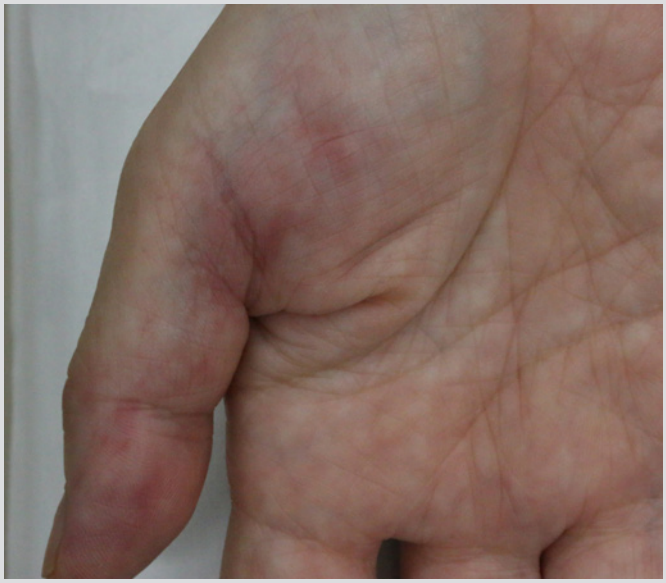

Figure 1. Erythema in the right thumb and thenar regions

Investigations revealed normal blood chemistry, including electrolytes such as potassium and sodium, and coagulation factor levels, except for elevated haemoglobin levels (18.2 g/dl). Further investigations revealed an erythropoietin level of 2.3 IU/ml (normal value 4.2–23.7 IU/ml) and a Janus kinase 2 (JAK2) mutation. Hence, we diagnosed the patient with erythromelalgia caused by polycythemia vera. After treatment with 100 mg/day aspirin, the patient's symptoms resolved. In addition, phlebotomy was performed to maintain a target haematocrit value of <45%, and oral aspirin was prescribed to avoid reoccurrence of thrombosis. The EM quickly improved after polycythemia vera treatment was started. Notably, blood pressure control also improved when oral spironolactone was increased for PA.

DISCUSSION

Erythromelalgia causes redness and pain in the upper and lower limbs. It is classified as primary (caused by gene mutations) and secondary erythromelalgia (associated with underlying factors, such as myeloproliferative causes including polycythemia, drug use, infection and collagen disease). It is diagnosed on the basis of clinical findings and medical history. If there are no specific findings, cellulitis and dermatitis must be excluded [1]. Antiepileptic drugs and selective serotonin reuptake inhibitors are often used to relieve symptoms in patients with secondary erythromelalgia; however, a complete cure is difficult. Moreover, it has been reported that treatment with aspirin improves erythromelalgia symptoms when polycythemia vera or essential thrombocytosis is the cause [1]. In the present case, the diagnosis of polycythemia was confirmed by detection of a mutation in JAK2, increased haemoglobin levels, and decreased erythropoietin levels, after elimination of the secondary causes of increased red blood cells [2]. Primary aldosteronism is an endocrine disease known to cause secondary polycythemia and systemic and persistent activation of the renin-angiotensin system (especially the AT1a receptor), which results in an increase in red blood cells [3]. AT1a receptors expressed in the kidney and bone marrow-derived cells and JAK2 mutations

are known to contribute to the expression of bone marrow renin-angiotensin proteins [4]. The AT1a receptor is also involved in the control of angiotensin II through JAK2 [5]. It is possible that mutated JAK2-associated polycythemia vera acts on the renin-angiotensin system, affecting blood pressure control in primary aldosteronism and exacerbating polycythemia. It is important to consider erythromelalgia in cases with undistinguishable redness and pain in the limbs. Although erythromelalgia is difficult to treat, secondary erythromelalgia caused by polycythemia vera may be effectively treated with aspirin.

REFERENCES

1. Cohen JS. Erythromelalgia: new theories and new therapies. *J Am Acad Dermatol* 2000;**43**:841–847.
2. Tefferi A. Polycythemia vera and essential thrombocythemia: 2012 update on diagnosis, risk stratification, and management. *Am J Hematol* 2012;**87**:285–293.
3. Kato H, Ishida J, Imagawa S, Saito T, Suzuki N, Matusoka T, et al. Enhanced erythropoiesis mediated by activation of the renin-angiotensin system via angiotensin II type 1a receptor. *FASEB J* 2005;**19**:2023–2025.
4. Vrsalovic MM, Pejsa V, Veic TS, Kolonic SO, Ajdukovic R, Haris V, et al. Bone marrow renin-angiotensin system expression in polycythemia vera and essential thrombocythemia depends on JAK2 mutational status. *Cancer Biol Ther* 2007;**6**:1434–1436.
5. Marrero MB, Schieffer B, Paxton WG, Heerdt L, Berk BC, Delafontaine P, et al. Direct stimulation of Jak/STAT pathway by the angiotensin II AT1 receptor. *Nature* 1995;**375**:247–250.

DOI: 10.12890/2020_001852