Secondary Erythermalgia Associated with an Autoimmune Disorder of Undetermined Significance

Abstract
A 50-year-old female patient is described with an acquired, persisting and yet incurable erythermalgia featured by symmetric burning pain and red congestion of the extremities secondary to cutaneous vasculitis. A weakly positive antinuclear antibody titer and high titers of antibodies against gastric parietal mucosa cells pointed to an underlying but unclassifiable autoimmune disorder. It is concluded that histopathology of lesional skin contributes to the differential diagnosis of primary and secondary erythermalgia.

Introduction
Erythromelalgia and erythermalgia are two distinct clinical syndromes of burning painful and red congested extremities [1-3]. The curable variant erythromelalgia is causally related to thrombocythemia and results from platelet-mediated arteriolar inflammation and thrombosis. Aspirin completely alleviates all symptoms by irreversible inhibition of platelet cyclooxygenase activity and aggregation [4-7].

The incurable variant of primary erythermalgia is a rare congenital disorder which spontaneously arises in childhood or adolescence as bilateral symmetrically burning extremities in the absence of detectable disease [8, 9]. The histopathology in primary erythermalgia is nonspecific and may show only slight perivascular infiltration with lymphocytes [9].

Secondary erythermalgia usually arises at the adult age either in association with cutaneous vasculitis or with the use of drugs. Secondary erythermalgia in these conditions responds to treatment of the underlying disorder or discontinuation of the incriminated drug [1, 8, 10, 11].

There also appears to be a persisting and incurable form of erythermalgia arising at the adult age [12]. However, the histopathology of incurable erythermalgia at the adult age has never been investigated. We have had the opportunity to study an adult woman who developed incurable erythermalgia in the setting of an unclassifiable autoimmune disorder. Evidence is presented that the specific clinical manifestations and the histopathological findings contribute to the differential diagnosis of primary and secondary erythermalgia.

Case Report
Since 1984, a 50-year-old woman has suffered from a unilateral painful erythema on the left heel, progressively extending to the foot, ankles and lower leg. In 1986, an erythema of the right foot, ankle and lower leg was noted. The condition progressed to bilateral burning distress and red swelling of both feet, ankles and lower legs. Since...
The complaints and signs in the presented patient with impaired function of the lower extremity, the burning and painful swelling of the toes and lower leg, as uncontrolled process and subsequent spread to both legs, are often associated with increased swelling at the ankle and severe numbness, which may be pronounced at night. Malignant tumors are a possible source of the swelling.

**Discussion**

Blood vessels with stenosis and endothelial cells and perivascular interstitial infiltrate composed of lymphocytes and plasma cells.

![Image](image_url)

**Fig. 2.** Blood vessels with stenosis and endothelial cells and perivascular interstitial infiltrate composed of lymphocytes and plasma cells.

**Fig. 1.** Peripheral neuropathy classified as diabetic neuropathy and symptomatic relief.

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**Footnotes:**

1. [Explain footnote 1 here.]
2. [Explain footnote 2 here.]
3. [Explain footnote 3 here.]

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**References:**


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**Tables:**

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<th>Table 1: Peripheral Neuropathy Prevalence</th>
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<td>Treatment with alpha-lipoic acid</td>
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**Images:**

1. Image of a diabetic foot showing signs of peripheral neuropathy.
2. Image of a foot with stenosis and perivascular infiltrate.

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**Figures:**

1. **Fig. 1:** Peripheral neuropathy classified as diabetic neuropathy and symptomatic relief.
2. **Fig. 2:** Blood vessels with stenosis and endothelial cells and perivascular interstitial infiltrate composed of lymphocytes and plasma cells.

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**Conclusion:**

The presented case highlights the importance of early intervention and appropriate management of peripheral neuropathy to prevent further complications and improve patient quality of life.
legs became a symmetric feature. At this stage, the symptoms superficially resembled the features of primary erythermalgia [9]. As in primary erythermalgia, the lesions had a bilateral distribution, there was aggravation by exercise and elevation of the ambient temperature worsened the symptoms. Also, the slight relief by cold, rest and elevation of the affected extremities and the resistance to treatment fit with the diagnosis of primary erythermalgia. However, particular symptoms are against the diagnosis of primary erythermalgia and are more in agreement with a secondary variant: the complaints and signs started as a unilateral process and spread subsequently to both feet and hands, whereas in primary erythermalgia the discomfort always starts bilaterally as a symmetric process. In contrast to a typical fluctuating course with frank exacerbations and symptom-free periods in primary erythermalgia, the symptoms in our patient became a constant and chronic clinical feature without any fluctuations. Moreover in our patient symptoms started at adult age unlike primary erythermalgia. Histopathology of erythermalgic skin showed perivascular inflammatory infiltrates of lymphocytes and plasma cells consistent with (peri)vasculitis, being different from fibromuscular proliferation and thrombotic occlusions in erythermalgia [7].

This pattern is similar to the histopathology of reporte cases in erythermalgia secondary to vasculitis, systemic lupus erythematosus in particular [10, 11]. Laboratory testing in our patient revealed a high antinuclear antibody titer and antibodies against gastric parietal mucosa cells which suggests a coexisting, but not yet clearly defined, autoimmune disorder. It is not clear whether the autoimmunity in our patient establishes a significant pathogenetic factor or even a link.

In this respect, it should be noted that antinuclear auto- bodies can be found in 10–37% of the healthy elderly and parietal cell antibodies are seen in up to 16% of the norma population [14, 15]. In another case of severe adult-onset erythermalgia, no autoantibodies were detectable [12]. Per sisting (secondary) erythermalgia arising at the adult age is very rare, and treatment is difficult. Histopathological examination of lesional skin contributes to the differentia diagnosis of primary and secondary erythermalgia.

References