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


Discussion

The complaints and signs in the presented patient with thrombosis cells and post vascular immunocompetent network consisting of lymphocytes and plasma cells.

FIG. 2. Blood vessels with epithelial smooth muscle endothelial cells and intima.

The condition was confirmed in the post mortem examination. The patient had a history of diabetes mellitus-type 2 and was a smoker. The patient was admitted to the hospital on October 15, 1998, with a history of numbness in the feet and pain in the legs. The patient was diagnosed with diabetic neuropathy and was treated with pain medication. The patient was discharged on October 29, 1998, with a recommendation for follow-up care.

FIG. 3. Autopsy findings. The pathological examination revealed a severe vascular lesion with thrombosis and intimal fibrosis. There was an absence of endothelial cells and a loss of smooth muscle cells. The lumbar vessels were narrowed and occluded, and there was a loss of intima. The renal vessels were narrowed and occluded, and there was a loss of medulla. The aorta was narrowed and occluded, and there was a loss of aortic wall. The femoral vessels were narrowed and occluded, and there was a loss of intima. The pedal vessels were narrowed and occluded, and there was a loss of medulla. The digital vessels were narrowed and occluded, and there was a loss of intima.
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 erythromelalgic skin showed perivascular inflammatory infiltrates of lymphocytes and plasma cells consistent with (peri)vasculitis, being different from fibromuscular proliferation and thrombotic occlusions in erythromelalgia [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 antibodies can be found in 10–37% of the healthy elderly and parietal cell antibodies are seen in up to 16% of the normal 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 differential diagnosis of primary and secondary erythermalgia.

References