Secondary Erythromelalgia in an HIV-infected Patient
Is there a Pathogenetic Relationship?

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The syndrome of red, warm, swollen and painful extremities has been divided into three types by Drenth & Michels: primary erythromelalgia, secondary erythromelalgia and erythromelalgia (1, 2). Erythromelalgia and erythromelalgia are two distinct entities and have to be separated. In all types the pain is relieved by cold, whereas exposure to warmth and physical exercise worsens the condition. Primary erythromelalgia is a very rare congenital disorder of unknown pathophysiology, which arises in young children and young adults and has a bilateral symmetrical distribution which is not treatable. An autosomal dominant inheritance pattern has been documented in a large family with 29 affected members over three generations (3). Secondary erythromelalgia is related to a variety of clinical conditions such as drug ingestion, cutaneous vasculitis, systemic lupus erythematosus, diabetes mellitus, rheumatoid arthritis and hypertension (4). Treatment consists of stopping a possibly causative medication and or improvement or healing of the underlying disease.

Erythromelalgia, the third type, is the most common variant and restricted to conditions with essential thrombocythemia or other myeloproliferative disorders associated with abnormal thrombocytopenic function. In the later patient group, treatment with aspirin leads to marked relief. Erythromelalgia due to thrombocythemia is typically asymmetric. Histopathology of erythromelalgia in thrombocythemia shows arteriole thrombosis and swollen endothelial cells with large nuclei, and narrowing of the lumen by proliferation of surrounding smooth muscle cells (5, 6). Erythromelalgia may progress to ischemic necrosis or necrosis of fingers and toes (7). In a previous study, we analyzed retrospectively 273 patients with essential thrombocythemia who were seen at the Mayo Clinic between 1975 and 1989 (8). Of the 273 patients with essential thrombocythemia, 62 had related skin manifestations. Fifteen patients had erythromelalgia, and in 11 it was an initial sign of essential thrombocythemia. As expected, a remarkable relief of symptoms was noticed after treatment with acetylsalicylic acid or after lowering the platelet count with chemotherapy or radiotherapy (8). Michels et al showed that erythromelalgia was the presenting symptom in 26 of 40 patients (65%) with thrombocythemia (7).

To the best of our knowledge no report on secondary erythromelalgia and HIV-infection exists. Here we present this association for the first time.

CASE REPORT
A 29-year-old female, who was known to be seropositive for HIV-infection as a result of intravenous drug abuse since 1996, was seen because of increasing pain at the distal arms and hands with redness and swelling which had developed within the last 9 months. The patient had advanced HIV infection and showed a history of recurrent Candida stomatitis. She had generalized lymphadenopathy and thrombocytopenia (124 x 10³/μL). Her dermatological history was remarkable for impetigo contagiosa in 1987, folliculitis, trichomycosis axillaris, molluscum contagiosum, flat warts at the dorsum of the hands and condyloma acuminata in the geno-anal area, linea pedis and seborrheic dermatitis. Antinuclear factors were slightly positive, with 1:5000s, but no antibodies against DNA were negative. Wassermann and VDRL test were negative. The leukocyte count was 3.0 x 10³/μL, hemoglobin 12.1 g/dL and thrombocytes 335 x 10³/μL. Her CD4 cell count was 140 x 10³/μL. The patient classified for B3 according to the revised CDC-classification system for HIV-infection (9). Her current medication included didanosine 2 x 200 mg daily and 3 x trimetropim 160 mg/sulfamethoxazole 800 mg once a week. The patient had documented palmar erythema since 1987, but starting at the beginning of 1995 increasing redness and swelling occurred on both hands. Pain increased in a warm environment and decreased under cold water rinsing. Physical exercise worsened the signs and symptoms. Clinical examination revealed hyperemic and warm hands (Fig. 1). The fingers were swollen and slightly painful. At the time of examination she showed dry skin, condyloma acuminata in the perianal and vulvar region, numerous molluscus contagiosus on the face and flat warts at the dorsum of the hands. Furthermore, she had marked seborrhoeic dermatitis and linea pedis.

DISCUSSION
The pathogenesis of red, warm, swollen and painful extremities remains unclear. In patients with essential thrombocythemia or polycythemia vera, erythromelalgia is caused by rheological problems. Medication against thrombocytotic aggregation leads to marked improvement. In patients with secondary erythromelalgia an autoimmune disease may be involved and has been discussed recently by Drenth et al. (10). Jain et al. (11) reported on a series of patients with periangual and acral erythema in those patients with HIV-infection. An autoimmune process was also suggested for this phenomenon. Secondary erythromelalgia is known under medication with calcium channel blockers but has not been observed in combination with didanosine or trimetropim/sulfamethoxazole. In a patient under didanosine Pedailles et al. (12) have observed acral erythema which appeared 9 days after the introduction of the drug. The erythema was painful and accompanied by swelling. However, bullous lesions with following desquamation were observed. The skin changes disappeared within a few days, although the drug was continued. In our patient the appearance of erythromelalgia and drug ingestion did not coincide. In addition, the natural course in our patient was persistent over 9 months. Erythromelalgia in HIV-infected patients may represent a major form of periangual erythema. Further studies are necessary to clarify the pathogenetic relationship of erythromelalgia and HIV-infection.

Fig. 1. Red, swollen hands which differ markedly from a control.
Multiple Facial Cylindromas in Twins

Sir,

We describe the clinical case of a pair of twin brothers and their mother, who presented with numerous, central-facial cylindromas, which had suddenly appeared.

CASE REPORT

Two 18-year-old men, twin brothers, attended our outpatient clinic because of the sudden progressive appearance of numerous solid tumours, normal skin-coloured, in the central facial area, around the nose and the internal cheek zone (Fig. 1a,b). The tumours had begun developing at the age of 15, and from then new tumours arose and other increased in size, forming a plaque with diverse papules and little nodules assembled. One of the patients presented a unique solid papule in the scalp. Any other clinically relevant antecedent, general or cutaneous, was absent. Since her youth their mother also suffered from a few tumours, in her face like those of her sons. Punch biopsies from the brothers were taken in the face and the scalp with the clinically oriented diagnosis of sebaceous adenoma. Histological examination confirmed the histological diagnosis of cylindroma in the face, but the nodule of the scalp was a trichoepithelioma.

DISCUSSION

The common location of cylindroma is in the scalp, but other areas, such as face, neck and trunk, can also be involved. They are occasionally associated with trichoepithelioma. In our patients the facial location in identical twin brothers and their mother as well is the presence of a solitary trichoepithelioma in the scalp in one are especially worth pointing out. Only one similar case was described of a pair of twin brothers, aged 45 years, with multiple cylindromas located in the scalp in turban distribution. Their mother, aged 92, had suffered from such a tumour since her thirties, and their sister presented trichoepitheliomas in the face (1).

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**Fig. 1a,b. Tumour in the central facial area of twin brothers.**