

Studies on Erythromelalgia

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Ole Magne Kalgaard, a dermatologist, defended his PhD thesis on erythromelalgia on 20 April 2012 at the University of Oslo, Norway. The thesis supervisor was Professor Knut Kvernebo, Department of Thoracic Surgery, Oslo University Hospital. The first opponent was Professor Mark Davis, Department of Dermatology, Mayo Clinic, Rochester, USA. The second opponent was Professor Knut Gjesdal, Department of Cardiology, Oslo University Hospital. Ole Magne Kalgaard was formerly a Research Fellow at the Department of Dermatology, Oslo University Hospital Rikshospitalet, and is now in private practice in Oslo.

The main aim of the thesis, which is entitled “Erythromelalgia – clinical aspects, pathology and therapy”, was to gain a better understanding of the clinical picture and pathogenesis of erythromelalgia.

The study reported in the paper “Erythromelalgia: a clinical study of 87 cases” demonstrated the heterogeneity of erythromelalgia in terms of its aetiology, severity and prognosis (1). This improvement in understanding of the clinical picture and classification of patients enabled further research to be carried out on pathogenesis and therapy.

The study reported in the paper “Nonspecific capillary proliferation and vasculopathy indicate skin hypoxia in erythromelalgia” found capillary proliferation and vasculopathy compatible with hypoxia in a smaller group of the total patient material, lending support to the vascular hypothesis of erythromelalgia, arteriovenous shunting and resulting hypoxia (2). These findings are compatible with the pre-study hypothesis that recurrent episodes of skin hypoxia in selected patients may lead to micro-vascular injury followed by vascular proliferation. However, it should be emphasized that most of the

histopathological findings were, in fact, normal, and that firm conclusions cannot be drawn. Histological examinations cannot be used for the diagnosis of erythromelalgia.

The data in the paper “Impaired neurogenic control of skin perfusion in erythromelalgia” demonstrate that asymptomatic patients with primary erythromelalgia have reduced cutaneous perfusion preceding provocation and impaired central sympathetic vasoconstrictor reflexes (3). Local autonomic reflexes and endothelial function are intact. These findings provide support for the existence of efferent thin fibre neuropathy and denervation hypersensitivity in at least some patients. Further studies are needed to determine whether the erythromelalgia-associated neuropathy is primary or secondary. The vascular and neuropathic hypotheses of pathogenesis are not mutually exclusive, as arterioles, shunts and venules are partially under neurological control. The findings in this paper are compatible with the hypothesis of a “final common vascular pathway”.

The paper “Prostacyclin reduces symptoms and sympathetic dysfunction in erythromelalgia in a double-blind randomized pilot study” demonstrated a positive effect on erythromelalgia



Fig. 1. Ole Magne Kalgaard defended his thesis in University of Oslo on 20 April 2012.



Fig. 2. Professor Mark Davis, from the Mayo Clinic in Rochester, USA, was first opponent.

patients of the prostacyclin analogue iloprost (4). This supported the performance of a subsequent therapeutic trial with commercially available oral prostaglandin E1 (misoprostol), which showed a positive effect of misoprostol on erythromelalgia patients and has become a well-documented treatment alternative in erythromelalgia. The mechanism of action of prostacyclin may, at least in part, be to redistribute skin perfusion, and thereby enhance the oxygenation of skin tissue.

Erythromelalgia should be considered a symptom diagnosis, due to a microvascular response with microvascular arterio-venous shunting, rather than a separate disease entity.

References

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4. Kalgaard OM, Mørk C, Kvernebo K. Prostacyclin reduces symptoms and sympathetic dysfunction in erythromelalgia in a double-blind randomized pilot study. *Acta Derm Venereol* 2003; 83: 442–444.