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Case Reports

Sweet's Syndrome in a Patient with Oral Cancer Associated with Radiotherapy

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Approximately 10–20% of the reported patients with acute febrile neutrophilic dermatosis (Sweet's syndrome) have an associated neoplasm. Oral findings of Sweet's syndrome are rarely reported, and no cases in patients with oral cancer have been reported to date. This report describes the clinico- and histopathological findings of Sweet's syndrome in a patient with oral cancer, treated with radiotherapy. After 10 fractions of external beam radiotherapy, treatment was interrupted because of severe oral mucositis which extended beyond the radiation fields. Two days later the patient developed multiple tender skin lesions and the diagnosis Sweet's syndrome was made. Skin and oral lesions resolved without additional treatment and did not recur upon resuming radiotherapy. As suggested in previous case reports, tumour antigens might play a role in the development of Sweet's syndrome. In this case, irradiation therapy may also have been a trigger for this syndrome. Copyright © 1996 Elsevier Science Ltd

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INTRODUCTION

Acute febrile neutrophilic dermatosis (Sweet's syndrome) was first described by Sweet in 1964 [1]. It is characterised clinically by the sudden appearance of multiple erythematous nodules and plaques on the skin, leucocytosis and fever. Histological examination reveals a dense dermal inflammatory infiltrate composed mainly of polymorphonuclear leucocytes. Systemic steroids are often used for treating this condition, but recurrences are commonly described [2–7].

Sweet's syndrome can be classified into three sub-types: (1) associated with haematological disorders; (2) associated with solid tumours; and (3) idiopathic or associated with various other disorders [2]. The last category accounts for most (80–90%) of the reported cases of Sweet's syndrome [3].

We report a case of Sweet's syndrome associated with radiotherapy in the treatment of an oropharyngeal squamous cell carcinoma, which, to our knowledge, has not previously been described.

CASE REPORT

In July 1994, a 58-year-old Caucasian female was seen by her family physician. She had a left earache radiating to the mandible and also noted an ulcer at the left lateral base of the tongue. She was a smoker (25 cigarettes a day for many years) and a non-drinker. Physical examination revealed a tissue defect on the lateral aspect of the anterior two thirds of the tongue ($4.0 \times 2.0 \times 1.5$ cm). There was no extension into the floor of the mouth, and no lymphadenopathy was noted. A biopsy under local anaesthesia showed squamous cell carcinoma, and the tumour was classified as T2N0M0. In August 1994 she was referred for treatment. It was planned to treat the tumour with a high dose rate iridium implant delivering a dose of 2000 cGy in five fractions over $2\frac{1}{2}$ days followed by external beam radiotherapy to a dose of 5000 cGy (unilateral wedge pair) in 20 fractions. On 30 August, she was admitted to hospital for implant placement under general anaesthesia. No complications occurred and she was discharged after 5 days. On 6 September, external beam radiotherapy was started.

After 10 fractions (=2500 cGy), radiotherapy was interrupted because of severe oral mucositis and on 21 September (day 1) she was re-admitted to the hospital. The oral mucositis was marked by ulceration within the treatment field and lesions which extended to the oropharynx and to the mucosa of the right-hand side of the tongue and cheek, beyond the radiation fields. There were isolated rounded areas of ulceration that were felt to be consistent with Herpes virus reactivation (Figs 1 and 2). She had no prior history of oral

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Fig. 1. Severe oral mucositis marked by ulceration within the treatment field.

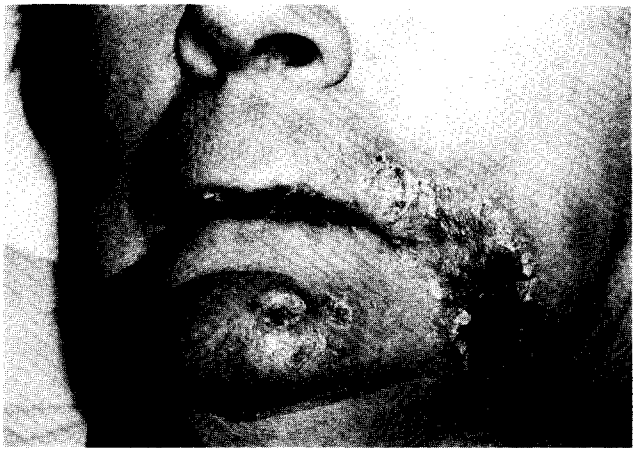

Fig. 3. A 7 cm ulcerated violaceous plaque covered with a haemorrhagic crust around the left corner of the mouth.

Fig. 2. Isolated rounded areas of ulceration on the oral mucosa and lower lip that were felt to be consistent with Herpes virus reactivation.

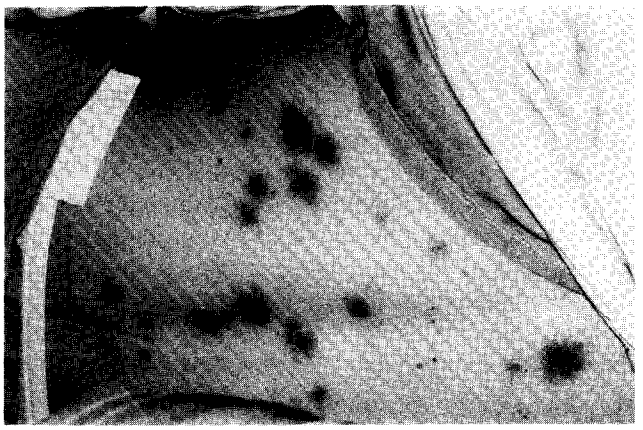

Fig. 4. Multiple erythematous, tender papules and plaques of Sweet's syndrome varying from 0.5 to 4 cm in diameter located on the back.

herpetic infection. White patches on an erythematous background suggested a secondary candidiasis. She experienced considerable pain and was unable to take anything by mouth other than small quantities of liquid. A percutaneous gastrotomy was placed and an intravenous (i.v.) line inserted. The patient was febrile (38.8°C/101.8°F). She was given fluconazole (100 mg, QD p.o.), acyclovir (250 mg, TID i.v.) and ciprofloxacin (500 mg, BID p.o.) until results of blood cultures, serology and oral swabs were available. She was also prescribed benzydamine HCl mouthrinse, chlorhexidine 0.2% mouthrinse, sucralfate suspension and morphine (15 mg q3h). Two days later she developed multiple erythematous, tender papules and plaques varying from 0.5–4 cm in diameter on the face, upper chest, back (Fig. 3) and posterior legs. These lesions were oedematous. There were scattered pustules within some plaques and some areas showed pseudo-vesiculation. Around the left corner of the mouth there was a 7 cm ulcerated violaceous plaque covered with a haemorrhagic crust (Fig. 4). The condition of the mouth remained unchanged with extensive non-specific mucositis. The neck was grossly swollen on the left side caused by lymphadenopathy. Radiographic examination of the chest revealed an infiltrate in the right lower lobe of the lung. At this time the patient was afebrile (37.2°C/99°F) and did not have any arthralgia, myalgia, conjunctivitis or recent upper respiratory tract infection. Pertinent laboratory findings included leucocytosis with neutrophilia (13.3×10^9 leucocytes/l with 79% neutrophils) and anaemia (haemoglobin = 9.8 g/dl). Specimens for

Fig. 5. Skin biopsy showing semidiffuse infiltrate, predominantly of neutrophils with perivascular accentuation (magnification ×30).

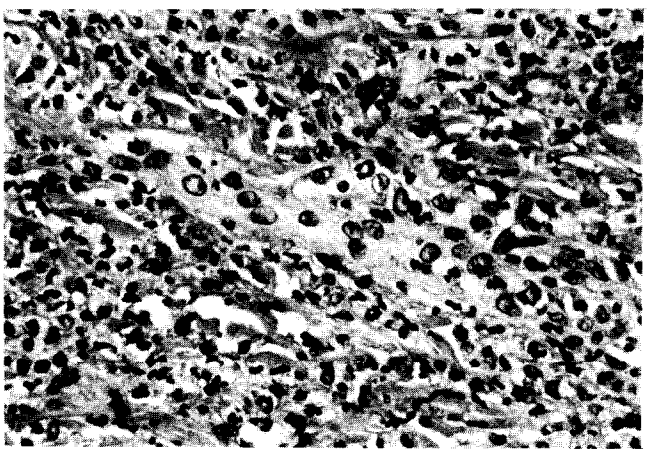

Fig. 6. Dermal blood vessel with endothelial swelling and perivascular infiltrate of neutrophils with scattered karyorrhexis (original magnification ×250).

Herpes Simplex and Varicella Zoster cultures and a biopsy were obtained from a lesion over the left upper back. Laboratory results were available on day 6. Viral cultures were negative and acyclovir was therefore discontinued. The biopsy (Figs 5–7) revealed a semi-diffuse infiltrate of neutrophils

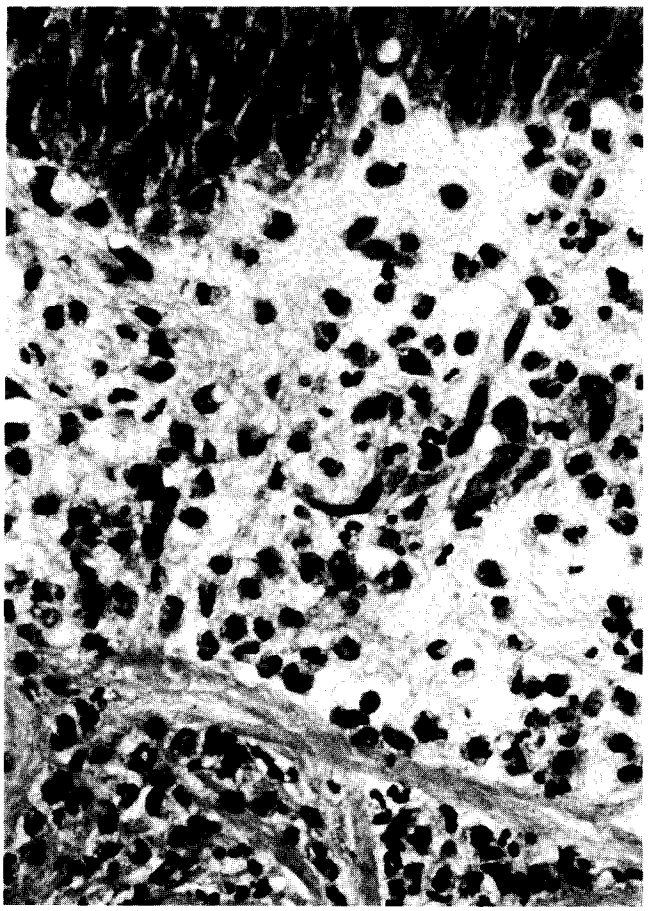

Fig. 7. Dermal oedema and neutrophilic infiltrate (original magnification ×350).

within the collagen and particularly around proliferating blood vessels with focal leucocytoclasis. In a few areas, the proliferating vessels were surrounded by reactive macrophages and lymphoid cells. The epithelium was benign and the upper dermis was oedematous. There was no evidence of microorganisms, and nothing suggestive of a viral effect. Based on clinicopathological findings the diagnosis of Sweet's syndrome was made.

On day 6, after re-admission, the skin and oral lesions showed improvement and the patient was afebrile. Over the next few days her situation improved further and a chest radiograph showed resolution of the lung infiltrate. On day 10 the patient resumed radiotherapy. Treatment was completed in 10 fractions over 6 days. On day 15 the medication was discontinued. The patient left the hospital in good condition 4 days later.

DISCUSSION

Su and Liu [8] proposed a set of two major and four minor criteria to be used in establishing the diagnosis of Sweet's syndrome. They suggested that a diagnosis requires that both major criteria as well as at least two minor criteria be fulfilled. The major criteria are: (1) an abrupt onset of tender or painful erythematous or violaceous plaques or nodules; and (2) a predominantly neutrophilic infiltration in the dermis without leucocytoclastic vasculitis. The minor criteria include: (1) illness preceded by fever or infections; (2) illness accompanied by fever, arthralgia, conjunctivitis or underlying malignancy;

(3) leucocytosis; and (4) a good response to systemic steroids and not to antimicrobials. Von den Driesch *et al.* [9] extended this system of criteria with the additional minor criterion of a erythrocyte sedimentation rate above 50 mm/h. In our opinion the diagnosis of Sweet's syndrome in the case presented above is justified because both major and three minor criteria were fulfilled.

Several investigators have suggested that an immunological mechanism has a role in the pathogenesis of Sweet's syndrome [10–12]. In contrast Cohen *et al.* [13] have suggested the possibility that pathogenesis may be secondary to an inappropriate secretion of one or more endogenous cytokines. Going [14] has also postulated that a cytokine may contribute to the aetiology of Sweet's syndrome. Although the cause of Sweet's syndrome is not yet clearly elucidated, it is widely believed to be a hypersensitivity reaction occurring after exposure to several possible triggers, such as viral, bacterial or tumour antigens. The case presented is the first case of Sweet's syndrome diagnosed in a patient with oral cancer and being treated with radiation therapy. Whether the tongue carcinoma or the radiotherapy was the trigger in this case is unknown. However, because the skin lesions healed after interruption of radiotherapy it may be likely that the radiation therapy was associated with the onset of Sweet's syndrome. The phenomenon of healing of the symptoms of Sweet's syndrome after removing the stimulus has been previously described. In one patient with recurrent episodes of Sweet's syndrome, all of the skin lesions were completely resolved within 4 days after resection of the tumour and did not subsequently recur [15]. In two other cases in which Sweet's syndrome was associated with kidney and liver disorders, clinical improvement occurred as a result of the treatment of the underlying disease [16]. Conversely, one might expect a recurrence of Sweet's syndrome upon resuming radiotherapy if radiation was assumed to be the only trigger in this case. An earlier onset of Sweet's syndrome would be expected if the presence of the tongue carcinoma was its only cause, because in the majority of the cases, solid tumour-associated Sweet's syndrome preceded the initial diagnosis of cancer [3]. On the other hand, cases have been reported in which Sweet's syndrome followed the development of a solid tumour [3, 4, 11, 17–19]. It seems likely that both radiotherapy and the presence of the tumour played a role in the aetiology in this case. A decreasing influence of tumour antigens as a trigger in course of time may then be an explanation for the fact that Sweet's syndrome did not recur upon resuming radiotherapy.

It is of particular interest that the clinical improvement occurred as a result of the interruption of the radiotherapy without treatment with corticosteroids. Healing of the skin lesions started on the day the results of the biopsy were available, making additional treatment unnecessary. A case with a similar short course of disease without steroid treatment was previously reported by Rahav *et al.* [20], who suggested the postponement of steroid treatment for 1 week in all patients with Sweet's syndrome.

Although oral lesions in Sweet's syndrome seem to occur more frequently than mentioned in earlier reports, involvement of the oral cavity is still rare. Cohen *et al.* [3] reviewed the world literature of 41 patients with solid tumour-associated Sweet's syndrome. They mentioned only one case with involvement of the oral mucosa. The oral and perioral manifestations in our case included extensive erythematous and ulcerated mucositis extending beyond the fields of radiation therapy, and angular cheilitis. The perioral lesions extended beyond the corner of the mouth and resulted in rounded ulcerations on the chin and the upper lip.

Another rare clinical manifestation in this case is lung involvement. To date, neither hepatic nor pulmonary manifestations of Sweet's syndrome have been described in patients with solid tumours. The clearance of the lung in connection with healing of the skin lesions was also remarkable.

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