Case reports

Hypertrichosis and multiple cutaneous squamous cell carcinomas in association with cyclosporin A therapy[1]

P S Mortimer MRCP
R P R Dawber FRCP
P J Morris FRCS
J F Thompson FRACS
T J Ryan FRCP
Department of Dermatology, The Slade Hospital, Oxford, and Transplant Unit, Nuffield Department of Surgery, Churchill Hospital, Oxford

The effectiveness of cyclosporin A (CyA) as an immunosuppressive agent in clinical organ transplantation is now clearly established. The immunosuppressive properties of the drug were first reported by Borel *et al.* in 1976, but its precise mode of action is still unknown. Present evidence suggests that it acts selectively against T lymphocytes, particularly the T helper cell subpopulation involved in graft rejection (for review *see* Morris 1983). This report concerns a renal allograft recipient who was changed to CyA therapy after 6 years of conventional immunosuppression with azathioprine and prednisolone and who, within 8 months of conversion, had developed 4 cutaneous squamous cell carcinomas and 3 premalignant keratoses, as well as marked hypertrichosis. Excessive hair growth is a well known yet poorly understood side effect of CyA therapy, but cutaneous tumour development has not previously been reported.

Case report

Mr AT (now aged 55) developed glomerulonephritis in 1967 and commenced maintenance haemodialysis in 1971. Following successful transplantation with a cadaveric kidney in 1976, immunosuppression was provided by azathioprine and prednisolone. Graft function was satisfactory during the following 6 years, but in March 1982 treatment was changed to CyA because of azathioprine intolerance, widespread purpura, and extreme skin fragility causing recurrent ulceration in response to trivial trauma. Azathioprine was discontinued at the time CyA was begun, and after 6 weeks a gradual reduction in the daily prednisolone dosage was commenced (Thompson *et al.* 1983). Within a month of conversion, before any reduction in the maintenance steroid dosage, a dramatic improvement in skin quality was noted, with decreased fragility and total disappearance of the purpura. Also apparent was a striking increase in body hair, particularly on the legs and forearms (Figure 1), and with significant regrowth on his bald scalp. By November 1982 the patient had developed several nodular skin tumours clinically resembling kerato-acanthomas on his forearms and face (Figure 2), having been completely free of skin lesions prior to conversion to CyA. Excision biopsies revealed 2 poorly differentiated squamous cell carcinomas (Figure 3), 2 well differentiated squamous cell carcinomas and 3 Bowenoid keratoses. The patient has since been converted back to azathioprine and prednisolone therapy, and has developed no further tumours.

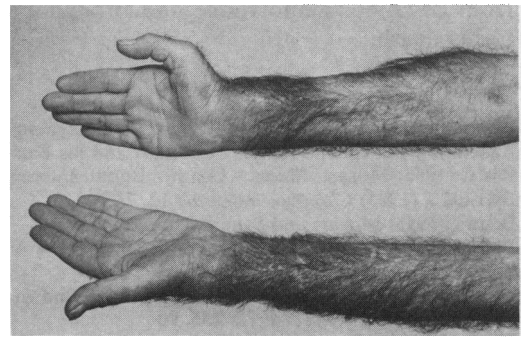

Figure 1. Hypertrichosis on forearms

Discussion

Excessive hair growth has been noted as a side effect in up to 44% of patients treated with CyA (European Multicentre Trial 1982, Canadian Multicentre Transplant Study Group 1983), and this has usually been referred to incorrectly as

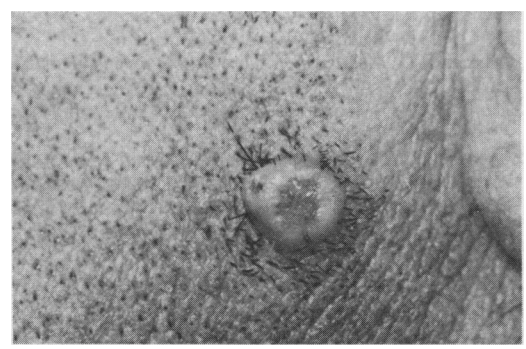

Figure 2. Squamous cell carcinoma anterior to left ear lobe

[1] Case presented to Section of Dermatology, 17 February 1983. Accepted 19 May 1983

0141-0768/83/090786-02/$01.00/0

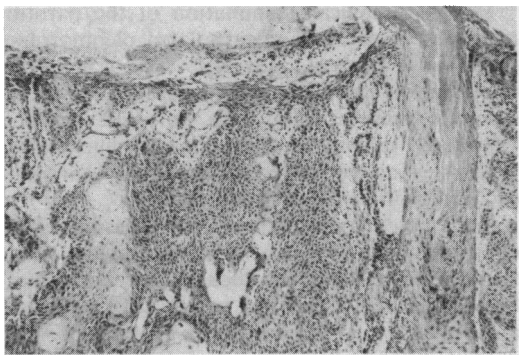

Figure 3. Photomicrograph showing moderately poorly differentiated squamous cell carcinoma. (× 160)

'hirsutism'. True hirsutism is hair growth restricted to part or all of the male sexual pattern, and implies androgen excess. In our patient and in others receiving CyA, excessive hair growth has not been restricted to the male distribution, and a recent report confirms that androgen levels are not raised (Margreiter *et al.* 1983). The term which should properly be used for the hair growth induced by CyA is 'hypertrichosis', meaning growth of hair excessive for the site on the body and for the age of the patient. The phenomenon has also been observed in nude mice treated with CyA (Pendry & Alexander 1982). As with other drugs such as phenytoin and minoxidil which cause hypertrichosis, the mechanism by which CyA stimulates hair growth is unclear.

The development of skin tumours in a patient receiving CyA has not previously been reported. Several forms of malignancy, including skin tumours, occur more frequently as a result of conventional immunosuppressive therapy (Penn 1981), but although an increased incidence of lymphomas has been recorded with CyA treatment (Morris 1983), no significant increase in the incidence of other neoplasms has been observed to date in patients receiving this drug. Our patient developed multiple synchronous squamous cell carcinomas and premalignant keratoses on light-exposed skin 8 months after conversion to CyA. It seems very likely that their development was related to administration of the drug, although the effects of 6 years of conventional immunosuppression and 55 years of ultraviolet light exposure presumably predisposed the patient to the development of skin malignancy (Sheil *et al.* 1979).

There is no known relationship between hypertrichosis and the development of cutaneous squamous cell carcinoma, but it would appear that in this patient CyA stimulated a proliferative response in both the skin and its appendages.

References

Borel J F, Feurer C, Gubler H U & Stahelin H
(1976) *Agents and Actions* **6**, 468–475
Canadian Multicentre Transplant Study Group
(1983) *New England Journal of Medicine* (in press)
European Multicentre Trial
(1982) *Lancet ii*, 57–60
Margreiter R, Spielberger M, Konig P, Steiner E, Kathrein H & Huber C
(1983) *Dialysis and Transplantation* **12**, 108–112
Morris P J
(1983) *Advances in Surgery* (in press)
Penn I
(1981) *Current Problems in Surgery* **18**, 713–720
Pendry A & Alexander P
(1982) In: Cyclosporin A. Ed. D J G White. Elsevier Biomedical Press, Amsterdam; pp 77–81
Sheil A G R, Mahoney J F, Horvath J S, Johnson J R, Tiller D J, May J & Stewart J H
(1979) *Transplantation Proceedings* **11**, 1052–1054
Thompson J F, Chalmers D H K, Carter N P, Wood R F M & Morris P J
(1983) *Transplantation Proceedings* (in press)

Dermatomyositis and salivary pleomorphic adenoma[1]

C A Holden BSC MRCP
R W Davis MB BS
D M MacDonald MA FRCP
Department of Dermatology
Guy's Hospital, London SE1

The previously unreported association of dermatomyositis and a salivary pleomorphic adenoma is described. Although considered overall to be benign, the parotid tumour showed some histological features typically associated with malignant mixed salivary gland tumour. Furthermore, the rapid response of the dermatomyositis to treatment following removal of the neoplasm may suggest a causative relationship.

Case report

A 71-year-old Caucasian woman was admitted with a three-week history of a florid red rash, typical of dermatomyositis, muscle weakness and general malaise. In addition, the patient had noticed swelling of the left-hand side of the face. Previously the patient had been well and had no other symptoms but was receiving thyroid extract for hypothyroidism, diagnosed in childhood.

[1] Case presented to the Section of Dermatology, 18 November 1982. Accepted 17 February 1983
Correspondence to D M MacDonald

0141–0768/83/090787–02/$01.00/0