

3. Morphologically it resembles acne conglobata, consisting of pustules and aggregations of nodules.

4. Culture of the abundant purulent discharge does not result in the growth of organisms recognised as pathogenic.

The affected areas are sharply demarcated from adjacent normal skin. The patients have no constitutional symptoms. The disease attains its maximum extent within a few weeks or months and usually resolves within a year, with minimal residual scarring. Discussion with our colleagues indicates that this disorder may be more common than is usually appreciated. It should be recognised as distinct from acne vulgaris but its pathogenesis remains a mystery.

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REFERENCES

1. Fulton, J. E., McGinley, K., Leyden, J. & Marples, R.: Gram-negative folliculitis in acne vulgaris. *Arch Dermatol* 98: 349, 1968.
2. O'Leary, P. A. & Kierland, P. R.: Pyoderma faciale. *Arch Dermatol Syphilol* 41: 451, 1940.
3. Plewig, G. & Kligman, A. M.: *Acne*. Springer-Verlag, 1975.

Malignant Angioendothelioma— Effect of Immunotherapy with *Corynebacterium Parvum*

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Abstract. An elderly patient with malignant angioendothelioma of the scalp is reported. Immunotherapy with killed *C. parvum* was used as an adjunct in treatment.

The majority of malignant vascular tumours are of subcutaneous or visceral origin and run a rapid

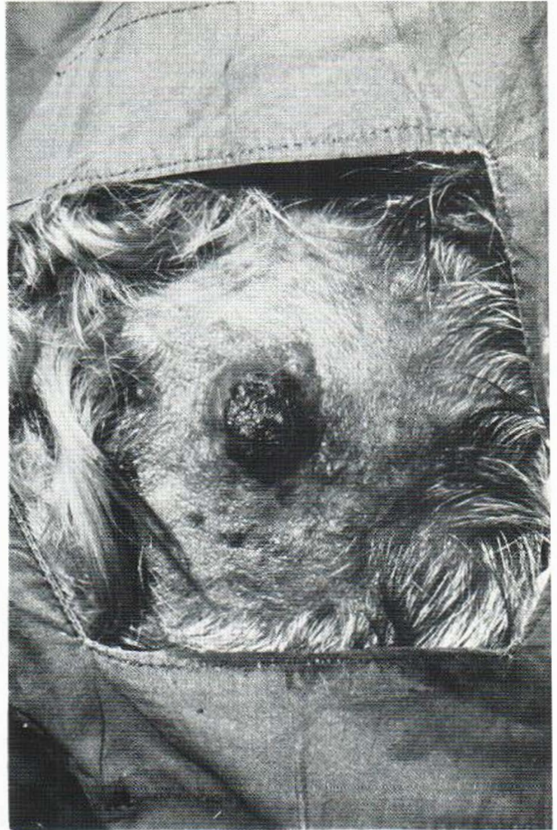


Fig. 1. Primary tumour.

course, with metastasis. Malignant angioendothelioma is a rare vascular tumour which Wilson Jones first delineated as a distinct clinical and histopathological entity (1). He reported nine elderly patients, seven of whom had rapidly progressive tumours of the face and scalp with metastases in unusual sites such as spleen, heart and intestines. Whilst radiotherapy may be palliative in most patients (2), wide excision with grafting appears to be the best form of treatment available at present.

This is a report of one patient with malignant angioendothelioma of the scalp who was treated initially by wide excision. Intratumour injection of killed *C. parvum* was then given in an attempt to control local recurrences.

PATIENT AND METHODS

A previously healthy man, aged 76 years, was seen in September 1974 with a three-month history of enlarging and bleeding nodules on the scalp. There had been no



Fig. 2. Histological appearances, $\times 50$.

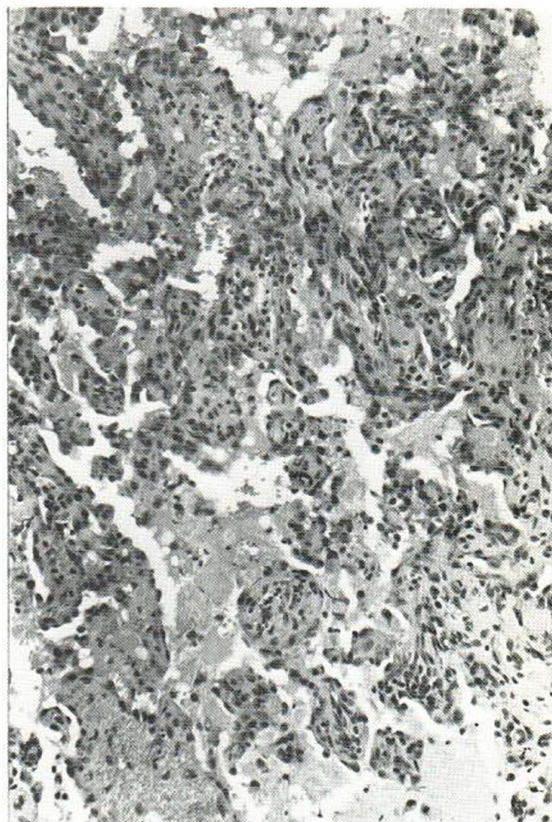


Fig. 3. Histological appearances ($\times 126$) showing numerous capillaries with ill-defined sheets of vasoformative spindle-shaped cells in the dermis.

preceding trauma or radiotherapy and no undue exposure to UVL. On examination three dark infiltrated and foul-smelling plaques with central crusts and a hyperpigmented edge were present (Fig. 1). In October 1974 the tumour was widely excised down to bone with a plastic repair of the defect. In January 1975 there was a local recurrence in the grafted area, with patchy infiltrated lesions in the centre of the graft which also had a violaceous edge. The patient subsequently developed several small haemoptyses and radiologically there were patchy opacities on the right upper and mid-zones and left mid- and lower zones. In January 1975 he was given cyclophosphamide intravenously 1 g daily for 5 days, but tolerated this treatment badly. It was then decided to try the effect of intralesional immunotherapy with *C. parvum*. However, his general condition continued to deteriorate and he died in February 1975.

Injection of killed C. parvum into tumour on the scalp

Dilutions of killed *C. parvum* in phosphate-buffered saline and 1% formaldehyde, 5.8 $\mu\text{g/ml}$, 46.9 $\mu\text{g/ml}$, 93.8 $\mu\text{g/ml}$ and 375 $\mu\text{g/ml}$ were prepared. This is the approximate range of doses which has been used to induce regression of tumours in mice (3). Each dilution (0.5 ml) was injected

into the tumour, the control being phosphate-buffered saline with 1% formaldehyde. The lesions were photographed and their outlines traced onto a transparent polythene sheet. Blood was taken to determine the titre of *C. parvum* antibodies.

It was planned to assess the area of the lesions weekly, reinject killed *C. parvum* on the 14th day, and repeat the blood titre of *C. parvum* antibodies on the 21st or 28th day.

Unfortunately, the patient died 7 days after the first injection of killed *C. parvum*. At post mortem there were foci of vascular tumour in lung, spleen and kidneys.

Histopathology

1. *Initial scalp biopsy.* Microscopically sections of both main and satellite nodules showed numerous capillaries along with ill-defined sheets of vasoformative spindle-shaped cells showing prominent mitoses in the dermis (Figs. 2 and 3).

2. *Scalp after injection of killed C. parvum.* Sections of the tumour from both injected and uninjected sites were obtained. The sections of uninjected tumour showed only a slight degree of necrosis, whereas those of the injected sites showed a much greater degree of necrosis of the



Fig. 4. Injection of killed *C. parvum*, $\times 75$.

tumour with an associated neutrophil polymorph infiltrate, but no lymphocytic reaction. The sections from tumour injected with 0.5 ml of 46.9 $\mu\text{g/ml}$ of killed *C. parvum* showed no viable cells (Fig. 4), whereas there were still viable tumour cells at the edge of the necrosis in all other sections.

DISCUSSION

Malignant angioendothelioma of the face and scalp in the elderly is a rare and rapidly spreading tumour which may metastasize to unusual sites such as the spleen (1). More than half of those affected are dead within 2 years of onset and many patients also suffer from unrelated medical conditions, as would be expected in the elderly (2). The best form of treatment of malignant angioendothelioma is wide excision with repair of the defect (4, 5).

The patient did well initially after wide excision with grafting which relieved his pain, bleeding and offensive odour.

The authors thought it worthwhile reporting the effects of local treatment with killed *C. parvum* on

the tumour recurrences. Intravenous injection of high doses of *C. parvum* has been shown to have antitumour effects in mice (6). However, intratumour injection of *C. parvum* is known to be more effective than intravenous injection in inhibiting tumour growth and prolonging survival time, producing systemic specific antitumour immunity and inducing complete regressions of tumours in mice (3). It appears that the mode of action of intratumour injected *C. parvum* is similar to that of B.C.G. in that a specific delayed hypersensitivity response to the infecting agent suppresses tumour growth non-specifically at the site of reaction (7, 8). However, *C. parvum* is effective in killed form, whilst with B.C.G. there is the danger of producing local and systemic infection.

Unfortunately, the patient died of disseminated disease before the effect of the injected *C. parvum* could be adequately assessed. However, this form of treatment appears safe and may be worth using earlier in the course of this almost universally fatal vascular tumour.

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REFERENCES

1. Wilson Jones, E.: Malignant angioendothelioma. *Br J Dermatol* 76: 21, 1964.
2. Wilson Jones, E.: Malignant vascular tumours. *Clin Exp Dermatol* 1: 287, 1976.
3. Scott, M. T.: *Corynebacterium parvum* as a therapeutic antitumour agent in mice. II. Local injection. *J Natl Cancer Inst* 53: 861, 1974.
4. Sanderson, K. V.: Tumours of the skin. In *Textbook of Dermatology* (ed. A. J. Rook, D. S. Wilkinson & F. J. Ebling), 2nd ed., vol. 2, p. 2000. Blackwell Scientific Publications, Oxford, 1972.
5. Mehregan, A. H. & Unsdck, H. E.: Malignant angioendothelioma. *Arch Dermatol* 112: 1565, 1976.
6. Scott, M. G.: *Corynebacterium parvum* as a therapeutic antitumour agent in mice. I. Systemic effects from intravenous injection. *J Natl Cancer Inst* 53: 855, 1974.
7. Zbar, B., Bernstein, I. D. & Rapp, H. J.: Suppression of tumour growth at the site of infection with living bacillus. Calmette-Guérin. *J Natl Cancer Inst* 46: 831, 1971.
8. Bartlett, G. D., Zbar, B. & Rapp, H. J.: Suppression of murine tumour growth by immune reaction to the bacillus strain of mycobacterium bovis. Calmette-Guérin. *J Natl Cancer Inst* 48: 245, 1972.