



Case report

'Proximal-type' epithelioid sarcoma: is Agent Orange still at large?

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Background and Aims: Proximal-type epithelioid sarcomas of the perineum are extremely rare. The authors provide an overview of this condition in relation to the history of exposure to Agent Orange.

Patient and Methods: A 54-year-old man presented with a rapidly growing perineal subcutaneous mass that was shown to be a proximal-type epithelioid sarcoma. The case is discussed. An Internet Medline search was performed and the current literature reviewed.

Results: Only 4 primary perineal sarcomas have been described in the literature. Epithelioid sarcomas are uncommon, aggressive tumours with a propensity for locoregional recurrence. They are recognised by the US Veterans Affairs department as linked to exposure to Agent Orange, an organochlorine defoliant containing the contaminant 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). However, the role of Agent Orange in sarcomagenesis is still controversial.

Conclusion: Unusual soft tissue swellings in a background of chemical exposure should be investigated thoroughly with a view to early, appropriate treatment.

Key words: Proximal-type epithelioid sarcoma – Agent Orange

Proximal-type epithelioid sarcoma is a rare variant of epithelioid sarcoma typically occurring in 'distal' locations like the hand or wrist.¹ Eighteen such cases are described in the literature,¹ as well as 4 primary perineal epithelioid sarcomas,² but no association between this entity and Agent Orange has been described.

Case report

A 54-year-old male presented with a 3-month history of an initially pea-sized perineal swelling gradually increasing in size. It was painless but uncomfortable on sitting. He had been exposed to Agent Orange for several hours at a time,

being unable to wash it off immediately during active military service in Vietnam.

Clinical examination showed a non-tender mobile, firm oval subcutaneous lump just to the right of the midline, measuring about 5 cm in size. Fine needle aspiration cytology (FNAC) of the specimen suggested a malignant tumour expressing both epithelial and mesenchymal immunohistochemical markers. Magnetic resonance imaging (MRI) of the pelvis confirmed an encapsulated 5-cm soft tissue mass (Fig. 1). A whole-body computerised tomographic (CT) scan showed no other lesions.

Resection revealed an encapsulated, haemorrhagic and focally fibrotic tumour (Fig. 2A) composed of large

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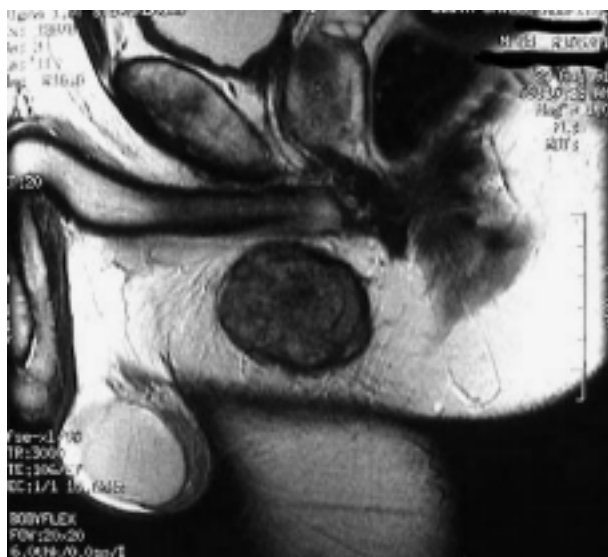


Figure 1 T2 weighted sagittal pelvic MRI scan showing the well-circumscribed lesion in the perineum.

ovoid cells with prominent nucleoli, with some cells showing spindle cell morphology (Fig. 2B). Immunohistochemistry was focally positive for cytokeratins – using antibodies MNF116 and AE1/AE3 (Dako) – and for vimentin. Endothelial markers (CD31, CD34 and factor VIII-RAg) were negative, excluding sarcomas of vascular origin.

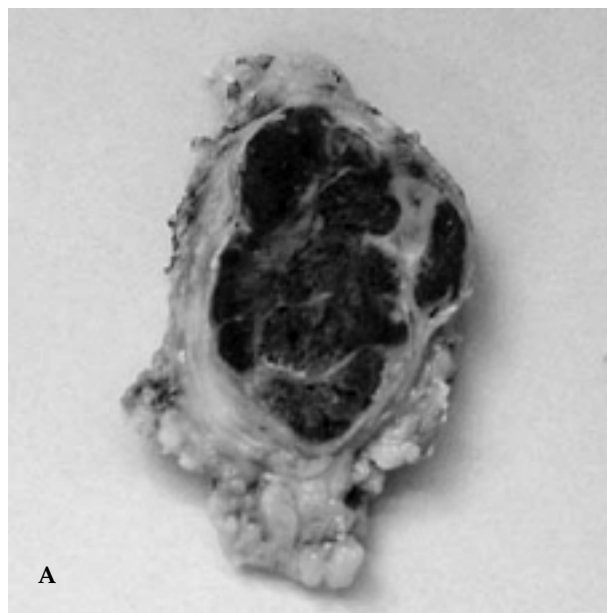
Overall morphological features and the pattern of immunohistochemical staining were those of an epithelioid sarcoma. The site of origin and clinical presentation were those of a proximal-type epithelioid sarcoma.

The patient remains well following chemoradiation.

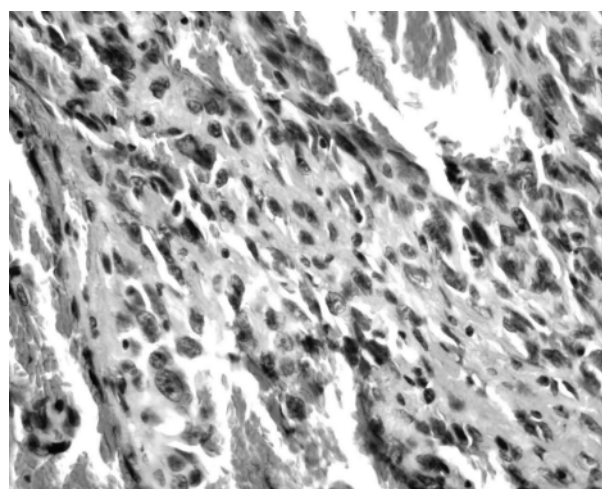
Discussion

Epithelioid sarcomas are aggressive, with a propensity for multifocal disease at presentation, local recurrence, regional (including lymph node) metastasis, and poor prognosis after regional or distant metastatic recurrence.³ Aggressive therapy including wide local excision and radiotherapy is therefore recommended.

Agent Orange is the name given to a herbicide used during the Vietnam War in ‘Operation Ranch Hand’. About 45 million kg of Agent Orange and other herbicides were used in Vietnam.⁴ It was used to defoliate base camps and other facilities in the US and other countries as early as the 1950s. Its constituents are 2,4-dichlorophenoxyacetic acid (2,4-D), 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), and its contaminant 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), otherwise known as dioxin. TCDD is implicated in the genesis of malignant tumours in Vietnam veterans. It is preferentially stored in body fat with an estimated half-life



A



B

Figure 2 (A) Gross section of tumour showing encapsulation, with prominent haemorrhagic spaces. (B) Micrograph of the tumour comprising of ovoid and spindle cells with vascular spaces (haematoxylin/eosin stain, high power).

of 11.3 years in Ranch Hand veterans.⁵ The role of Agent Orange in the genesis of soft tissue sarcoma (STS) remains controversial and not definitely proven,^{6,7} though TCDD has been categorised as a Group 1 carcinogen by a Working Group at the International Agency for Research on Cancer in Lyon, France.⁸ There are still on-going case-control studies looking into this.⁹ However, STSs are recognised by the US department of Veterans Affairs as related to herbicide exposure [Internet links: www.vba.va.gov/bln/21/benefits/Herbicide/AOno3.htm#top, www.va.gov/agentorange/docs/D04brief.pdf].

TCDD is known to suppress both innate and acquired immunity in humans,¹¹ but there have been no studies to show if this is linked to sarcomagenesis. Bacterial studies have not shown any TCDD mutagenicity,¹² though extrapolation of these results to humans remains speculative.

Kang *et al.* showed that Vietnam veterans had a higher incidence of STS though this was not statistically significant.¹³ Thoracic STSs have been described in patients exposed to Agent Orange, and an increased risk of STS in case-control studies on Swedish lumberjacks exposed to phenoxy herbicides has also been noted.⁴

Prolonged contact with our patient's perineal skin may have been a factor in the development of subsequent tumour, which may parallel the reported link between skin exposure to dioxin and development of basal cell carcinoma.¹⁰ However, there is no direct causal evidence that the authors can provide in this case. This is due to the rarity of the lesion and the unusual nature of the exposure.

Conclusions

Proximal type epithelioid sarcomas are uncommon and have not been described in a background of Agent Orange exposure. Clinicians presented with an unusual soft tissue lump in patients, particularly with a military background, need to look for a history of chemical exposure; this may extend to non-military personnel as well, such as Vietnamese immigrants. An accurate diagnosis is essential so as to institute early, appropriate treatment.

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