

# Squamous cell carcinoma of the palm after chronic organophosphate exposure

## Introduction

Squamous cell carcinoma of the palm is a rare cutaneous tumour of the hand (Rayner, 1981). While exposure to organophosphate flame retardant constituent chemicals such as tetrakis-hydroxymethyl phosphonium chloride (THPC) causes cutaneous squamous cell carcinoma in mice (Loewengart and Van Duuren, 1977), there is insufficient evidence to classify these chemicals as carcinogens in humans.

Figure 1. Palmar keratotic lesion at time of presentation.



Figure 2. Wide local excision of lesion with 1 cm margin.



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The authors present a case of squamous cell carcinoma of the palm in an elderly man who had had chronic dermal exposure to organophosphate flame retardants that may represent a potential causal factor.

## CASE REPORT

An 87-year-old retired research chemist and avid golfer (skin type Fitzpatrick type II) was referred to his regional plastic surgery unit by dermatology for treatment of a longstanding palmar keratotic lesion on his left non-dominant hand overlying his ring and little finger metacarpal heads (Figure 1). This had become painful during the preceding year and developed within a pre-existing golf-related callus which had been present since the age of 11 years.

As part of his national service at the age of 24 years, the patient had been recruited to a government-sponsored job taskforce to develop flameproof military uniforms using tetrakis-hydroxymethyl phosphonium chloride (THPC)-containing organophosphate flame retardants. According to the patient, over a 2-year period he had regularly wrung out clothing fabrics soaked in THPC using his bare hands.

Other relevant past medical history included basal cell papillomata of the back treated with cryotherapy 12 years earlier. His current medications included warfarin 5 mg once daily for atrial fibrillation and prednisolone 5 mg once daily for chronic pruritus. He had no known allergies. He had no family history of skin or other types of cancer. He was a lifelong non-smoker, drank approximately 7 units of alcohol per week, and had occasional unprotected sun exposure up until the age of 10 years and again at the age of 45 years when he lived in Hong Kong for 3 years. He did not report any background of significant skin damage secondary to sun exposure or human papilloma virus-related skin changes anywhere on his body.

His GP initially referred him to dermatology who prescribed keratolytic moisturisers to treat a presumed wart. He would cover his hand with duct tape to enable him to continue playing golf. He revisited his GP a year later with persisting symptoms of palmar pain and

## Discussion

Squamous cell carcinoma of the palm is a rare cutaneous tumour of the hand (Rayner, 1981). Reported potential risk factors include immunosuppression, excessive sun or

was re-referred to dermatology who arranged an urgent shave biopsy. Histology demonstrated a moderately differentiated squamous cell carcinoma extending to the deep margin of the shave with a minimal thickness of 1.2 mm. There was no evidence of lymphovascular or perineural invasion. The patient's case was discussed at the skin multidisciplinary team meeting.

A magnetic resonance imaging scan measured the lesion at 3x2x1.5 cm extending down to the flexor tendons and close to the palmar metacarpophalangeal joint capsules of the little and ring fingers. A wide local excision of the lesion using a 1 cm margin (including the metacarpophalangeal joint palmar plates and tendon sheaths of the little and ring fingers) was performed (Figure 2). A full thickness skin graft was used to reconstruct the defect pending histological analysis and hand therapy exercises were started 3 weeks after his operation so that at 2-month follow up, movement and grip strength were comparable to preoperative clinical examination (full range of active and passive movement and above average grip strength) allowing a return to usual activities of daily living including golf.

Although histology initially demonstrated complete excision (1.1 mm deep and 6 mm peripheral margins) of his moderately differentiated squamous cell carcinoma with no angiolymphatic or perineural invasion, he unfortunately developed recurrence as evidenced by the presence of a painful red nodule detected within his healed full thickness skin graft at his 4-month follow up (Figure 3). An urgent incision biopsy confirmed recurrence of squamous cell carcinoma (same histological sub-type to that initially excised) and it was decided at the following skin multidisciplinary team meeting that he should have an amputation of his little finger (Figure 4).

Figure 3. Resected area reconstructed with full thickness skin graft demonstrating signs of local recurrence.



Figure 4. Post-amputation of left little finger.



radiographic exposure, chronic burn injury, certain skin conditions (e.g. porokeratosis and/or hyperkeratosis, eczema, psoriasis, acrodermatitis chronica), and chronic exposure to chemical irritants such as arsenic (Swanbeck and Hillström, 1970).

While exposure to organophosphate flame retardant constituent chemicals such as THPC has been shown to cause cutaneous squamous cell carcinoma in mice, with a higher incidence of cellular atypia seen in mice exposed to ultraviolet B radiation and organophosphates (Loewengart and Van Duuren, 1977), there is insufficient evidence to classify organophosphate flame retardant constituent chemicals as carcinogens in humans (International Agency for Research on Cancer, 1990; National Research Council (US) Subcommittee on Flame-Retardant Chemicals, 2000).

The proposed mechanisms of carcinogenicity have been thought

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to relate to the possible formation of bis(chloromethyl)ether or reaction with guanosine at the 2-amino position to give N-[[bis(hydroxymethyl)phosphine]methyl], both potent human carcinogens (Van Duuren et al, 1978).

Flame retardants are a group of chemicals commonly used to coat household furniture, electronics and clothing to prevent or delay fire spread. Organophosphate flame retardants have widely replaced polybrominated diphenyl ethers as a result of concerns regarding carcinogenicity secondary to polybrominated diphenyl ether exposure (Linares et al, 2015). Exposure to organophosphate flame retardants can occur via inhalation, ingestion or dermal contact. A significant source of exposure occurs worldwide through polluted environments (World Health Organization, 1997) and in association with certain occupations (Bruchajzer et al, 2015).

The potential for delayed carcinogenic effects following chronic exposure to organophosphate flame retardants has been widely anticipated (Blum and Ames, 1977), despite relatively low risk assessment reports issued by both the World Health Organization and the European Union. However, high-level evidence supporting the carcinogenic potential of organophosphate flame retardants in humans is currently lacking. This case report supports further investigation into the carcinogenic potential of organophosphate flame retardants in humans. **BJHM**

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### LEARNING POINTS

- Squamous cell carcinoma of the palm is a rare tumour that should be managed by a skin multidisciplinary team including dermatology, plastic surgery, pathology, radiology and hand therapy.
- Early identification, surgical treatment and physiotherapy are often key to obtaining a favourable outcome with return to baseline function where possible, but despite these measures, there is still a high risk of recurrence.
- Organophosphate flame retardants are present on domestic furnishings, including electronics and clothing, and can be inhaled, ingested or absorbed through dermal exposure.
- There is currently no high-level evidence to support the carcinogenic potential of organophosphate flame retardants such as tetrakis-hydroxymethyl phosphonium chloride.
- This case report adds to the literature and supports further investigation into the relationship between organophosphate flame retardants and skin cancer.

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