

# Cutaneous haemangioendothelioma: a possible link with chronic exposure to vinyl chloride

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## Abstract

A patient who worked with polyvinyl chloride developed a malignant haemangioendothelioma of a toe. This rare tumour is more commonly found in the liver where it has been reported to arise in association with exposure to the vinyl chloride monomer.

Malignant haemangioendothelioma, or angiosarcoma, is a rare tumour of vascular endothelium. It may arise in any tissue but has been reported most commonly in muscle, bone, breast, and liver.<sup>1,2</sup> Cutaneous forms, first described by Wilson-Jones,<sup>3</sup> may arise in the scalp and face of elderly patients.<sup>4,5</sup> Both previous trauma and radiotherapy have been implicated in their aetiology.<sup>2,6</sup> The histological features are identical with those of the postmastectomy angiosarcoma (Stewart-Treves syndrome) that may occur in a chronically oedematous arm after mastectomy and radiotherapy.<sup>1,7</sup> Our patient developed a cutaneous haemangioendothelioma after working for many years with polyvinyl chloride (PVC); the monomeric form of which, VCM, has been incriminated in the development of similar tumours found in the liver.<sup>8,9</sup>

## Case report

A 55 year old man presented with a three month history of an ulcerating lesion affecting the nail bed of his third left toe. This had not responded to simple dressings and antifungal agents. He had worked in the plastics industry for many years first as a welder and then for 28 years as a moulder of polyvinyl chloride. His medical history was unremarkable, although two years previously he had developed a rash, thought to be psoriasis, which had spontaneously resolved. He had been a heavy drinker in the past and still consumed 20-30 pints of beer a week.

Examination of his toe showed the nail bed to be split by a raised moist lesion (fig 1). There was no

inguinal lymphadenopathy and no hepatomegaly. Radiographic examination of the toe was unremarkable and, with the exception of a mild rise in the hepatic enzymes, both haematological and biochemical results were normal, as was ultrasonic examination of the liver. The lesion was biopsied under local anaesthesia. Histological examination showed a malignant haemangioendothelioma with plump cells in a loose connective tissue stroma. In some places they were in clumps; in others they formed capillary sized channels with open lumina. There was pronounced cellular pleomorphism and many bizarre mitotic figures. Reticulin fibres were seen frequently around the cells (figs 2 and 3) and many of the cells were stained positively with factor VIII related antigen with silver enhancement and with a special lectin stain (UEA-1), a feature typical of tumours arising from vascular endothelium.<sup>10</sup> Amputation was carried out through the metacarpophalangeal joint. Twelve months later there was no evidence of local or distant recurrence.

## Discussion

Malignant haemangioendothelioma or angiosarcoma, although uncommon, may arise after exposure to certain chemical agents—for example, arsenic and thorium dioxide.<sup>10</sup> More recently a link has been well established between haemangioendothelioma of the liver and the production of polyvinyl chloride (PVC),



Figure 1 Tumour at presentation.

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that molecules from both VCM and, perhaps more important, its metabolites, appear in the skin of rats within hours of inhalation of  $^{14}\text{C}$ -labelled VCM.<sup>13</sup> and epidermoid carcinomas have been described in the facial areas of rats experimentally exposed to vinyl chloride.<sup>14</sup> There seems no doubt that some elements of the skin are susceptible to the oncogenic effects of VCM although, with the exception of liver malignancies, no increase in the incidence of deaths from cancers has been observed in man in association with exposure to VCM.<sup>15</sup>

To date, cases of haemangioendothelioma have been identified exclusively in workers engaged in the process of polymerising VCM to PVC but not in those exposed only to the finished polymer or processing it into plastic products. Although high levels are required, exposure need not be continuous.<sup>12,16</sup> Those who clean the pressure vessels used to polymerise vinyl chloride at high temperatures seem particularly at risk but hepatic tumours may also occur in production workers and others engaged in the industry.<sup>4</sup> During the manufacture of PVC some of the VCM remains absorbed on the finished polymer at a concentration of 0.005% or higher.<sup>19,20</sup> Release of small amounts of monomer may subsequently occur during handling and processing finished articles from raw PVC. The significance of this small exposure is uncertain.<sup>19,21</sup> Our patient had direct contact with PVC over many years and in moulding or welding PVC at high temperatures it seems likely that small quantities of the monomer may be released, although for practical purposes it is considered to be infinitesimally small and to be undetectable (B Bennett, personal communication).

The possibility that the lesion on the toe was a cutaneous metastasis from a primary hepatic tumour is excluded by the normal ultrasound of the liver and the continuing good health of the patient. The biochemical evidence of mild hepatic dysfunction probably reflects excessive alcohol consumption rather than exposure to VCM.<sup>22</sup> That the tumour in the present case was a subungual amelanotic malignant melanoma is excluded by the positive staining by specific histochemical markers for tumours of vascular endothelium. It is of interest, however, that Heldass *et al* raised the possibility that a causal relation might exist between exposure to VCM and the development of cutaneous malignant melanoma.<sup>23</sup> This association has not been confirmed by more recent studies.<sup>16</sup>

The relation of PVC manufacture to hepatic angiosarcoma was only firmly established in 1974 and the tumour is known to have a long latency (20–30 years). More cases may be expected to arise over the next three decades despite changes in legislation

to ensure that workers are exposed to lower levels of VCM.<sup>16</sup> If the cutaneous angiosarcoma in the present case has occurred as a result of exposure to VCM then similar lesions may be encountered in the future.

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July 9, 1986

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Re: JECFA Evaluation of  
Vinyl Chloride and DEHP

Dear Mike:

As you may be aware, the Food and Agricultural Organization (FAO) and World Health Organization (WHO) of the United Nations operates a group known as the Joint FAO/WHO Expert Committee on Food Additives (JECFA). This committee evaluates food additives and, while its decisions have no binding legal effect, it is quite influential in the United States and around the world. JECFA recommendations are used by other UN groups such as the Codex Committee on Food Additives (CCFA) and the Joint FAO/WHO Codex Alimentarius Commission as a basis for decisions on the safety of substances that are added to or contact food.

I recently became aware of the enclosed toxicological evaluations of vinyl chloride and bis(2-ethylhexyl) phthalate (DEHP). Although these evaluations are about two years old, I understand that they represent JECFA's current view. I thought that you might appreciate having a copy of this material to add to your data base. I have also included the introduction and index in the event you are interested in any other portions of the publication.

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