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Nasal squamous carcinoma in an undertaker – Does formaldehyde play a role?

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INTRODUCTION

There has been much public concern over the perceived health hazards of prolonged formaldehyde exposure. Formaldehyde resins are ubiquitous industrial chemicals present in adhesives utilized in particle board, veneer and plywood production, production of leather goods, permanent press fabrics, plastics, rubbers, shampoos and cigarette smoke. The release of formaldehyde vapour from urea formaldehyde foam insulation sparked much controversy, leading to the ban of this form of insulation in the United States in 1981. While it is well known that formaldehyde exposure may act as an irritant causing such symptoms as rhinitis, dermatitis and asthma, its affect as a carcinogen in humans is yet to be proven definitively.

Studies by Swenberg (1980) and Kerns (1983) have shown that high concentrations of formaldehyde vapour (5.6 ppm and 14.2 ppm) can induce squamous metaplasia and squamous cell carcinoma of the nasal cavity in rats. However, retrospective epidemiological studies fail to correlate formaldehyde exposure with death from nasal carcinoma in humans. Such has been the case in studying the mortality of embalmers (Levine et al., 1982; Walrath and Fraumeni, 1984), chemical plant workers (Liebling et al., 1984; Marsh, 1982), and pathologists (Harrington and Oakes, 1984), as well as numerous other epidemiological studies. The inherent error in studies based on mortality statistics in that squamous carcinoma of the nose is not always fatal, especially when diagnosed early. In addition, nasal carcinoma is altogether a rare lesion compromising 0.25 to 0.50% of all cancers so that even large cohort studies have a small chance of evaluating excess risk. Alternatively, publication by Olsen et al. (1984) and Hayes et al. (1986) utilizes case control studies in an attempt to sort out the independent variable of exposure to formaldehyde and wood dust, a known carcinogen. The findings suggest a small but statistically significant rise in relative risk of developing nasal squamous carcinoma in workers exposed to formaldehyde vapour with low or nil exposure to wood dust.

A solitary case of nasal carcinoma in a worker exposed to formaldehyde has been documented in the literature. Halperin et al. (1983) reported the case of a 57 year

old man with a 25 year exposure history to low concentrations of formaldehyde in a fabric finishing plant. Similarly, we report here a case of nasal carcinoma in a patient who had two sources of formaldehyde exposure, as an embalmer, and as an occupant for a home with recently installed urea foam insulation. While case reports do not establish causality, they serve to indicate the potential for health hazard posed by this ubiquitous chemical. It is therefore encumbent upon the otorhinolaryngologist to document a detailed exposure history for both home and workplace when faced by similar such cases.

REPORT OF CASE

Occupational History

The patient is a 63 year old white Italian male who was the proprietor of a funeral home established in 1950. He embalmed cases until his retirement in 1974, for a sum total of 728 cases. During embalming procedures, formalin was instilled through a closed pumping system. The attendents would usually wear paper "operating room-like" masks. Prior to becoming an embalmer, the patient worked in the United States Armed Forces as a diver. He states that only occasionally he would do pipe fitting work, involving welding. The patient smoked a pipe for approximately 40 years. He also did wood working as a hobby which involved occasional drilling and generation of wood dust. In September, 1980, his home was insulated with a urea foam compound. He states that the formaldehyde fumes were severe enough to prevent anyone from entering the top floor of his home. The instillation of exhaust fans in his home did not remedy this. Subsequent measurements in July, 1980 revealed formaldehyde levels of approximately .6ppm.

CLINICAL HISTORY

The patient noticed bleeding and soreness of his nose in June, 1980. Examination revealed an ulcerated mass on the right anterior nasal septum, extending approximately 2 cm from the mucocutaneous border of the columella to the superior margin of the nasal valve. No adenopathy was palpated. Biopsy was positive for well differentiated squamous cell carcinoma. The tumour was approached via an alar incision and excised in its entirety. Histology revealed in situ, well differentiated squamous cell carcinoma with microinvasion, margins free of tumour (Figure 1).

In October, 1981, he presented with a right upper cervical mass, present and increasing in size over a few months. Right radical neck dissection was performed with five lymph nodes found to be positive for metastatic carcinoma. He was then treated with 5400 rads to the right neck. He remains free of tumour to this present date.

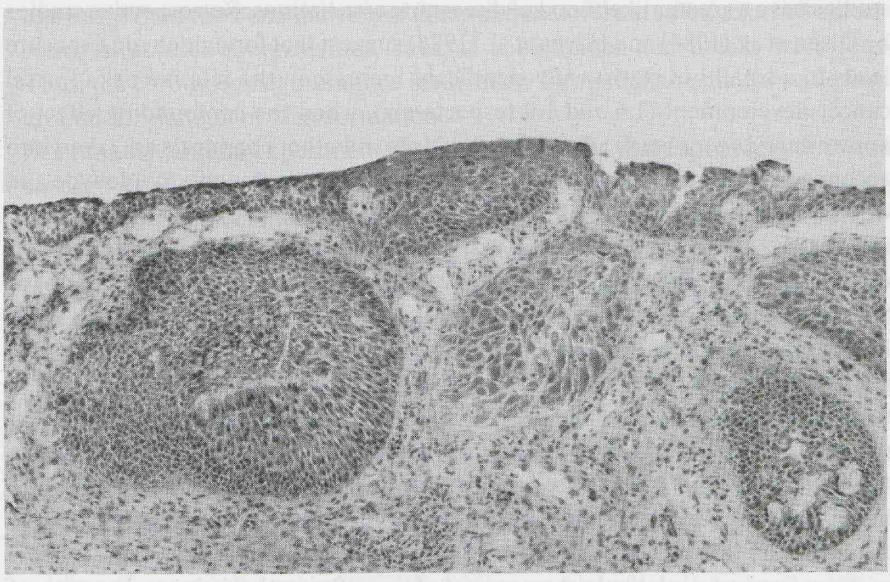

Figure 1. Photomicrograph of surgical specimen showing microinvasion of well differentiated squamous cell carcinoma. (Hematoxylin and eosin, 40X original magnification.)

DISCUSSION

The difficulty in detecting an increased risk to the development of nasal carcinoma after prolonged formaldehyde exposure lies in the rarity of this lesion in the general population and in the prolonged induction period. The patient had well documented exposure to formaldehyde over 24 years that he worked as an embalmer. The use of formaldehyde solution in the embalming of human bodies lasts from 1/2 hour to 1 hour per case with an estimated exposure level of .25 to 1.3ppm. For the eight months prior to the discovery of his nasal tumour, he was further subjected to exposure of formaldehyde vapour from newly installed urea foam insulation in his home. Ambient formaldehyde levels of approximately 0.6ppm were found in the home. The maximum accepted concentration of formaldehyde in the work place was determined to be 1.0ppm by OSHA (Occupational Safety and Health Agency). However, this figure is thought to decrease for homes insulated with urea foam. In addition, this patient had brief or occasional exposure to other risk factors such as welding and woodworking (Hernberg, 1983).

Early epidemiological studies searching for an increase in nasal carcinoma by utilizing death certificates in cohort with known formaldehyde exposure lack statistical power and have been unsuccessful. This approach is also limited by the generally non-fatal nature of this disease, as in this present case. Case control

studies have a greater likelihood of discerning associations. Retrospective studies by Olsen et al. (1984) and Hayes et al. (1986) suggest that formaldehyde exposure leads to a small but statistically significant increase in the relative risk of nasal cancer development (1.6 and 1.9 respectively), when the confounding effect of known carcinogens, such as wood dust, paints and other chemicals are taken into account. It has been suggested that the combined exposure to formaldehyde and wood dust has an additive effect (Olsen, 1984). Soft wood dust (birch, aspen, spruce, pine) have been associated with the development of nasal squamous cell carcinoma (Hernberg, 1983) while hardwood exposure (furniture woods) have been associated with adenocarcinomas (Acheson, 1972; Heinberg, 1983; Klintenberg, 1984).

It is generally held that the latency period for the development of an upper airway tumour is at least 10 years; and the latency period for development of nasal carcinoma has been suggested to be as long as 15–25 years (Olsen et al., 1984) and even 40–45 years (Willis, 1982) after primary exposure. Our patient had an exposure history starting 35 years before the development of this tumour. It is speculative as to whether the urea foam insulation in his home further promoted this tumour as it was present a relatively short period of time (9 months) prior to diagnosis of the tumour.

Compelling evidence as to the carcinogenicity of formaldehyde comes from rat and mouse studies. Swenberg et al. (1980) demonstrated a nasal tumour incidence of 20% in rats killed after 18 months of exposure to high levels (15ppm) of formaldehyde. Epithelial dysplasia and squamous metaplasia were found at all concentration exposures (2,6 and 15ppm) and were dose related. The incidence of nasal carcinoma in mice in these studies was lower. This was thought to be due to a lower delivered dose which is dependent upon minute volume and nasal surface area (both less in mice). In addition, formaldehyde does induce a greater degree of cell turnover in rat respiratory epithelium than it does in that of mice. It is known that formaldehyde may increase cell turnover rates in rats nasal mucosa 10–20 times (Kerns et al., 1983). While there is no comparable study in humans, this prospect is not unlikely.

Experimental work has shown that formaldehyde acts as a weak mutagen. The property which makes it quite useful to the pathologist and histologist also may case it to be an inducer of neoplasia; that is, its ability to covalently bind DNA. Chromosomal rearrangement and gene mutagenesis have been found in Drosophila fed with formaldehyde treated food or injected with formaldehyde solution. It has also been shown to produce mutations in neurosporia and aspergillus, and in some mammalian cell cultures (Griesemer et al., 1982). Formaldehyde has been utilized in sterilizing dialyzers and dialysis machines. Goh and Cestero (1982) studied 40 patients undergoing dialysis and estimated as much as 126.75 ± 50.84 mg of formaldehyde may be received during maintenance hemo-

dialysis. When the bone marrow of these patients were studied, marked chromosomal structural abnormalities, such as aneuploides and breaks were found. Thus, the chromosomal mutations incurred by formaldehyde may provide fertile ground for malignant transformation.

In summary, animal experiments have demonstrated that formaldehyde is a carcinogen when inhaled in high concentrations. Cohort studies to date have shown but a minimal association between formaldehyde exposure and development of nasal carcinoma. This may be due to the rarity of this tumour and long latency period. Squamous cell carcinoma is most probably the result of multiple promotors, chemical and possibly viral; but this remains to be experimentally defined. In this case a nasal squamous carcinoma was observed in a retired undertaker after a latency period of 36 years. Additional prospective long term epidermological studies are necessary before the role of formaldehyde in the development of human nasal carcinoma can be fully evaluated. In the meantime, the practicing otorhinolaryngologist should carefully consider and document all possible risk factors when faced with a patient with nasal carcinoma.

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