

## Chromium-induced carcinoma in the nasal region. A report of four cases\*†

Nobukiyo Satoh, Satoshi Fukuda, Masahiko Takizawa, Yasushi Furuta, Masaaki Kashiwamura, Yukio Inuyama

Department of Otolaryngology, Hokkaido University School of Medicine, Sapporo, Japan

### SUMMARY

*The carcinogenicity of chromium is well established in chromium-induced lung cancer. As of yet, however, there have been only few reports of head-and-neck cancer induced by chromium. We report four cases of carcinoma in the nasal region which seemed to be induced by chromium. All patients have worked at the same chromate factory for 19 to 32 years. The first patient has suffered from squamous cell carcinoma of the left nasal cavity, starting 11 years after his retirement. He received radiotherapy followed by surgery. A malignant fibrous histiocytoma occurred in his left upper gingiva in a previously irradiated region, 7 years after the previous treatment. Surgery and chemotherapy for palliation failed to control the tumour, and he eventually expired. The other three patients underwent lobectomy for lung cancer. In cases 2 and 3, the tumour occurred in the left nasal cavity six and ten years, respectively, each after the lobectomy. In case 4, the tumour arose from the nasopharynx 15 years after the lobectomy. These patients are alive and well without any sign of tumour. The presented cases seem to be induced by long-term exposure to chromium. We conclude that regular physical examination of chromate workers is mandatory for the early detection not only of lung cancer but also of head-and-neck cancer.*

*Key words: chromium, carcinoma, nasal cavity, carcinogenicity*

### INTRODUCTION

Chromium has been identified as a possible carcinogenic agent, particularly in the lower respiratory tract (Pheil, 1935). Although the upper respiratory tract is considered to be the most likely site for direct exposure to chromium, there have been only few reports of chromium-induced carcinoma in this region. Hueper (1966) has reported 187 cases of respiratory tract cancer in chromate workers. Among these, cancer of the nasal cavity is limited to six cases.

In this paper, we report four cases of carcinoma of the nasal region which seem to be induced by chromium, and we review the literature.

### SUBJECTS

All patients were male workers of the same chromate factory for 19 to 32 years. Table 1 summarizes the clinical data of the patients.

The first patient, 56 year old, suffered from squamous cell carcinoma of the left nasal cavity, starting 11 years after his retirement. He received radiotherapy followed by surgery. A malignant fibrous histiocytoma occurred in his left upper gingiva in a previously irradiated area, 7 years after the previous treatment. Surgery and chemotherapy for palliation failed to control the tumour, and he eventually expired.

The other three patients underwent lobectomy for lung cancer induced by chromium. The histological typing of the lung tumour was squamous cell carcinoma in all cases. In cases 2 and 3, the tumour occurred in the left nasal cavity six and ten years, respectively, each after lobectomy.

In case 4, the tumour arose from the nasopharynx 15 years after lobectomy. These three patients have been free of tumour. (Two typical cases are presented in the following case reports.)

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Table 1. Summary of four patients with chromium-induced carcinoma in the nasal region.

No.	case	region	histology	(1)	(2)	(3)	(4)
1.	56y. M	left middle turbinate	moderately differentiated SCC	28y	-	-	40y
2.	53y. M	left nasal floor hard palate	moderately differentiated SCC	25y	+	30y	36y
3.	67y. M	left middle turbinate	poorly differentiated SCC	19y	+	21y	31y
4.	74y. M	nasopharynx	poorly differentiated SCC	32y	+	34y	49y

(1) period of working for the industry; (2) complication of lung carcinoma; (3) time of origination of lung carcinoma after first exposure to chromium; (4) time of origination of nasal carcinoma after first exposure to chromium.

### Case 1

A 56-year-old man was referred from the Department of Internal Medicine to our department in January 1982. He had worked in the chromate factory of Nihon Denkoh, Co., Ltd. from 1942 to 1970. He had received regular lung examinations at the factory since his retirement. The result of sputum cytology revealed atypical cells in December 1981. He had noticed epistaxis and nasal obstruction for a long time.

Rhinoscopic examination showed a perforation of the nasal septum and a papillomatous tumour on the middle turbinate. An X-ray demonstrated a massive lesion in the left nasal cavity (Figure 1). A biopsy of the left middle turbinate revealed a moderately-differentiated squamous cell carcinoma.



Figure 1. X-ray of the nose of case 1. Massive lesion in the left nasal cavity and slight sinusitis in the left maxillary antrum were demonstrated.

He was admitted to our hospital and underwent partial resection of the left maxilla in February 1982. Recurrence occurred in the posterior wall of the maxillary sinus 7 months after surgery. The tumour was resected again followed by radiotherapy at a dose of 52.5 Gy with  $^{60}\text{Co}$ .

Although the patient had been tumour-free for 7 years since the initial treatment, a dark-red and easily bleeding tumour occurred on the left upper gingiva and in the left

maxillary sinus in July 1989. Computed tomography (CT) showed a distinct tumour mass with bone destruction (Figure 2). Histological examination of the tumour revealed a spindle cell carcinoma. So he underwent partial maxillectomy; microscopical examination of the surgically resected specimen showed proliferation of spindle and oval atypical cells with polymorphism (Figure 3). The final diagnosis was malignant fibrous histiocytoma. Although the patient twice underwent surgical resection and cisplatin-based chemotherapy, the primary tumour could not be controlled and lung metastasis occurred. He died on January 24, 1990.

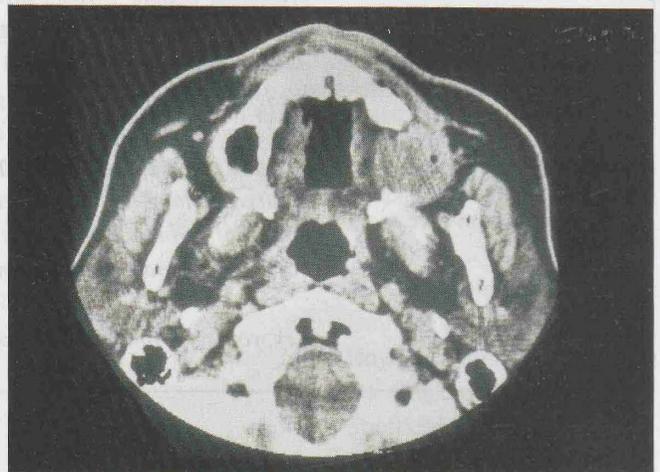


Figure 2. CT of case 1. The distinct tumour mass has destroyed the left maxillary bone.

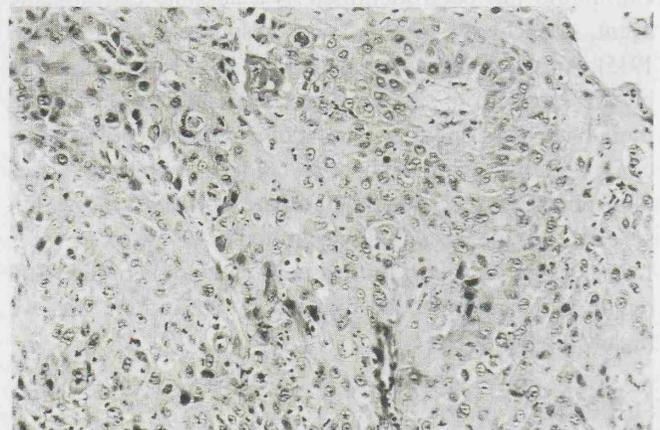


Figure 3. Microscopical finding of case 1. The proliferation of spindle and oval atypical cells with polymorphism were demonstrated. The final diagnosis was malignant fibrous histiocytoma.

### Case 2

A 53-year-old man was referred to our department in March 1984, because he had noted a mass on the left hard palate and bloody sputum since one month. He had worked in the same factory as the other patients from 1948 to 1973. He underwent lobectomy for squamous cell carcinoma of the lung which seemed to be induced by chromium.

Rhinoscopic examination revealed a perforation of the nasal septum as well as an easily bleeding and whitish tumour on the floor of the left nasal cavity. On the hard palate there was a necrotic tumour mass with the size of 2×2.5 cm. Biopsy specimens of the left nasal cavity and hard palate revealed squamous cell carcinoma. CT showed dense soft tissue in the nasal cavity with bone destruction (Figure 4). He received radiotherapy at a dose of 19.8 Gy with <sup>60</sup>Co followed by partial maxillectomy in April 1984. Then, the patient received the post-operative radiotherapy at a dose of 33 Gy. He has been free of tumour for 7 years now.

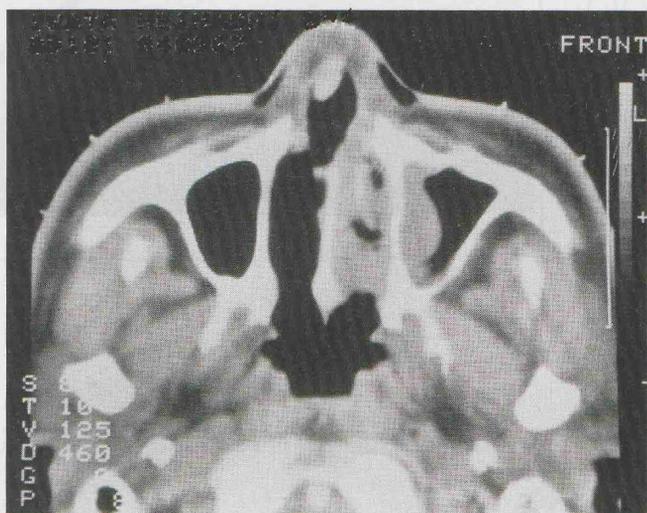


Figure 4. CT of case 2. A dense area of soft tissue in the nasal cavity with bone destruction was seen.

### DISCUSSION

The carcinogenicity of chromium is well established in chromium-induced lung cancer since Pheil's report in 1935. Cancer of the respiratory tract among chromate workers has been reported in Great Britain, Czechoslovakia, Italy, Japan, Norway, the former Soviet Union, and the United States. The death rate from lung cancer among chromate workers in the United States was 10- to 20-times higher than in the general population (Sunderman, 1976). In Japan, Ohsaki et al. (1978) reported a similar high incidence of lung cancer in chromate workers. According to Tsuneta's report (1982) of the follow-up study in this factory, lung cancer occurred in 25 out of 623 workers during the period between 1936 to 1972. He pointed out that the incidence of lung cancer in this factory was about 16-times as high as the general incidence of lung cancer in Japan.

Hueper (1966) presented a world-wide survey of 187 cases of respiratory tract tumours among chromate workers, including 180 cases of lung cancer, six cases of cancers of

the nasal cavity, and one case of laryngeal cancer. The histological types of lung cancer were squamous cell carcinoma in 46 cases, undifferentiated carcinoma in 66 cases, and adenocarcinoma in 11 cases. Most tumours in the nasal cavity were squamous cell carcinomas.

Experimental studies of chromium carcinogenesis in animals have been reviewed by Sunderman (1976). The injection of chromium powder and hexavalent chromium compounds has produced local sarcomas in rodents. Kushner and Laskin (1971) have succeeded in producing squamous cell carcinoma by implanting small pellets of calcium chromate. They have compared the carcinogenicity of several types of chromium compounds, and found that calcium chromate appears to be the most potent respiratory carcinogen. There is some controversy concerning the degree of carcinogenicity of trivalent and hexavalent chromium compounds. Recent reports (Abe et al., 1980; Levy and Venitt, 1986) have suggested that soluble hexavalent chromium compounds are more carcinogenic.

In the present cases, the period required for occurrence of nasal tumours was 39 years, on average, from the first exposure to chromium. Sano (1987) reported that the period required from the first exposure to chromium to death of lung cancer was 24.6 years on average, and that of other tumours 32.4 years. In 3 out of 4 cases in this series, nasal carcinomas arose at 10.3 year, on average, after the occurrence of lung cancer.

There are few reports of head-and-neck cancer induced by chromium. Sato (1985) has reported that the incidence of cancer of the nose and paranasal sinuses was 0.9 per 100,000 population. So, the incidence of cancer in the nasal region is to be regarded quite high in this factory. The presented cases seem to be induced by long-term exposure to chromium, with mean exposure times of 26 years.

One explanation for the higher incidence of lung cancer as opposed to that of nasal carcinoma in chromate workers is that chromium will more easily reach the lung than the nasal cavity. In other words, the concentration of chromium might be much higher in the lung than in the nasal cavity. Therefore, chromium appears to be toxic rather than carcinogenic to the nasal mucosa, resulting in nasal septal perforation. Interestingly, it seems that the malignant fibrous histiocytoma in case 1 was induced by a combination of factors, i.e. irradiation and chromium exposure.

We conclude that careful and long-term follow-up is mandatory for the chromate workers in order to detect not only lung cancer but also head-and-neck cancer as early as possible.

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Dr. N. Satoh  
 Department of Otolaryngology  
 Hokkaido University School of Medicine  
 Kita-15, Nishi-7, Kita-ku,  
 Sapporo 060  
 Japan

