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Pathology in Focus

Early radiation-induced malignant fibrous histiocytoma of the oral cavity

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Abstract
With an incidence of less than 0.3 per cent, post-radiation sarcomas are rare malignant neoplasms with a very poor prognosis. On average, they occur after a latency period of at least 15 years following radiation therapy with doses ranging from 24 to 80 Gy. We present the case of a post-irradiation malignant fibrous histiocytoma (MFH) on the floor of the mouth in a 79-year-old male patient arising only five and a half years after radiation therapy. The primary tumour was classified as a well differentiated squamous cell carcinoma of the right rim of the tongue. Primary therapy was surgical resection of the tumour and post-operative radiation with 50 Gy. Five and a half years later, the patient developed a rapidly progressing MFH within the field of radiation.

Key words: Head and Neck Neoplasms; Radiotherapy; Histiocytoma, Fibrous; Sarcoma

Introduction

Post-irradiation sarcoma is a rare complication after radiotherapy of head and neck carcinomas. In the literature only few cases have been reported.[1–3] The percentage of soft tissue sarcomas arising in the head and neck in adults is less than five per cent.[4] Malignant fibrous histiocytoma (MFH) of the head and neck has a five-year mortality of 40 to 45 per cent with most deaths occurring within the first two years of diagnosis.[3] The incidence of radiation-induced sarcomas ranging from 0.03 to 0.3 per cent with MFH being one of the most common ones.[5] Generally post-irradiation MFH occur after a latency period of 15 years following radiation with total doses ranging from 24 to 80 Gy. The median age of the patients is 43 years.[5–11] We report an unusual case of radiation-induced MFH after five and a half years.

Case report

A 79-year-old man underwent excision with margins free of tumour of a $pT_1N_0M_0$ well differentiated squamous cell carcinoma of the right rim of the tongue in 1994, followed by post-operative radiation of the excision region of the tumour and the adjacent area of lymphatic drainage with a total of 50 Gy. In 1997 and 1998 a lesion of the right rim of the tongue affecting the floor of the mouth was biopsied. Histology revealed ulcerous glossitis. In 1999 an exophytically growing tumour was observed in the same area. The tumour measured approximately 2.5 cm in diameter and was entirely resected. The histopathological findings revealed a suspect cell proliferation, however, malignancy could not be assured. Two months after resection a new mass with 3 cm in diameter was observed and biopsied. This time a high-grade malignant sarcoma was diagnosed. The patient underwent wide local excision and ipsilateral neck dissection. The histology revealed a MFH. The patient died of heart failure six months later. No autopsy was performed.

Histopathological findings

The histological examination in 1994 of the original carcinoma of the right rim of the tongue established a mainly exophytic-verrucously growing squamous cell carcinoma of low (GI) grading (Figure 1(a)–(c)).

Histological examination of the biopsy in 1997 and 1998 showed chronic hyperplastic ulcerous glossitis without evidence of epithelial dysplasias or malignant cells. In 1999 conventional histology revealed a suspect spindle-cell proliferation. Further immunohistochemical staining was performed.[12] Immunohistology showed a proliferation index of approximately 60 per cent as detected by Ki67 immunostaining. Melanoma antigen, epithelial markers as well as desmin, actin and S-100 protein were not expressed. The mesenchymal character of the lesion was confirmed by vimentin expression including a positive staining for alpha-1 antichymotrypsin (Figure 1 (d)–(f)). These additional immunohistological findings led to the diagnosis of a malignant fibrous histiocytoma (GIII). Multiple subsequent biopsies confirmed the diagnosis of MFH.

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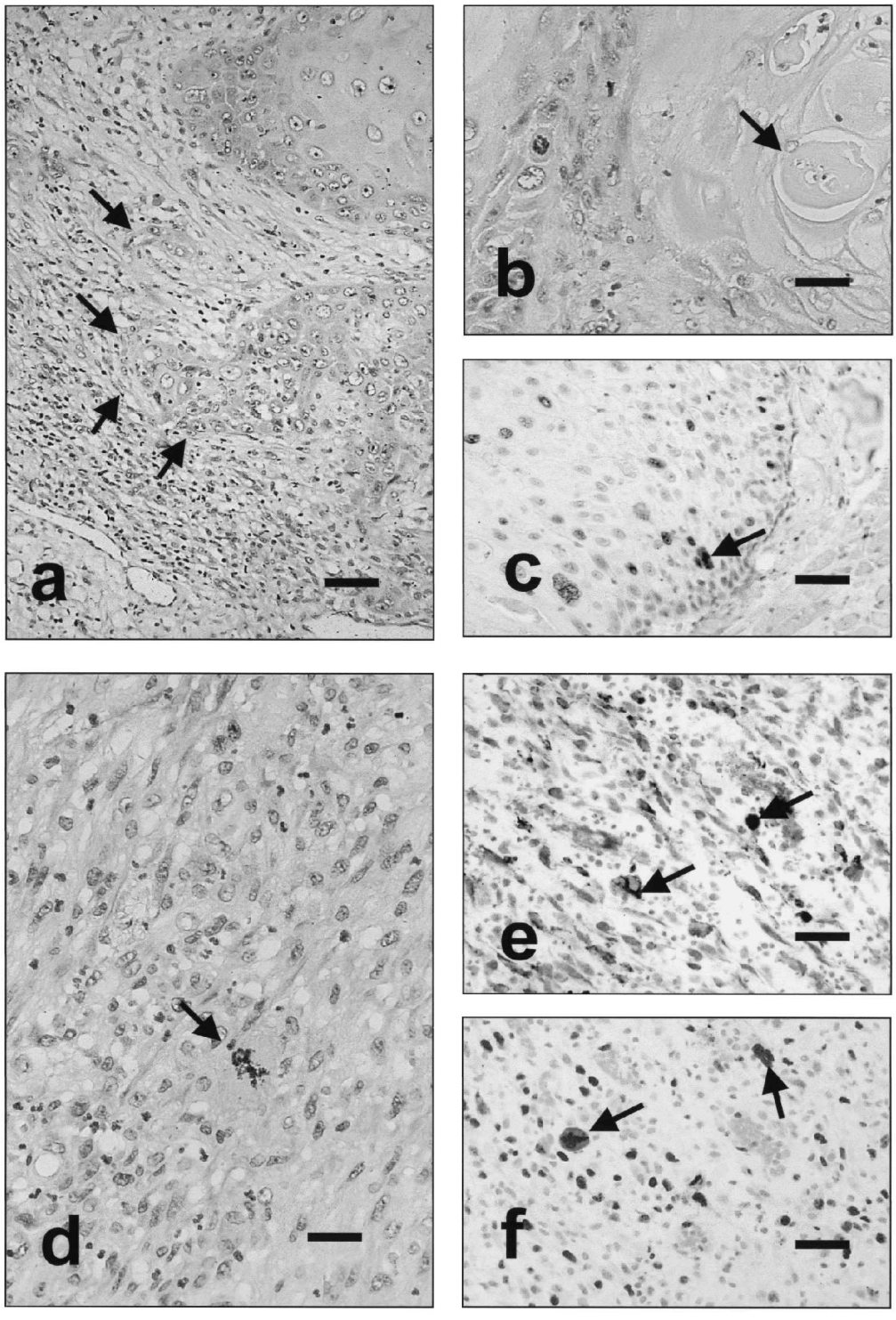

FIG. 1(a)–(c)

Histomorphological spectrum of the squamous cell carcinoma of the tongue in 1994. (a) Conventional histology reveals with a H & E stain a well differentiated squamous cell carcinoma (GI) with infiltration of the adjacent tissue (see arrows; bar = 180 μ). (b) The tumour cells show a moderate polymorphism with marked differences in nuclear size and formation of typical keratin pearls (arrowhead; bar = 40 μ). (c) Immunohistology reveals a positive staining (black dot) of the nuclei for the Ki67 antigen in less than 10 per cent of the tumour cell population, indicating a low mitotic rate (see arrow; indirect streptavidin/biotin-peroxidase method clone Mib-1, Dako, Hamburg, Germany; bar = 40 μ).

FIG. 1(d)–(f)

Histomorphology of the malignant fibrous histiocytoma of the tongue in 1999 (d) The tumour cell population shows marked pleomorphism with varying size of nuclei and prominent nucleoli. An atypical mitosis is seen (arrowhead; bar = 40 μ). (e) Immunohistology by staining with a monoclonal antibody for vimentin shows a strong positive signal in the cytoplasm of large part of the tumour cell population, confirming the diagnosis of a malignant fibrous histiocytoma (see arrowhead; indirect streptavidin/biotin-peroxidase method, clone VIM3B4, Camon, Wiesbaden Germany; bar = 40 μ). (f) The proliferation rate is high as detected by immunostaining for the Ki67 antigen. About 40 per cent of the tumour cells give a strong black signal of the nuclei marking the active phase of the cell cycle of the respective cell (see arrowheads; bar = 40 μ).

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TABLE I
OVERVIEW ON POST-IRRADIATION SARCOMA (PS)

Author(s) and year of publication	Number of cases	Age at diagnosis of PS (median)	Radiation dose in Gy (median or range)	Entity and site of post-radiation sarcoma of the head and neck	Latency period in years (median)
Patel *et al.*[5]	1	35	40	OS maxilla	15
Ko *et al.*[8]	8	50	70–80.1	MFH maxilla; MFH nasal cavity	10
Van der Laan *et al.*[6]	5	53	36–70	MFH neck, MFH larynx, FS neck, SCS nose	18
Maisel *et al.*[9]	4	30	59.5	MFH maxilla, MFH mandible, MFH larynx, FS mandible	9
Garner *et al.*[10]	1	50	66	MFH temporal bone	22

MFH = malignant fibrous histiocytoma; FS = fibrosarcoma; SCS = spindle cell sarcoma; OS, = osteosarcoma.

Discussion

It is generally accepted that radiation therapy increases the relative risk of subsequent sarcoma even though that risk appears to be small.[13,14]

For diagnosis of radiation-induced MFH, the following criteria must be fulfilled:[5–7] documented history of irradiation at the respective site, a latency period greater than five years, a histologically proven malignant tumour arising within the field of radiation with different histology from the original tumour.

In the literature the median latency period is 15 years following radiation doses ranging from 24 to 80 Gy. The median age of the patients with radiation-induced sarcomas is 43 years.[5–11] The total dose of radiation is supposed to influence the incidence of post-radiation sarcomas.[13,15] Several studies showed that higher radiation doses may be followed by longer latent periods.[16] Regarding the occurrence of post-irradiation tumours, age seems to affect the incidence but does not seem to alter the latency period.[17,18] The incidence of radiation-induced sarcomas varies between 0.03 and 0.3 per cent.[3,5] Patel *et al.*[5] report MFH as one of the most common types of post-irradiation sarcoma of the head and neck (Table I).

Conclusions

Even though the median time of latency of post-irradiation sarcoma is reported to be approximately 15 years,[5–11] we show that this can occur even after as short a period as five and a half years. Therefore, after radiation therapy regular clinical controls should be started immediately and suspect lesions should be controlled by biopsies, in order to recognize and control the emergence of secondary neoplasms within the field of radiation.

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