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Short communication

Metastasis of carcinoma ex pleomorphic adenoma to the brain without previous metastasis to the lungs or bones: a case report

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Abstract

Carcinoma ex pleomorphic adenoma is a rare type of cancer of the salivary gland that involves the malignant transformation of a primary or recurrent pleomorphic adenoma, which often metastasises to the lungs or bones, or both. To the best of our knowledge, however, nobody has reported a distant metastasis of this lesion to the brain without such previous metastasis. We report a case in a 64-year-old man.

Keywords: Carcinoma ex pleomorphic adenoma; Cetuximab; Bioradiotherapy; Brain metastasis; Blood-brain barrier

Introduction

Carcinoma ex pleomorphic adenoma is a relatively rare neoplasm that comprises a carcinomatous component (derived from the epithelium or myoepithelium, or both) of a long-standing pleomorphic adenoma. These lesions often develop in association with a primary or recurrent pleomorphic adenoma.[1] Generally, salivary gland tumours such as this undergo haematogenous metastasis to the lungs or bones, or both, through the systemic and pulmonary circulation.[2–5] In contrast, they rarely metastasise to the brain because of the blood-brain barrier. This barrier is a tight structure that consists of microvascular endothelial brain cells, strictly controls both the uptake of nutrients and excretion of waste matter, and prevents the entry of some pathogens and other toxic substances into the central nervous system.[6]

Case report

A 64-year-old man was referred to our department with pain in the right side of his neck and rapid swelling in the submental region, and the clinical diagnosis was cancer of the right sublingual gland (T3N3M0). Histopathological examination showed carcinoma ex pleomorphic adenoma with adenocarcinoma that was not otherwise specified (Fig. 1). A radical operation was not indicated, as magnetic resonance imaging (MRI) showed that the infiltrated supraclavicular metastatic lymph nodes had adhered to the right scalenus anterior muscle adjacent to the brachial plexus.

We gave him bioradiotherapy that comprised concurrent radiotherapy and a molecular-targeted drug (cetuximab,[7] Merck & Co), and intensity-modulated radiation to the primary lesion and the bilateral neck at a total dose of 66 Gy. Cetuximab was then given weekly at a loading dose

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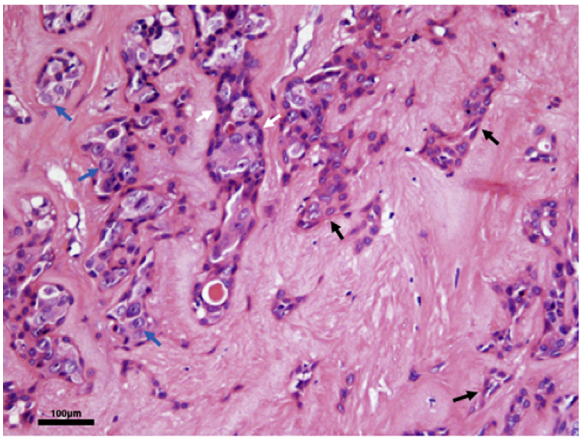

Figure 1. Histopathological analysis of tissues. This image shows the co-localisation of both benign and malignant components of carcinoma ex pleomorphic adenoma. The image on the right side shows pleomorphic adenoma (black arrows) infiltrating into the surrounding fibrous stroma, accompanied by extensive hyalinisation; in contrast, the left side of the image shows the malignant transformation of granular epithelial cells (white arrows) to adenocarcinoma cells (blue arrows).

of 400 mg/m^2 in the first week of radiation, and then at 250 mg/m^2 intravenously for four more weeks during radiotherapy. Both the primary lesion and metastases in the cervical lymph nodes were successfully treated with this regimen. He continued to take a single weekly dose of 250 mg/m^2 for 31 weeks after discharge.

Eleven months after bioradiotherapy had finished, he complained of headaches, vomiting, and difficulty in walking. Positron emission tomography/computed tomography (PET/CT) showed distant metastases to the right supraclavicular lymph nodes and lymphadenopathy of the right axillary and mediastinal lymph nodes (Fig. 2). MRI of the brain showed nodules in the left cerebellum and left frontal lobe, as well as meningeal seeding (Fig. 3). Systemic weekly paclitaxel monotherapy (PTX; Bristol-Myers Squibb) at a dose of 100 mg/m^2 for two months was begun for the lymph node metastases. After two months, PET/CT showed a strong antitumour effect on the distant lymph node metastases, and no metastases in the lungs or bones. He also had whole-brain radiation therapy at a total dose of 45 Gy for multiple brain lesions. Despite this treatment, his level of consciousness began to decline, and he died of respiratory failure at six months after the metastases in the brain had been identified.

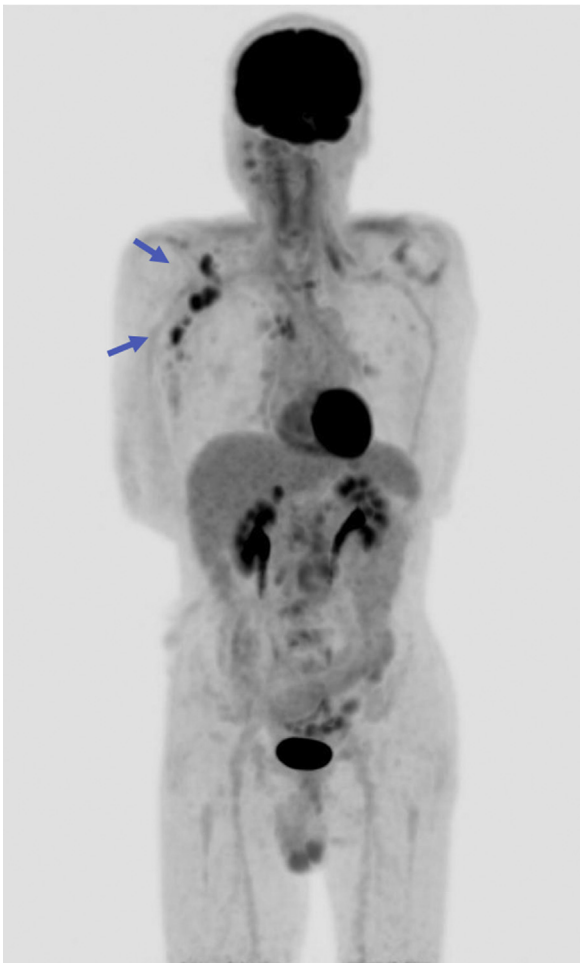

Figure 2. Follow-up positron emission tomographic/computed tomographic image. Multiple distant lymph node metastases were detected 11 months after the completion of bioradiotherapy (blue arrows).

Discussion

Metastatic disease to the lungs is common because most metastatic cancer cells are transported through the pulmonary circulation and become trapped there.[4,5] According to a study by Ali et al, 90% of distant metastases of cancer of the salivary glands occur in the lungs and bones.[2] To our knowledge, only two cases of brain metastasis of carcinoma ex pleomorphic adenoma have been reported previously.[8,9] In our patient, metastases were detected in both the brain and distant lymph nodes. This suggests either a direct inflow of cells from the primary lesion into the systemic circulation (and, consequently, metastasis to the brain), or a haematogenous process that was mediated by the venous system and transmitted through the lymphatic tract from the bilateral metastases in the cervical lymph nodes. In either circumstance, metastatic cancer cells would have bypassed the lungs. Ultimately, the cancer cells would have been delivered to premetastatic niches in the brain through the circulation of cerebrospinal fluid, unless they were subsequently delivered to various other organs through the systemic circulation instead.[4,5]

Such transmission would first require the destruction of the blood-brain barrier by circulating metastatic cancer cells. Tominaga et al reported that metastatic breast cancer cells could secrete exosomes that induce brain tropism as the result of an autocrine effect. These exosomes may contain a microRNA that can destroy the blood-brain barrier, and result in metastasis to the brain.[10] We suspected, therefore,

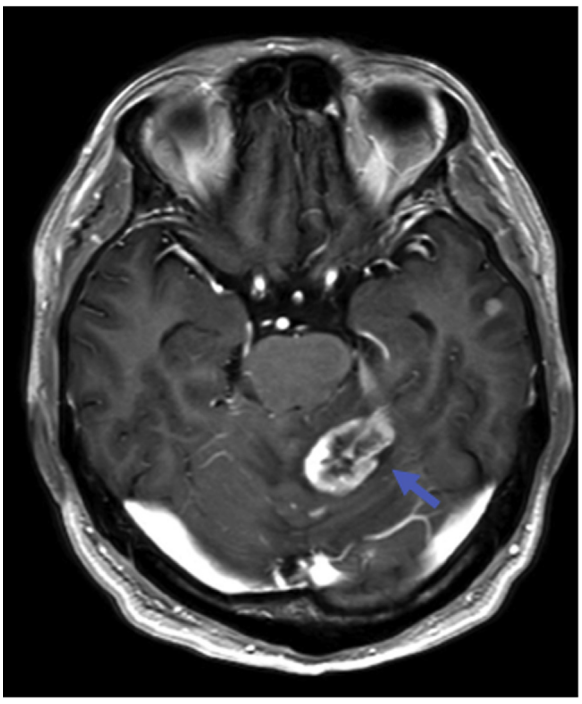

Figure 3. T1-weighted brain magnetic resonance imaging with Gd-DTPA as the contrast. Nodules are visible in the left cerebellum (blue arrow).

that salivary cancer cells may have induced the destruction of the blood-brain barrier in our patient in a similar way.

Ethics statement/confirmation of patient's permission

The rules regarding medical ethics at our institution do not require an ethics review for a case report. We obtained the permission of the patient's wife for the publication of this paper.

Author contribution

Yukio YOSHIOKA conceived of the case presentation and drafted the manuscript. Seiya HAYASHI (sh0522@hiroshima-u.ac.jp), Atsuko HAMADA (hamaco@hiroshima-u.ac.jp), Shigeaki TORATANI (tora@hiroshima-u.ac.jp), and Tetsuji OKAMOTO (tetsuok@hir**oshima-u.ac.jp) participated in the treatment of this patient. All authors read and approved the final manuscript.

Guarantor

Yukio YOSHIOKA accepts full responsibility for this article.

Conflict of interest

We have no conflicts of interest.

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