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CASE REPORT

Fungal Infection Mimicking Nasopharyngeal Carcinoma Recurrence: a Case Report

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CASE REPORT

In May 2016, a 55-year-old Chinese man presented with headache to Tuen Mun Hospital, Hong Kong. He was otherwise asymptomatic and had no known history of diabetes mellitus. The patient previously received neoadjuvant chemotherapy and concurrent chemo-irradiation 70 Gy / 33 fr / 6.5 weeks for nasopharyngeal carcinoma in 2009. Clinical and endoscopic examinations until late 2015 showed no recurrent disease.

Positron emission tomography–computed tomography scan showed increased uptake in the sphenoid and skull base. Endoscopy did not show any nasopharyngeal mass and an initial random biopsy was negative for significant pathology. Plasma Epstein-Barr virus DNA was undetectable. Tissue biopsy obtained by endoscopic sphenoidotomy was sent for pathology examination. The results revealed tissue invasive fungal hyphae (Figure 1). Tissue samples were not sent for microbiological examination at that time.

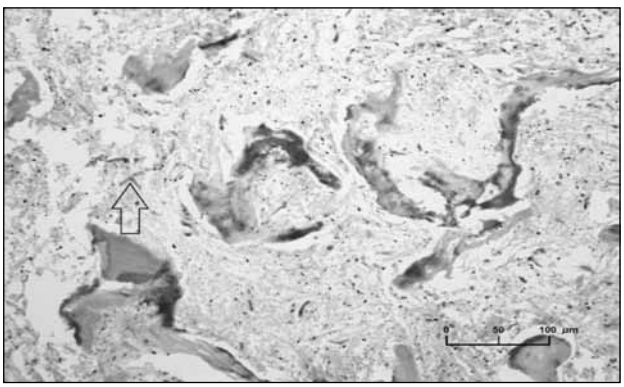

Figure 1. Photomicrograph showing trabeculae of woven bone in a background of fibrillary stromal matrix. Many fungal hyphae (diameter 5-8 µm) are seen scattered in the tissue. Hyphae that branch at right angles are identified (arrow). Septation is hardly observed. One possible type of fungus is Rhizopus, which fits the size, non-septation of hyphae, branch angle, and the predilection for the upper respiratory tract (haematoxylin and eosin stain, x 100).

The patient underwent magnetic resonance imaging (MRI) scan of the brain and pituitary in May 2016, which revealed that his sphenoid sinus was completely filled by materials with mixed signal intensity and heterogeneous

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enhancement. T1-weighted hyperintense signal (Figure 2a) was noted inside the right side of the sphenoid sinus, likely representing proteinaceous material. Differential diagnosis was sphenoid sinusitis or tumour recurrence. He was admitted to our hospital in May 2016 and treated with liposomal amphotericin B 300 mg every 24 hours as advised by our microbiologist.

The patient had a second biopsy by sphenoidotomy in July 2016. The pathology was again negative for malignancy. Tissue samples were sent for fungal culture, and the results were negative this time. He completed a 3-week course of amphotericin B 1 month before the biopsy.

The patient had a seizure in August 2016 and computed tomography scan performed at that time revealed a right occipital lobe infarct. Subsequently, MRI scan of the brain and MR angiography were done. The MRI of the brain showed an enhancing mass at the posterior aspect of sphenoid sinus with significant intracranial extension to bilateral cavernous sinuses, sellar region, and suprasellar region (Figure 2b). The enhancing soft tissue was significantly T2-weighted hypointense (Figure 2c) and T1-weighted iso/hypointense in signal. The basilar artery, the cavernous segment of the right internal carotid artery, and the petrous to cavernous segments of left internal carotid artery were also occluded (Figure 2c to e). There was evidence of subacute infarction within the posterior circulation (Figure 2f). The overall picture was most compatible with fungal infection complicated by stroke as a result of vascular encasement.

In view of the finding of tissue invasive fungal hyphae on initial microscopic examination, absence of malignant cells in repeated biopsies, undetectable Epstein-Barr virus DNA, and MRI findings favouring fungal infection, the patient was treated for extensive fungal invasion of skull base with vascular involvement. Surgical debridement was offered but declined by the patient. He was started

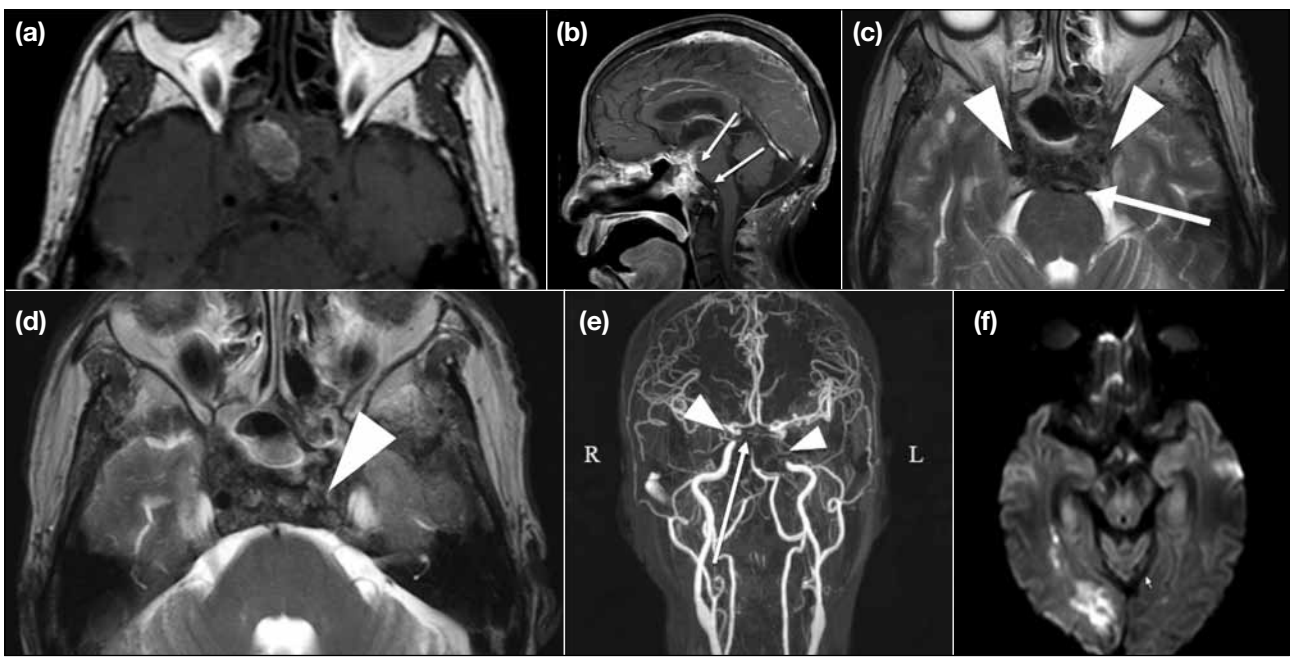

Figure 2. Magnetic resonance (MR) images of a 55-year-old Chinese man with a fungal infection mimicking recurrence of nasopharyngeal carcinoma. (a) Axial T1-weighted (T1W) MR image showing a T1W hyperintense mass over the right side of the sphenoid sinus. (b) Sagittal T1W contrast-enhanced MR image showing an enhancing mass at the sphenoid sinus with extension to the sellar and suprasellar regions and the prepontine cistern (arrows). (c) Axial T2W MR image showing the involvement of bilateral cavernous sinuses with T2W hypointense signals (arrowheads). Cavernous segments of bilateral internal carotid arteries are significantly narrowed. There is also extension of the T2W hypointense lesion into the prepontine cistern with occlusion of the basilar artery (arrow). (d) Axial T2W MR image showing involvement of bilateral cavernous sinuses with T2W hypointense signals. Loss of flow void in cavernous segment of the left internal carotid artery due to significant narrowing (arrowhead). (e) MR angiography showing occlusion of the basilar artery (arrow), the petrous to cavernous segments of the left internal carotid artery, and the cavernous segment of the right internal carotid artery (arrowheads). (f) Diffusion-weighted MR image, showing increased signal at the right posterior circulation territory due to infarction caused by the basilar artery occlusion.

on long-term antifungal treatment posaconazole 400 mg twice a day by our microbiologist.

At 3-month follow-up examination, the patient reported improvements in the headache and his general condition. One month after he was last seen in our oncology clinic, he was admitted for chest infection and septic shock. His condition quickly deteriorated and he succumbed within a day. Autopsy was not performed.

DISCUSSION

In patients with nasopharyngeal carcinoma after radiation, diagnostic difficulties often exist when lesions of the nasopharynx and surrounding structures are found on imaging studies. Differential diagnosis of a nasopharyngeal mass in a patient given radical radiotherapy for nasopharyngeal carcinoma would include the following.

Recurrent Tumour

Recurrent tumour is typically expansile in appearance, and demonstrates intermediate T2-weighted signal (higher than the muscle signal), low T1-weighted signal, with moderate contrast enhancement on non–fat-saturated images (enhancing to a lesser degree than normal mucosa).[1]

Radiation-induced Sarcoma

The imaging characteristics of radiation-induced sarcoma are similar to those of recurrent nasopharyngeal carcinoma. The presence of calcification or ossification, often better seen on CT than MRI, would favour the diagnosis of radiation-induced sarcoma. In addition, radiation-induced sarcoma may occur at a site away from the original tumour, though still within the radiation field.[2] A rapidly enlarging mass occurring after a long latent period following radiotherapy would also raise the suspicion of radiation-induced sarcoma.

Radiation-induced Granulation Tissue

Formation of polypoid granulation tissue after radiotherapy mimicking tumour recurrence has been reported.[3] Radiation-induced granulation shows intense enhancement after intravenous gadolinium, compared with the more moderate enhancement expected from nasopharyngeal carcinoma.

Post-radiotherapy Fibrosis

Mature fibrotic tissue typically shows retraction, low T2-weighted signal and no contrast enhancement, in contrast to recurrent tumour.[1]

Sphenoid Sinus Mucocoele

Sphenoid sinus mucocoele has previously been reported in patients who have had radical radiotherapy for nasopharyngeal carcinoma.[4] Imaging findings of a mucocoele typically show expansion of the sinus and MRI signals of a mucocoele depend on the proportion of its proteinaceous content.

Fungal Sinusitis

Chronic invasive fungal sinusitis may mimic malignancy. The most characteristic imaging feature of fungal sinusitis is marked hypointense signal intensity or signal void on T2-weighted MR images, which is caused by high concentrations of various paramagnetic substance concentrated by fungal organisms, including iron, magnesium and manganese. High protein concentration and low free-water content in fungal sinusitis also attribute to the characteristic imaging feature.[5] The signal intensity of the lesion in our case is most compatible with fungal sinusitis.

Vasculopathy related to sinusitis leading to stroke has also been described in the literature.[6] Sinusitis can trigger perivascular inflammatory reaction and may result in arterial thrombosis and occlusion, typically in the internal carotid and basilar arteries as they lie close to the sphenoid sinus.

Fungal infection mimicking newly diagnosed nasopharyngeal carcinoma has been reported before.[7] To the best of our knowledge, this is the first reported case of fungal infection mimicking disease recurrence in a patient given radical radiotherapy for nasopharyngeal carcinoma.

Invasive fungal infection of paranasal sinus most commonly occurs in immunocompromised hosts such as patients with AIDS, diabetes or haematological malignancy.[8] Radiotherapy has been known to affect the mucosal immunity and predisposes to fungal infection such as oral candidiasis.[9]

In our patient, the negative fungal culture may be related to sampling error or prior antifungal treatment. Microscopic examination of the first sphenoidotomy biopsy established that fungal hyphae were present in viable bony tissue, not only fungal colonisation of necrotic tissue debris in the nasopharynx. The absence of fungal culture makes definitive interpretation of the clinical picture difficult. Unfortunately, surgical debridement for both diagnostic and therapeutic purposes was declined by the patient.

Fungal infection should always be included as a differential diagnosis in patients with sphenoid sinus soft tissue mass after irradiation for nasopharyngeal carcinoma. Biopsy specimens should be sent for fungal culture, in addition to bacterial culture and pathological examination. If there is suspicion of fungal infection, early treatment should be initiated to prevent devastating sequelae.

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