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Tzu Chi Medical Journal

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Case Report

Recurrent Nasopharyngeal Carcinoma Presenting as a Positron Emission Tomography False-negative Scan

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Article info

Article history:
Received: December 27, 2008
Revised: January 7, 2009
Accepted: January 19, 2009

Keywords:
Cavernous sinus
Diplopia
Magnetic resonance imaging
Nasopharyngeal carcinoma
Positron emission tomography

Abstract

Positron emission tomography (PET) is valuable for detecting locoregional recurrences of nasopharyngeal carcinoma (NPC) with a high sensitivity and fair specificity. A negative PET result is generally thought to confidently exclude the presence of a tumor. However, a false-negative PET scan is more dangerous than false-positive results because an undiscovered recurrent tumor may eventually lead to the patient's death without proper treatment. In this report, we describe a false-negative PET scan in a NPC patient with a recurrent tumor in the left cavernous sinus, presenting as a new onset of left 6th cranial nerve palsy 1 year after irradiation. The first magnetic resonance imaging (MRI) and PET scan failed to disclose any abnormalities. The second MRI performed 3 months after the first scans demonstrated a new abnormal lesion in the left cavernous sinus, which had resolved in the following MRI after re-irradiation. Therefore, clinical observation with suggestive symptoms is still important, even with negative imaging results. Close follow-up with a series of imaging studies must be performed when indicated. (*Tzu Chi Med J* 2009;21(4):327–330)

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1. Introduction

Nasopharyngeal carcinoma (NPC) is endemic in Southern China, Hong Kong, Singapore and Taiwan (1,2). Because NPC is highly radiosensitive and chemosensitive, concurrent chemoradiotherapy is currently the standard treatment for NPC with a high cure rate, especially during the early stage (3–6). However, locoregional failures still occur after definitive treatment (3–6). In clinical practice, local examinations of the nasopharynx and computed tomography (CT) scans or magnetic resonance imaging (MRI) are performed regularly to detect these locoregional recurrences. However, it is sometimes difficult to distinguish between a recurrent tumor and post-irradiated changes (7) in the CT scans and MRI. In recent years, positron emission tomography (PET) with 18-fluoro-2-deoxyglucose (^{18}F-FDG) has been shown to be useful in the detection

of tumors by identifying regions of accelerated glucose metabolism. It has been proven effective in detecting recurrent NPC at the primary site, with a very high sensitivity of 100% and fair specificity of 64–100% (7–10). However, PET scans still have some diagnostic problems, especially with false-positive results, which are not uncommon because post-irradiated tissue effects may also result in high glucose metabolism (7,11–13). In contrast, false-negative PET scan results have been rarely reported (7). In this report, we describe a case in which a PET scan failed to detect a recurrent NPC occurring in the cavernous sinus, which presented as diplopia and was disclosed and confirmed later using the results of serial MRI examinations.

2. Case report

A 45-year-old man with NPC presenting as diplopia for 3 months with the initial stage of T4N2M0 came to our hospital in January 2003. He received a 7-week course of concurrent chemoradiotherapy at a dosage of 7000 centi-Gray (cGy) to the nasopharynx and 6000 cGy to the bilateral neck immediately after the diagnosis of NPC was confirmed. After complete treatment, diplopia resolved and MRI showed that the nasopharyngeal tumor had vanished. However, 12 months after completion of his treatment, he complained of diplopia for 3 weeks, and presented with limitation of lateral movement of his left eye, which was similar to the initial symptom. The initial MRI did not show any abnormal signals in the nasopharynx, skull base or cavernous sinus (Fig. 1).

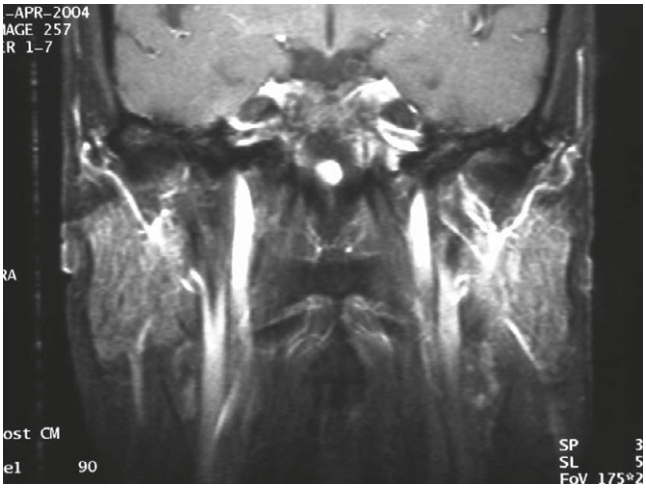

Fig. 1 — Coronal view of T1-weighted magnetic resonance imaging with gadolinium enhancement, which was performed when the patient had diplopia again. No significant lesions in bilateral cavernous sinus or the skull base were observed.

At the same time, PET scan showed no ^{18}F-FDG uptake in the nasopharynx or in the left cavernous sinus (Fig. 2). However, diplopia did not improve during the next 3 months of observation. Therefore, MRI was performed again. This time, it showed an obvious tumor in the left cavernous sinus near the left internal carotid artery (Fig. 3). Concurrent chemoradiotherapy was administered again with a dosage of 5000 cGy covering the cavernous sinus. Lateral movement of the left eye and diplopia began to improve soon after the treatment. When MRI was repeated 3 months after treatment, it demonstrated that the left cavernous sinus lesion had disappeared (Fig. 4).

Fig. 2 — Coronal view of an 18-fluoro-2-deoxyglucose positron emission tomography scan at the level of the cavernous sinus shows no significant uptake in the cavernous sinus, skull base, or nasopharynx.

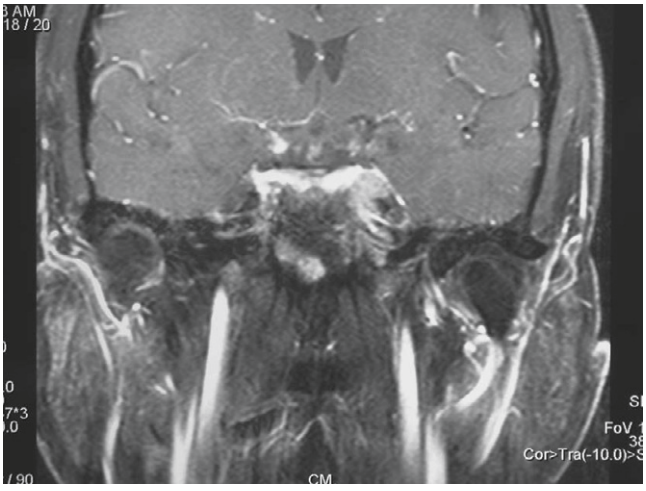

Fig. 3 — Coronal view of T1-weighted magnetic resonance imaging with gadolinium enhancement, which was performed 3 months after the initial imaging, shows a tumor in the left cavernous sinus.

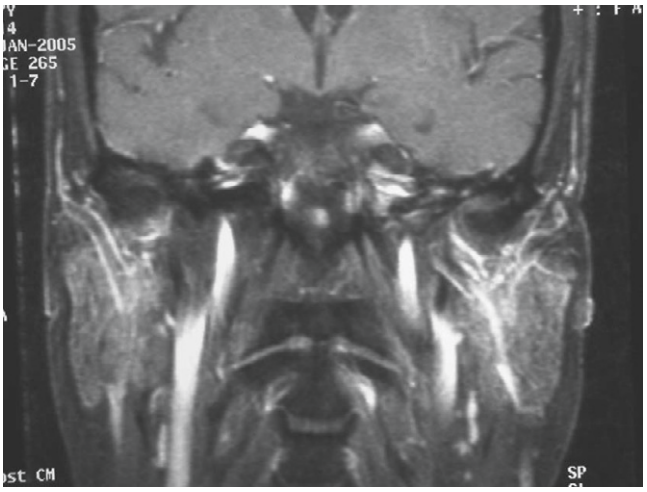

Fig. 4 — Coronal view of T1-weighted magnetic resonance imaging with gadolinium enhancement, which was performed 3 months after re-irradiation, shows that the recurrent tumor had disappeared.

3. Discussion

Although NPC is curable with a 5-year survival rate of 50–90% after curative radiotherapy [6,14], locoregional recurrences, with rates of 10–30% [6], remain a problem. Locoregional failures usually lead to the patients' death. However, early detection and prompt treatment of these recurrences still present a chance to attain successful salvage. In the clinical practice, local mirror examination or direct endoscopic observation of the nasopharynx is performed regularly to detect recurrent tumors in the nasopharynx, and it is not difficult to take a biopsy of the nasopharyngeal lesion for pathological diagnosis. However, physical examinations cannot be used to detect recurrent NPC occurring in the base of the skull or the intracranial space such as the cavernous sinus. Therefore, a CT scan or MRI is usually arranged for the patients having suggestive symptoms or signs of recurrent tumors in the regions mentioned above [15,16]. However, these morphological imaging studies sometimes cannot be used to distinguish between the recurrent tumor and post-irradiation changes, such as fibrosis, tissue edema, or osteoradionecrosis [17,18]. Furthermore, even when lesions suggestive of recurrence are discovered in imaging studies, it is not feasible to do a biopsy of the tumor in these areas [16,17]. Therefore, repeated imaging studies to follow tumor growth are the only reliable way to confirm tumor recurrence [15,16] before a PET scan is carried out.

PET is a functional imaging technique, which can provide information about the metabolic rate in lesions. Because the cancer cells of NPC have high glucose utilization, an ^{18}F-FDG PET scan can be applied to detect tumors, under the basis of a higher glycolytic rate of the viable cells. Previous studies have shown that PET scans are valuable in detecting locoregional recurrences of NPC with a high sensitivity and acceptable specificity, especially when the clinical findings are uncertain or the morphological imaging results are controversial [7–10]. However, many false-positive results can occur due to other benign conditions, such as active inflammatory processes, osteoradionecrosis or other granulomatous lesions, which also have a high glucose metabolism [7,12,13,19]. False-positive results are now the main problem of PET scans in the detection of recurrent NPC at the primary site in clinical practice [12,19].

In contrast, a false-negative PET result has rarely been reported. A negative PET scan is generally thought to confidently exclude a tumor. However, false-negative scans still may occur when the tumor is small (>0.5 cm) or when the tumor itself has lower intracellular accumulation of ^{18}F-FDG [7]. In the management of cancers, a false-negative result is more dangerous than a false-positive report. This is because there is no tumor in a false-negative situation, but an undiscovered recurrent tumor will grow more advanced without proper management and will finally lead to the patient's death. Therefore, negative PET scans must be carefully interpreted.

Here, we describe a false-negative PET scan in a patient with NPC with a recurrent tumor in the left cavernous sinus, who presented with new onset of left 6th cranial nerve palsy only 1 year after irradiation. Sixth cranial nerve palsy is one of the late complications of irradiation, but usually occurs more than 5 years after treatment [20,21]. Even after achieving complete tumor regression for many years, patients with recurrent disease may still present with cranial nerve palsy [21]. In the patients who present with recurrent cranial nerve palsy after receiving radiotherapy, tumor recurrence is possible and investigations should be carried out unless the recurrence is excluded [21]. Therefore, in our case, despite the fact that MRI failed to reveal any significant lesion, a PET scan was performed, but this also showed no significant ^{18}F-FDG uptake. Because a recurrent tumor was not confidently excluded, a second MRI scan was performed 3 months later. This MRI demonstrated a new abnormal lesion in the left cavernous sinus region, which was compatible with the patient's clinical symptoms. Despite the fact that pathological evidence was not available because of the difficulty of obtaining tissue from this region, recovery of left 6th cranial nerve function and the resolution of the cavernous sinus lesion as shown by the following MRI 3 months after the second dose of irradiation implied that the cavernous sinus lesion was really a recurrent tumor [22,23]. From the treatment experience of this patient, it is possible that a PET scan may fail to detect a small recurrent tumor, which is

not shown by other imaging modalities. Although initial imaging studies may not be compatible with a patient's clinical symptoms, close observation with a high index of suspicion for a tumor is very important. Regular and long-term follow-up with a series of imaging studies must be performed when indicated [15,24–26], especially for patients who have persistent, even progressive, symptoms or signs that cannot be solely explained just as early or late complications of their previous treatments.

4. Conclusion

The clinical value of PET scans for diagnosis of recurrent NPC has been well-established. However, PET scans still have limitations. False-negative PET results must be carefully interpreted because they are more dangerous than false-positive results. Clinical pictures are still important, especially for those patients who have discrepancies in the physical examinations and the image results. The image studies must be performed repeatedly to detect small recurrent tumors early when the PET scans are negative in a high risk patient.

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