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Clinical Record

Synchronous bilateral tonsillar carcinoma: role of fluoro-deoxyglucose positron emission tomography scanning in detecting occult primary tumours in metastatic nodal disease of the head and neck

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Abstract

We present the second case of primary synchronous bilateral tonsillar squamous cell carcinoma reported in the English literature and evaluate the role of fluoro-deoxyglucose positron emission tomography scanning in the search for the occult primary tumour in a patient presenting with metastatic nodal disease in the head and neck.

Key words: Tonsillar Neoplasms; Squamous Cell Carcinoma; Positron Emission Tomography; Head and Neck; Neoplasms, Occult Primary

Introduction

Most head and neck tumours are clinically obvious, but 5 per cent of patients present with neck metastasis without an obvious primary lesion.[1–3] A further 1–6 per cent will have a second, synchronous tumour at the time of presentation.[2,4]

The reported detection rate of these occult primary tumours in the head and neck by the use of computed tomography (CT) and magnetic resonance imaging (MRI) is 15–20 per cent. Some studies have shown that fluoro-deoxyglucose positron emission tomography (FDG-PET) imaging improves the detection rate of occult primary tumours by a further 30 per cent.[5]

Positron emission tomography exploits the abnormal metabolism of malignant cells. The technique makes use of radionuclides which decay, with the emission of positively charged particles (positrons). These positrons travel a few millimetres in tissue and combine with negatively charged electrons. This converts mass to energy and two high-energy photons (gamma rays) are released. These rays are emitted at approximately 180 degrees to each other and are detected by opposing detectors, and a three-dimensional image of these events is reconstructed as the PET image.

Cancer cells have an increased glucose metabolism, and the radionuclide analogue of glucose, 2-[^{18}F] fluoro-2-deoxy-D-glucose, can be utilized to investigate tumours *in vivo* by exploiting the increased FDG metabolism of malignant cells compared with non-malignant cells.[2,5,6]

There are a variety of nucleotides which allow studies of other metabolic processes, but FDG is most commonly used when studying head and neck squamous cell carcinoma (SCC).

The technique therefore provides a non-invasive method of studying tumour pathophysiology *in vivo*, with the added advantage that the information can be displayed in a manner similar to that of conventional imaging.[5]

Case report

A 56-year-old patient, a non-smoker and non-drinker, was referred to the head and neck clinic with a two to three month history of an asymptomatic, left-sided neck lump which was thought, by the referring clinician, to be a possible branchial cyst. On examination, there was a 2 × 3 cm, mobile, cystic lump in the left jugulodigastric area, consistent with a branchial cyst. The rest of the ENT examination was unremarkable and fine needle aspiration cytology (FNAC) was requested.

Fine needle aspiration cytology showed features of a necrotic lesion suggestive of an underlying SCC. Arrangements where made for an MRI and a PET scan, which were reported independently of each other.

The MRI scan reported a soft tissue mass lying inferomedial to the lower pole of the parotid gland. It was a loculated lesion and the morphology was consistent with a metastatic level two or three lymph node (Figure 1). No other pathology suggestive of a primary tumour was identified.

The PET scan was reported as showing intense, abnormal uptake in the left upper neck corresponding to the site of the 'known branchial cyst'. The appearances were consistent with malignancy. In addition, there was asymmetrical uptake in the tonsils. The significance of this was uncertain and was reported as a possible variant of normal (Figure 2).

In the past, a number of PET scan reports had indicated some uptake in the tonsils; this had always been due to inflammation. Therefore, the tonsils were not immediately suspected as being the source of the tumour. Instead, a

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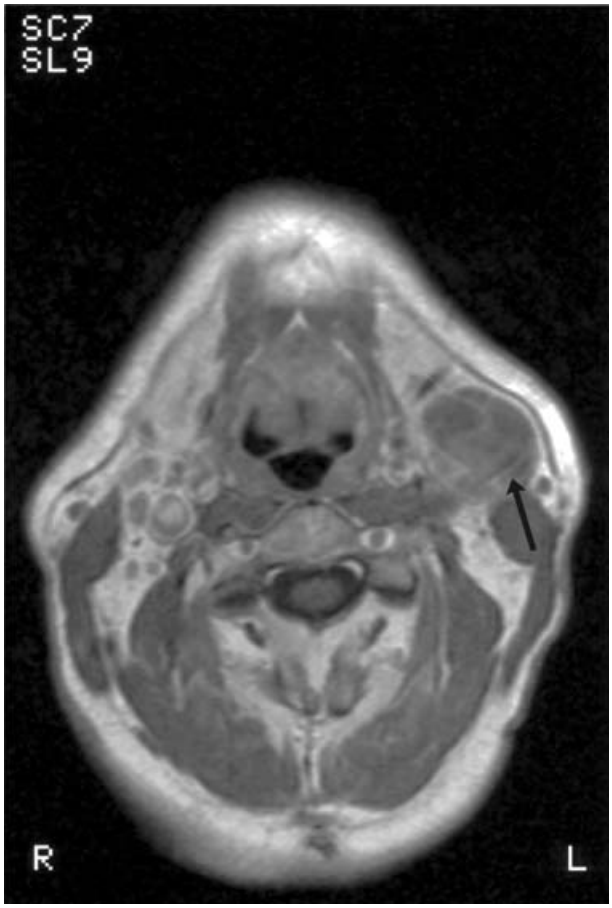

FIG. 1
Magnetic resonance imaging scan showing a loculated lesion consistent with a metastatic level 2/3 lymph node (black arrow).

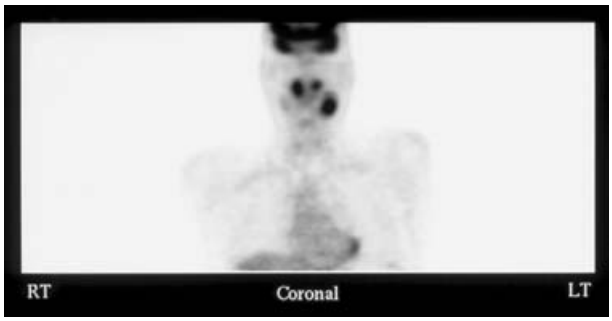

FIG. 2
Positron emission tomography scan showing uptake in the left neck mass and asymmetrical uptake in the tonsils.

tentative working diagnosis of malignant transformation in a branchial cyst was made.

The patient underwent a panendoscopy, with the intention of removing the left tonsil. Under general anaesthetic, both tonsils appeared normal but both felt firm to digital palpation. In view of this and the PET scan findings, a bilateral tonsillectomy was performed. Both tonsils were adherent to the pharyngeal muscle and sharp dissection was necessary to remove them.

Histology assessment showed primary, invasive SCC in both tonsils.

The patient underwent a left modified radical neck dissection. Histological assessment showed no other nodal involvement apart from the clinically obvious tumour. Post-operative radiotherapy was given to the left neck and both tonsillar fossae. There was no sign of tumour recurrence at 12-month follow up.

Discussion

There are a number of interesting and important issues relating to this case.

Firstly, this is a rare case of synchronous bilateral primary tonsillar SCC. There has been only one other reported case in the English literature, in 1999; there has also been a Polish case (1995) and a German case (1971).[4]

Squamous cell carcinoma of the oropharynx is in itself uncommon. It represents 10–15 per cent of all head and neck cancers and accounts for 0.3–0.5 per cent of all registered malignancies. The incidence in the UK is approximately 6–8 per million. There is a 4:1 male predominance and the peak incidence is in the sixth to seventh decades. The incidence appears to be increasing and the peak in age range decreasing towards the fourth and fifth decades.[7]

In the oropharynx, the tonsil is the most common subsite involved (50 per cent), followed by the tongue base (35 per cent), soft palate (10 per cent) and posterior pharyngeal wall (5 per cent).

The most common presenting feature in tonsillar tumours is that of tonsillar asymmetry. This may be associated with soreness of the throat and otalgia. Lymphatic spread is common, affecting 50 per cent of patients at presentation. The most common nodes affected are the ipsilateral jugulodigastric and upper deep cervical nodes. Spread is then down the chain of nodes around the internal jugular vein. The discovery of a cystic SCC in the neck is highly suggestive of a primary tonsillar carcinoma.[7–9]

A significant number of cases are asymptomatic and, as in the case presented, are uncovered during investigation for an occult primary in a patient presenting with a metastatic neck node.

The second important aspect of our case is the question of which biopsies to take during panendoscopy. It has been suggested that blind biopsies of the lymphoid tissue of Waldeyer's ring (i.e. postnasal space, tonsils and tongue base) be taken.[10] However, such blind biopsies may not be adequate, as representative areas of the tonsil may not have been sampled. Most ENT surgeons in daily practice would at least remove the ipsilateral tonsil for histological assessment.[11] However, in view of the case presented, we would advocate careful inspection and palpation of both tonsils, and if there is any suspicion about the contralateral tonsil we would recommend that bilateral tonsillectomy be performed.

The third issue raised by our case concerns the use of PET scans in the investigation of the head and neck for an occult primary tumour. Despite using conventional diagnostic procedures, including panendoscopy with blind biopsies and radiological investigations such as ultrasound, CT and MRI, approximately 5 per cent of patients with cervical metastasis have no detectable primary lesion.[3] The use of CT or MRI is said to improve the detection rates of clinically occult tumours by up to 20 per cent, and additional diagnostic methods, such as PET scanning, are also useful.[5]

Studies using FDG-PET have shown that the detection rate of occult tumours improves by a further 30 per cent, compared with use of other methods alone.[5] That is to say that, in a group of patients with a clinically occult primary tumour, PET scanning was able to uncover a

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primary site of cancer in 50 per cent, compared with 15–20 per cent when using CT and MRI. In another study, the detection rate reached 73.3 per cent.[3] There was one false positive result due to an inflamed lymph node. The other false positive results reported in the literature also appear to be due to inflammatory changes.[2,12–14] It is important to perform PET scans before doing a biopsy as areas of recent surgical trauma also show increased uptake on these scans.

The similarity between the PET scan appearance of severe inflammation and tumour is due to white blood cells and macrophages, which also take up increased amounts of glucose compared with normal tissue. Therefore, a focus of infection will show increased uptake on PET scanning in a similar way to a tumour.[2,14] However, there is a discrepancy in glucose uptake between white cells and tumour cells, and it may therefore be possible to distinguish between them by using visual and semi-quantitative analysis of the glucose uptake, in the form of standardized uptake values (SUVs).[2,6,14] This method has been successful in differentiating reactive lymph node hyperplasia and lymphoma nodal involvement.[6] Another way of distinguishing between inflamed tissue and tumour is by performing early and delayed FDG-PET imaging in order to contrast the relative glucose uptake, over time, in the tissues.[3]

As far as the tonsils are concerned, there is usually some uptake on PET images and at present the range of normal SUVs is not known. When the PET scans from our case were reassessed in hindsight, one could conclude that there was quite significant asymmetrical uptake in the tonsils, but no definite conclusions could be made. This is, therefore, an area for future research.

Future research should also address the minimum tumour load (size) which will permit detection by FDG-PET, as this has implications for the detection of small, occult primary tumours in the head and neck.[14]

The use of computer combining or co-localization of CT/MRI images with PET images may be helpful in the detection of occult primary tumours. In one study, CT-PET FDG and MRI-PET FDG were shown to have respectively 97 per cent and 100 per cent accuracy in tumour staging, as compared with CT (69 per cent) and MRI (40 per cent) alone. Similarly, CT-PET FDG (98 per cent) and MRI-PET FDG (100 per cent) were better than CT (70 per cent) and MRI (80 per cent) alone for identifying tumour invasion of specific structures.[15]

When the MRI scans of this case were reviewed, both tonsils appeared slightly more bulky than normal and there was a slightly brighter signal on T2-weighted images (Figure 3). As this is detectable with the naked eye, it is conceivable that computer co-localization could improve detection rates for occult primary tumours and may hold the key to future developments in this field.

Conclusion

It is standard practice at our institution to perform FDG-PET scans on all patients presenting with metastatic nodal disease in which there is no obvious primary tumour, before performing a panendoscopy and blind mucosal biopsies. The results of the PET scans have often successfully directed us to specific biopsy sites, even when there is no tumour clinically visible, palpable or evident on an MRI scan. Positron emission tomography is most frequently useful in deep-seated tongue-base tumours (anecdotal evidence).

As FDG-PET technology becomes cheaper and more widely available, it is hoped that more ENT departments will be able to make use of this valuable imaging tool.

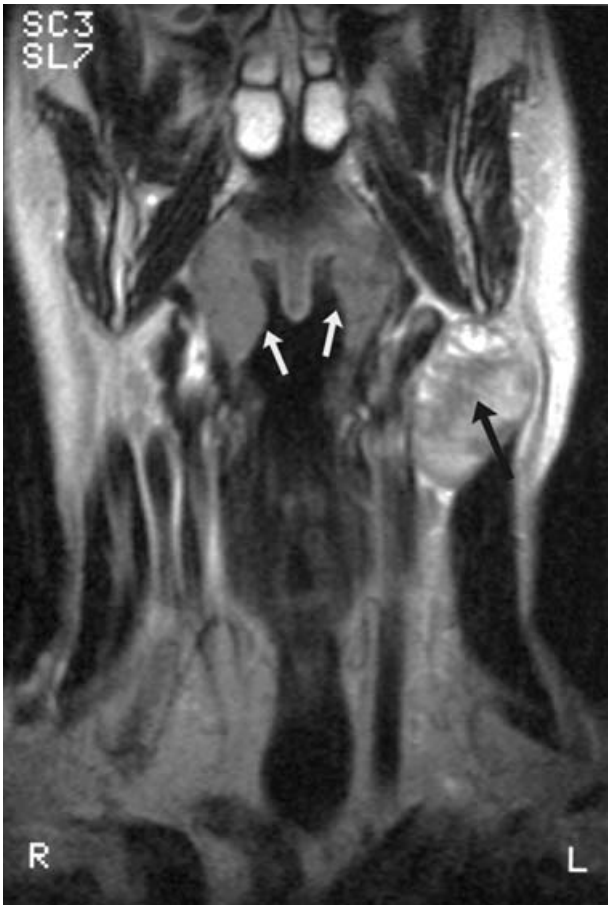

FIG. 3

T2-weighted magnetic resonance imaging scan showing slightly higher signal in both tonsils (white arrows) than 'normal'. The metastatic node is indicated by the black arrow.

- **This report describes a case of synchronous bilateral primary tonsillar carcinoma presenting initially with a cystic cervical metastasis**
- **The authors discuss the role of fluoro-deoxyglucose positron emission tomography (FDG-PET) scanning in the investigation of patients presenting with metastatic squamous carcinoma from an occult primary**

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