Post treatment imaging in head and neck tumours†

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Abstract

Cancer is a leading cause of death in most parts of the world. Most patients will undergo multiple imaging studies following treatment. The regular follow up of these patients often leads to the early detection of tumour recurrence or the onset of treatment complications. Early diagnosis may result in the timely institution of appropriate therapy thereby improving the survival and morbidity rates. This review addresses difficulties related to demonstrating early tumour recurrence and nodal metastasis and focuses on the complications seen in the central nervous system, cranial nerves and brachial plexus following radiotherapy.

Keywords: Radiation-induced neuritis; radiation-induced brain necrosis; nodal metastasis.

Introduction

Post treatment physical examination or endoscopic evaluations are often more difficult to perform and to interpret because of fibrosis, loss of anatomical landmarks or pain. The role of imaging is often crucial under such circumstances. Imaging can provide information that cannot be obtained by clinical means or provide further information that may affect the choice of treatment options[1].

The accurate interpretation of imaging studies rests upon several factors. First, radiologists must be familiar with the treatment modalities and treatment techniques that are commonly used. Second, they should be familiar with the expected post treatment findings that will enable them to differentiate expected post treatment changes from tumour recurrence. Lastly, radiologists should be aware of the various treatment complications and separate them tumour recurrence.

Interpreting post treatment imaging studies is often a daunting task. This is because surgery alters the normal anatomy, tissue planes and landmarks. To complicate matters, these changes are frequently accompanied by complex or confusing magnetic resonance (MR) signal intensity alterations. Very often it is impossible to arrive at a definitive diagnosis based on a single examination. It should be emphasised that the cheapest and most effective method of resolving a diagnostic dilemma is to compare the confusing findings with an earlier imaging study. If one is not available, a further follow up study or an imaging-guided biopsy may lead to a definitive diagnosis.

Imaging the primary tumour site

Clinical examination (supplemented by endoscopy and laboratory tests when necessary) is the mainstay of follow up. In general (for surveillance of the upper aerodigestive tract), these measures are usually sufficient. It should be noted that mucosal recurrence is best assessed by direct vision. Both computed tomography (CT) and MRI have poor sensitivities in detecting early mucosal changes[2].

The role of imaging, therefore, is the assessment of submucosal recurrence or tumour relapse in the deep tissue planes. Imaging supplements the advantages of endoscopy. In formulating a follow up strategy, malignancies that tend to recur superficially need only have clinical assessment. Primary lesions involving the buccal mucosa, glottis and tongue require no imaging studies on routine follow up.

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Tumours that have a propensity to have submucosal recurrence should have imaging studies performed regularly. Nasopharyngeal carcinoma, for instance, has a known tendency to recur in deep tissue planes and the mucosa may reveal no evidence of disease in spite of gross submucosal relapse. Thus, nasopharyngeal cancer should have 6-monthly imaging surveillance for the first year and yearly for the next 3 years. It is known that the vast majority of recurrence occurs during the first 3 years.

In the management of the primary tumour, various reconstructive techniques have been introduced to close the surgical defects. Tumour recurrence deep to the flap cannot be visually examined. Hence, imaging studies are often required. It is therefore important to recognise the normal appearances of flaps and not to confuse them with tumour recurrence. Flap reconstruction is best evaluated with MRI. Flaps show a wide spectrum of contrast enhancement characteristics ranging from almost no enhancement to diffuse intense enhancement. These enhancement characteristics do not predict flap reconstruction failure or signal the presence of tumour recurrence. T2-weighted images may also show high signal intensities but this observation does not necessarily indicate failure. The reason for the high T2 signal intensity changes is uncertain but may be due to post surgical oedema or the result of denervation.

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Nodal metastasis
Squamous cell carcinoma of the upper aerodigestive tract has a high incidence of occult metastasis (oral cavity 41%, oropharynx 36%, hypopharynx 36% and supraglottic 29%). Loco-regional failure (due to nodal recurrence) is a major cause of treatment failure in head and neck cancers. It is important to examine carefully for nodal recurrence. The imaging strategy depends on the type of cancer under surveillance. Tumours with low incidence of nodal relapse, such as paranasal sinus or parotid malignancies, need only clinical assessment. Tumours with high incidence of nodal metastasis should have imaging surveillance especially when previous radiation therapy or surgery has rendered the neck difficult to carry out satisfactory palpation. In addition, serial studies can document nodal enlargement even though the absolute measurements of the nodes are still within normal limits.

Neurological consequences following radiation therapy
Radiation damages DNA and cells die only after failed attempts at mitotic division. The observed rate at which injury develops is related to the tissue proliferative activity. Actively proliferating tissues such as mucosa, glands and bone marrow will manifest early changes. Tissues with slow proliferative activities such as those seen in the central nervous system, muscles and bone typically show delayed changes.

Neurons do not divide and are therefore considered radiation insensitive. However, neurons do perish as a consequence of oligodendrocyte and endothelial cell injury. As the turnover of these proliferative cells of the central nervous system is slow, radiation injury is typically that of the delayed type. Radiation therapy for skull base, orbital, ethmoid and sphenoid sinus tumours invariably include brain tissue within the target volume. Irradiation of these primary sites also affects the cranial nerves found within the target volume.

Radiation-induced cerebral necrosis
The irradiation of skull base tumours often injures the adjacent brain tissues. For esthesioneuroblastomas, the inferior portions of the frontal lobes are affected. In nasopharyngeal carcinoma irradiation invariably affects the medial and inferior portions of the temporal lobes. Cerebral oedema is often the earliest radiological sign and it preferentially affects the white matter. Enhancing foci in the grey matter may therefore exist without associated cerebral oedema.

The most important differential diagnosis of cerebral necrosis is tumour recurrence. An important point of distinction is that whereas skull base tumour recurrences are extra-axial lesions, cerebral necrosis is an intra-axial pathological process. Magnetic resonance spectroscopy (MRS) may be used to separate radiation-induced necrosis from tumour recurrence with brain invasion. It is important to note that skull base tumours are not expected to show N-acetyl-aspartate (NAA) since NAA is a neuronal marker. In the early delayed phase of cerebral necrosis, the levels of NAA and creatine are reduced but choline may be raised thus mimicking a primary brain tumour. The increased choline level is the result of demyelination secondary to injury to oligodendrocytes. The late delayed phase of radiation injury shows a decrease of NAA, choline and creatine. Positron emission tomography (PET) will show decreased metabolic activity in cerebral necrosis.

Brainstem encephalopathy
It is widely known that radiation therapy can damage the brainstem and cervical cord in up to 3% of patients. The frequency of cord injury is now considerably less with the introduction of improved radiation techniques and shielding. The patients usually present with clinically unmistakable symptoms and signs of corticospinal tract damage. The majority of patients will develop severe motor disability. Findings on CT are usually unremarkable. Brainstem lesions are well demonstrated...
by MRI. The cervical cord usually shows some degree of swelling and contrast enhancement.

Cranial nerves

Cranial nerves are relatively radioresistant and the reported frequencies of radiation-induced palsies range from 0.3 to 6%. Radiation-induced blindness may be seen following irradiation for skull base, orbital, ethmoid or sphenoid sinus tumours. The optic nerve is usually radiologically normal. However, radiation-induced optic neuritis may be seen as nerve thickening that shows contrast enhancement. The sixth cranial nerve is frequently affected but the nerve injury itself is seldom demonstrable on imaging studies. The XII cranial nerve is reportedly the most commonly affected nerve following irradiation for nasopharyngeal carcinoma. The affected hypoglossal nerve usually appears radiologically unremarkable.

Brachial plexopathy

Patients who had previous irradiation to the neck may develop brachial plexus symptoms and signs as a result of tumour recurrence affecting brachial plexus or as a consequence of radiation-induced plexopathy. Disease recurrence is usually a painful entity, whereas painless weakness of the shoulder abductors, arm flexors, and lymphoedema favour radiation-induced plexopathy. This complication of radiation therapy is unlikely to develop with radiation doses below 60 Gy.

Radiation-induced plexopathy usually shows MRI features of fibrosis. On T1- and T2-weighted images, the signal intensity is low to intermediate. Contrast enhancement tends to be minimal. However, occasionally, the nerves may show swelling, high signals on T2-weighted images and strong contrast enhancement. However, the nerves maintain their normal tubular morphology. Recurrent tumours usually show mass-like features.

Conclusion

Clinical examination is the mainstay of post treatment evaluation in cancer patients. When follow up clinical examination (physical or endoscopic) is difficult because of fibrosis, loss of anatomical landmarks or pain, imaging can often play a crucial role under such circumstances. Imaging can provide information that may lead to confirmation (or exclusion) of tumour recurrence or provide further information that may affect the choice of treatment options.

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