

Subdural empyema post-chemoradiotherapy for nasopharyngeal carcinoma

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ABSTRACT

Nasopharyngeal carcinoma is a common malignancy in the Asian Chinese population. The first-line treatment for Stage III/IV disease has in recent times shifted from radiotherapy to that of concurrent chemoradiotherapy. The treatment is not infrequently associated with in-field complications. We describe a rare case of one such complication – subdural empyema developing post-chemoradiotherapy in a 56-year-old man with Stage IVB nasopharyngeal carcinoma.

Keywords: chemoradiotherapy, nasopharyngeal carcinoma, subdural empyema

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INTRODUCTION

The acute and late complications of concurrent chemoradiotherapy (CRT) for Stage III/IV nasopharyngeal carcinoma (NPC) are recognised to be higher than that of radiotherapy⁽¹⁻³⁾. We describe a patient presenting with subdural empyema two months after completion of concurrent chemoradiotherapy for Stage IVB NPC.

CASE REPORT

A 56-year-old Chinese man with T2N3M0 (Stage IVB) NPC was treated with concurrent CRT that had been completed in March 2005. Routine pre-CRT and post-CRT otorhinolaryngological examination did not reveal any clinical evidence of sinusitis, otitis media, otitis externa or mastoiditis. He also had type 2 diabetes mellitus that was well-controlled on diet. He presented in May 2005 with a five-day history of fever and drowsiness. He initially had a Glasgow Coma Scale score of 15. There was no evidence of meningism or focal neurological signs. There was no evidence of any head and neck trauma or oropharyngeal

source of sepsis. The septic workup showed the patient to have *Klebsiella pneumoniae* urosepsis (positive blood and urine cultures with identical bacteriological identity).

The patient was treated with high dose intravenous ceftriaxone. Computed tomography (CT) of the brain (with and without intravenous contrast) was done the following day in view of the patient's persistent drowsiness. CT showed a left subdural iso/mildly hypodense fluid collection that was consistent with a subacute subdural haematoma (Fig. 1). There was also mild cerebral atrophy with associated mild ventricular dilatation. The working diagnosis was thus urosepsis with septic encephalopathy. In spite of appropriate antibiotics, the patient became drowsier and thus had an urgent magnetic resonance (MR) imaging of the brain done later in the day, before a planned lumbar puncture. MR imaging of the brain showed a left parietal subdural fluid collection that had high

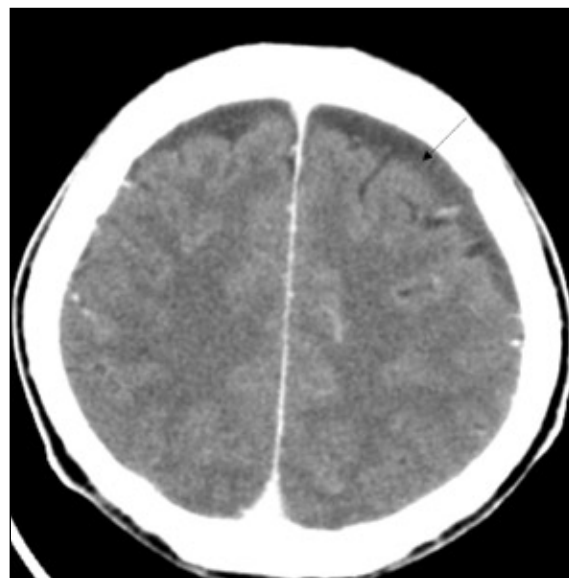


Fig. 1 Contrast-enhanced CT image of the brain taken near the near vertex shows an isodense subdural fluid collection compatible with a subacute subdural haematoma (black arrow).

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signal on T2-weighted (Fig.2) and fluid attenuated inversion recovery (FLAIR) (Fig.3) sequences. The fluid collection did not show any susceptibility artifacts on the gradient-echo sequence or any enhancement post-Gadolinium administration. These imaging characteristics were atypical of a subdural haematoma or an abscess.

The patient continued to deteriorate and was intubated and sent to the intensive care unit for further management (on the same day as the CT and MR imaging) after he started to have right-sided focal seizures. A neurosurgical consult was obtained and the decision was made to perform an exploratory left frontal burr hole. The burr hole surgery revealed a subdural empyema. The evacuated fluid microscopy showed abundant (3+) polymorphs but the culture of the fluid was negative due to the administration of systemic high dose antibiotics for the prior 24-36 hours. However, in spite of intensive care unit support, appropriate antibiotics and anticonvulsants, the patient continued to have periods of status epilepticus. The patient subsequently died of complications from the ensuing hypoxic brain damage. No autopsy was performed.

DISCUSSION

Complications post-radiotherapy for NPC have been well described⁽⁴⁾. They can be divided into early and late complications. Examples of early complications include infection, odynophagia, mucositis, xerostomia, dermatitis, asthenia and emesis. Examples of late complications⁽⁵⁻⁹⁾ include sinusitis (due to eustachian tube dysfunction), osteoradionecrosis, temporal lobe necrosis (and associated cognitive impairment), radiotherapy-induced lung apical fibrosis, dysphagia, cranial nerve palsies, carotid artery stenosis, dental and oral hygiene problems, sensorineural hearing deficit and hypothalamic-pituitary dysfunction.

Complications post-CRT for NPC have now been recognised to be more common than that occurring post radiotherapy alone⁽¹⁻³⁾. Lee et al⁽²⁾, in the NPC-9901 trial, defined late toxicities as occurring more than 90 days after commencement of RT. Our patient thus had a late toxicity of CRT for NPC. They reported higher crude rate of acute toxicities (84% versus 53%) and higher actuarial rate of late toxicities (28% versus 13%) in CRT and RT patients, respectively. The increase in late toxicity reported in that study was mostly because of increased otologic toxicities (14% versus 8%), peripheral neuropathy (2% versus 0%) and endocrine dysfunction (4% versus 1%).

Rhinosinusitis post-RT is a common side effect in NPC patients⁽¹¹⁾. Subdural empyema occurring after sinusitis is an uncommon but serious complication of

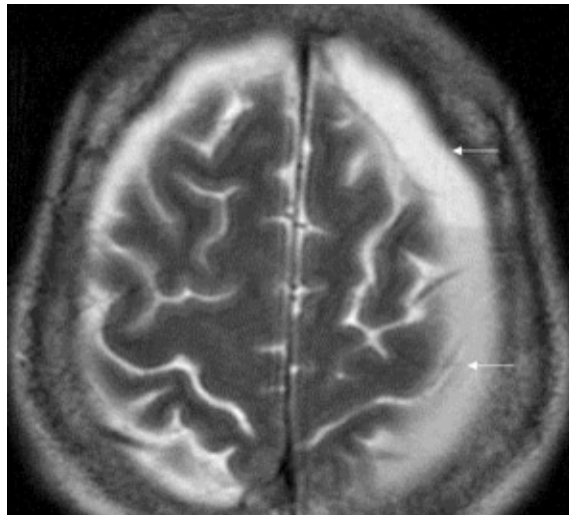


Fig. 2 T2-W MR image of the brain taken near the vertex shows high-signal fluid collection with fluid-fluid level (white arrows) consistent with a fluid collection.

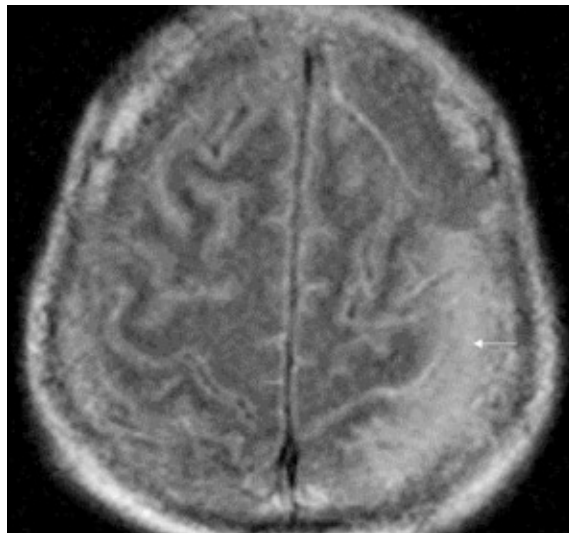


Fig. 3 FLAIR MR image of the brain taken near the vertex shows proteinaceous component of fluid collection sedimenting out (white arrow).

paranasal sinus infections⁽¹²⁾. There was however no clinical evidence of rhinosinusitis which could have predisposed this patient to developing a subdural empyema. Furthermore, in a review of 178 patients with sinusitis-associated subdural empyema, gram-negative rods was the causative agent in only 5% of cases⁽¹³⁾. 95% of cases had staphylococcus, streptococcus or anaerobes as the causative agent. Hence in this patient, it would favour haematogenous seeding of the subdural space leading to subdural empyema rather than a sinusitis-associated empyema. In addition, a PubMed search did not reveal any reported case of serious central nervous system infection (including subdural empyema) post RT or post-CRT for NPC as in this patient.

This case report of late onset toxicity post-CRT for NPC is both unusual in its presentation

and also illustrates the pitfall in the care of such patients. Gram-negative bacilli are an uncommon aetiology of community-acquired meningitis (and its associated sequelae ie. subdural empyema) in adults, but are a common cause of nosocomial meningitis, often occurring as a complication of head trauma and craniotomy. Spontaneous non-traumatic Gram-negative bacillary meningitis (as in this patient) is usually community-acquired, being two-thirds of cases in one series, and most frequently occurs in patients who are elderly or have underlying conditions, such as alcohol-induced cirrhosis, diabetes mellitus, malignancies, splenectomy and steroid therapy⁽¹⁰⁾.

The mucosal integrity, blood-brain barrier and lymphatics integrity of the head and neck region of patients who have undergone radiation to the head and neck region are often altered adversely, more so in those post-CRT than those post-RT. This patient developed a Gram-negative organism subdural empyema most likely due to seeding from a urosepsis source due to the above factors. The diagnosis of *Klebsiella pneumoniae* urosepsis with septic encephalopathy, as supported by the bacteriological investigations and CT brain findings consistent with subacute subdural haematoma, was unfortunately a false reassurance. The absence of post-Gadolinium enhancement of the fluid collection was against the fluid collection being that of an empyema. The fluid-fluid level seen on the T2-weighted and FLAIR MR images (Figs. 2 & 3) was in retrospect most likely due to the purulent material sedimenting out, although it in itself could be due to blood from a subdural haematoma sedimenting out in a haematocrit-like fashion. The definitive diagnosis of a subdural empyema was ultimately clinched on surgical evacuation of the fluid collection.

In conclusion, our case report recognises a rare but potentially rapidly-progressing and fatal complication arising from CRT for NPC. We await the long-term results of complications post-CRT for Stage III/IV NPC in the other concurrent CRT trials for a more detailed description of the late toxicities.

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