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Case Report

Skull base or cervical vertebral osteomyelitis following chemoradiotherapy for pharyngeal carcinoma: A serious but treatable complication



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ABSTRACT

Osteomyelitis, infection of the bone and marrow, following high dose (chemo-)radiotherapy for head and neck cancer is uncommon and rarely seen in the cervical spine or temporal bone. Due to its proximity to critical structures, osteomyelitis in the latter regions could carry potentially important consequences. Furthermore, involvement near the skull base (e.g. temporal bone and high cervical vertebrae) presents unique challenges in diagnosis (especially in the differentiation from disease recurrence) and treatment, making early detection and timely intervention critical. In this report, we describe two cases of osteomyelitis, one involving the temporal bone and the other affecting the 2nd and 3rd cervical vertebrae, diagnosed and treated with good outcome in the setting of definitive chemoradiotherapy for locally advanced pharyngeal carcinomas. We suggest that for new or evolving post-radiotherapy osseous changes in regions that have received a high dose of radiotherapy, associated with unexpected and deteriorating spinal symptoms such as pain and spasm, radiation-related osteomyelitis should be considered in the differential diagnosis from tumor progression. Timely referral to a surgical oncologist and infectious diseases specialist is paramount in achieving satisfactory clinical outcomes.

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Introduction

The treatment of locally advanced head and neck malignancies usually entails radical radiotherapy augmented by concurrent chemotherapy [1–4]. This approach permits organ preservation as an alternative to surgery in many advanced oropharyngeal cancers, or curative treatment for nasopharyngeal carcinoma where surgery is not ordinarily employed due to anatomic considerations. Unfortunately, the sequelae of radiation treatment often include stromal and vascular fibrosis with subsequent decreases in micro-circulation [5]. The clinic-pathologic result of these changes may include delayed mucosal healing within the irradiated volume. In turn, persistent mucosal breakdown can serve as both a nidus

and a portal of entry for infection due to loss of mucosal barrier function and compromised vascular supply [6].

Following active cancer treatment, patients generally undergo long-term surveillance. Post-radiotherapy radiographic changes in osseous and non-osseous tissues may occur for several reasons including radiotherapy-induced inflammation, fibrosis, osteonecrosis or disease recurrence. In this report, we present an additional entity that should be considered in the differential diagnoses of evolving symptomatic radiologic bone abnormalities. We describe two cases of osteomyelitis, one involving the temporal bone and the other affecting the 2nd and 3rd cervical vertebrae (C2–C3), diagnosed and treated with good outcome in the setting of definitive chemoradiotherapy (CRT) for locally advanced pharyngeal carcinomas.

Case 1

A 54-year-old male current smoker with a 40-pack year smoking history, peripheral vascular disease and polycythemia requir-

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ing repeated phlebotomies presented with a 6-week history of sore throat caused by an infiltrating lesion in the right posterior pharyngeal wall. The lesion involved the right posterior tonsillar pillar and soft palate with extension across the midline, and with posterior thickening at the junction of the oropharynx and hypopharynx measuring 6.4 cm in craniocaudal dimension. Biopsy confirmed a high-grade p16 negative mucosal squamous cell carcinoma. An associated 1.3 cm necrotic retropharyngeal node was also evident on magnetic resonance imaging (MRI). The disease was staged as a T3N1M0 posterior pharyngeal wall HPV-negative oropharyngeal carcinoma and the patient was offered definitive concurrent CRT (IMRT 70 Gy in 35 fractions [Fig. 1A] and elective bilateral neck irradiation (not shown in the figure) with concurrent high-dose cisplatin [100 mg/m²] on weeks 1, 4, and 7). However, he developed ototoxicity after one cycle of chemotherapy and an acute lower extremity vascular occlusion after 26 Gy of radiotherapy. His right lower extremity abruptly became cold and pulseless and a Doppler ultrasound demonstrated external iliac artery occlusion extending into proximal common femoral artery pelvic vessels that was managed without surgical intervention. For these reasons, his chemotherapy was discontinued but radiotherapy continued to a full dose of 70 Gy without interruption.

After completion of radiotherapy, the patient had a good response to treatment on imaging, although, a flexible nasopharyngoscopy showed a persisting area of ulceration along the posterior pharyngeal wall mucosa [Fig. 1B and C]. Biopsy by an experienced head and neck surgical oncologist (JI) confirmed that there was no residual carcinoma. Continued monitoring of the area showed persistent but improving ulceration, and he was instructed frequently about smoking cessation which remained a challenge for him. Two years after completion of radiotherapy, he developed acute onset bilateral neck pain, radiating to the occipital area. Examination revealed that the mucosal ulcer appeared deeper and was associated with a mild foetor. A repeat biopsy of the area of ulceration revealed no evidence of malignancy. A bone scan showed no uptake in the cervical spine. MRI showed a slight increase in the extent of ulceration as well as new abnormal signal changes in the C2 and C3 vertebral bodies [Fig. 2A]. However, no signs of septicemia or neurological compromise were evident. A repeat MRI performed after three months showed further progression of the ulcerated area as well as increased marrow abnormalities in the cervical spine with development of an epidural collection abutting the anterior margin of the spinal cord [Fig. 2B–D].

Although cancer recurrence was again considered, the findings were more consistent with a probable discitis complicated by an epidural abscess, likely introduced through the ulcerated mucosa. The case was thought to be too risky for surgical drainage following

neurosurgical consultation. After assessment by an infectious disease specialist (CR) a decision was made that the patient should be started on high dose IV antimicrobial therapy for osteomyelitis. Initially this involved amoxicillin/clavulanic acid for a period of one week and then switched to intravenous piperacillin/tazobactam 4.5 grams every 8 h for an additional 8 weeks once a peripherally inserted central catheter was placed. Within 2 weeks of commencing antibiotic therapy, there was significant improvement in neck pain and stiffness, with complete resolution of symptoms after completion of antimicrobial therapy. Simultaneously, the posterior pharyngeal mucosal ulceration started to improve within 2 weeks, and was documented to be completely healed 2 months following completion of a 77-day course of antimicrobial therapy. The patient remains disease-free without other late sequelae 10 years following his original head and neck cancer treatment.

Case 2

A 53-year-old non-smoking Asian female with a two-year history of a right neck mass associated with nasal obstruction and epistaxis presented with severe temporal headache and marked diplopia. On clinical examination, the patient had a right-sided upper-lid ptosis with complete eye closure, trismus, and unilateral cranial nerve three, six, and twelve nerve palsies. Flexible nasopharyngoscopy revealed a large nasopharyngeal mass. Subsequent biopsies of the lesion and right neck node confirmed a nonkeratinizing carcinoma of undifferentiated type, positive for Epstein-Barr virus-encoded RNA (EBER). Plasma Epstein-Barr viral (EBV) load by PCR was elevated (1627 copies per ml). MRI and positron emission tomography (PET) imaging revealed an extensive nasopharyngeal mass involving the entire nasopharynx with extension through the foramen ovale and foramen lacerum into the right cavernous sinus juxtaposed to the pituitary gland [Fig. 3A and B]. The bony central skull base was extensively replaced by tumor. Bilateral enlarged lymph nodes were evident, the largest of which was 2.5 cm in the right level 2 region. The disease was staged as a T4N2 nasopharyngeal carcinoma with extensive encroachment adjacent to critical skull base anatomy that included cranial nerves, the optic apparatus, and the brain stem. The patient was treated with a course of high-dose concurrent CRT consisting of 70 Gy in 35 fractions to all gross disease [Fig. 3C] and elective radiotherapy to adjacent tissues and both necks (not shown in figure), delivered with concurrent cisplatin (100 mg/m² on weeks 1, 4, and 7) and adjuvant cisplatin and 5-fluorouracil for 3 cycles. The disease responded successfully with

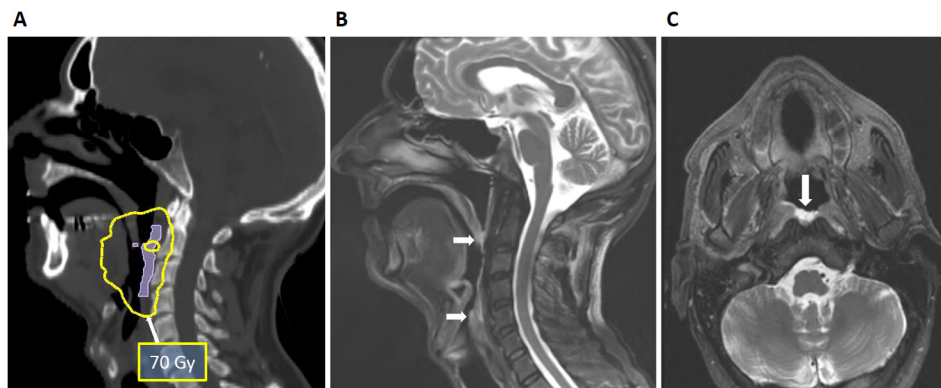


Fig. 1. Sagittal view of radiotherapy planning computerized tomography (A) depicting the original gross tumor volume (colour wash) and 70 Gy isodose line encompassing the anterior components of C2–C3 vertebral bodies where osteomyelitis occurred. Sagittal (B) and axial (C) fat-saturated T2-weighted magnetic resonance images show evolving tumor ulceration along the posterior oropharyngeal wall (arrows).

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