

Case Report

Patients with Spondylodiscitis following Chemoradiotherapy for Head and Neck Cancer in a Portuguese Cancer Hospital: A Case Report

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Keywords

Spondylodiscitis · Chemoradiotherapy · Head and neck cancer · Clinical management

Abstract

Introduction: Head and neck cancer is an umbrella term for tumor manifestations across the head and neck regions, including the oral cavity, pharynx (including the naso, oro, and hypopharynx), larynx, and sinuses. Treatment options for head and neck cancer include surgery, radiation therapy, chemotherapy, and immunotherapy, with specific treatment plans depending upon individual tumor location and staging, together with overall patient health status. Furthermore, definitive chemoradiotherapy (CRT) has emerged as a highly effective therapeutic option for locoregional advanced head and neck squamous cell cancer. However, such therapy has also been linked to the development of spondylodiscitis. Spondylodiscitis consists of an infection starting at the vertebral endplates and spreading into the intervertebral discs, typically manifesting in adults. **Case Presentation and Conclusion:** This case report describes our clinical team's experience in managing three separate cases of spondylodiscitis following CRT for head and neck tumors that presented at our clinic for diagnosis and treatment in order to identify predisposing factors that underlie the link between CRT and spondylodiscitis.

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Introduction

Head and neck cancer is an umbrella term for neoplasms across the head and neck regions, including the oral cavity, pharynx, larynx, and sinuses, with squamous cell carcinoma being the most common histologic subtype [1]. Treatment options for head and neck cancer include surgery, radiation therapy, and chemotherapy, with specific treatment plans depending upon individual tumor location and tumor stage, together with overall patient health status [1]. Furthermore, definitive chemoradiotherapy (dCRT) has emerged as a standard-of-care treatment for locoregional advanced head and neck squamous cell cancer [2]. In summary, dCRT consists of a complex combination of chemotherapy and radiation, that is highly successful in treating non-metastatic head and neck squamous cell cancer, whenever the condition is unresectable and requires organ preservation or when patients refuse surgery [3]. However, dCRT can lead to acute and late toxicities, more than radiotherapy alone, and has also been linked to the development of spondylodiscitis within a subgroup of head and neck tumor patients, with several cases being reported across the literature [4–9].

Spondylodiscitis consists of an infection that starts within the vertebral endplates and spreads secondarily to the adjacent vertebral discs, typically manifesting in adults [6]. Spondylodiscitis differs from spondylitis, as the latter is an inflammatory condition, without any elements of infection [10]. Furthermore, spondylodiscitis can be sub-classified as pyogenic, brucellar, or tuberculous in origin, often acting as an insidious infection that requires prolonged antimicrobial therapeutic measures for successful recovery [6].

This case series describes our clinical team's observations and efforts in managing three separate cases of spondylodiscitis, following CRT for head and neck tumors, within patients hospitalized at our clinical center (2018–2022). Such case reports could possibly identify novel predisposing factors that underlie the mechanistic links between head and neck cancer CRT and spondylodiscitis.

The CARE checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000535712>).

Case Series Reports

Patient 1

This first case was a 68-year-old male presenting with cardiovascular risk factors (ischemic heart disease, essential hypertension, dyslipidemia), a heavy tobacco and alcohol user, and a diagnosis of right-sided keratinizing oropharyngeal squamous cell carcinoma (p16 negative/T3N2bM0). The patient started chemoradiotherapy and completed 33 fractions of treatment with 69.96 Gy (2.12 Gy/fraction) on the tumor and metastatic cervical lymphadenopathies on the right, prophylactic 59.4 Gy (1.85 Gy/fraction) on the unaffected cervical lymph node chains on the right and levels II and III on the left, and 54 Gy (1.64 Gy/fraction) on level IV on the left, with concomitant administration of carboplatin AUC 5 on days 1 and 22, skipping day 43 due to cutaneous and hematologic toxicity. Twenty weeks later, the patient complained of severe odynophagia, and clinical observation showed an ulceration of the posterior wall of the oropharynx. Biopsy excluded tumor recurrence, and a cervical CT scan confirmed a complete response to treatment. Further 8 weeks later, chest CT revealed a cavitated lesion in the posterior segment of the left upper lung lobe, measuring 23 mm in diameter. Concomitantly, the patient complained of progressively worsening cervicalgia. A cervical spine CT revealed signs of spondylodiscitis at the C3-C4 intervertebral space, with

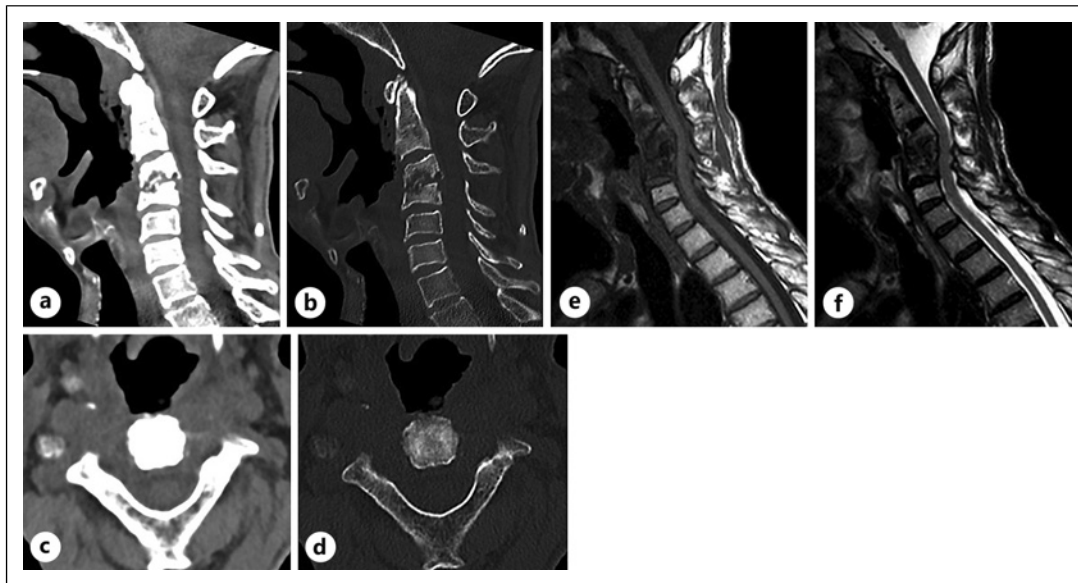


Fig. 1. CT of the cervical spine sagittal reconstructions in soft tissue (a) and bone (b) windows and axial sections in soft tissue (c) and bone (d) windows display disc-vertebral changes centered on the C3–C4 disc with extensive erosions in the vertebral endplates and with a small soft tissue component in the epidural and paravertebral spaces. In the immediate proximity, there is an ulceration of the posterior wall of the oropharynx with a fistulous tract extending to the pre-vertebral space, consistent with radiation necrosis. Also noteworthy is the cervical kyphotic deformity contributing to the stenosis of the central spinal canal. The corresponding MRI sagittal sections in T1W (e) and T2W (f) images show more accurately the extent of the inflammatory process and the bone marrow edema of the vertebrae extending from the lower third of C2 to the lower endplate of C4, as well as the stenosis of the central spinal canal with effacement of the pre- and retromedullary subarachnoid space. However, no areas of spinal cord edema or foci of myelomalacia are seen to suggest spinal cord distress.

vertebral endplate erosions and slight kyphotic angulation, together with mild peri-vertebral and anterior epidural inflammatory thickening (shown in Fig. 1). The patient was hospitalized for 6 weeks with a diagnosis of spondylodiscitis (C3–C4). The neurosurgery team considered that there was no surgical indication, and the patient completed 42 days of IV antimicrobial therapy (ceftriaxone 2 g/day and vancomycin with target serum concentrations of 15–20 µg/mL), with clinical improvement. He also used a cervical collar and was treated for 12 days with fluconazole for a concomitant pulmonary fungal infection. Meanwhile, the patient lost status for the single lung metastasis surgery and passed away in a palliative care unit about 8 months following hospital discharge.

Patient 2

This was a 60-year-old male with a history of type II diabetes mellitus and hypertension, a former smoker, and a heavy drinker. The patient had undergone cervical spine surgery for a disc protrusion, and an iliac bone graft was placed. Twenty years later, he was referred for a biopsy, following dysphonia and was diagnosed with laryngeal squamous cell carcinoma. He became tracheotomized due to worsening dyspnea and underwent a total laryngectomy, bilateral cervical lymph node dissection, and right hemithyroidectomy (pT4aN2b). Then, he received adjuvant chemoradiotherapy (60 Gy on the surgical bed and 50 Gy on bilateral cervical lymph node chains with concomitant cisplatin 100 mg/m² on days 1, 22, and 43), with a complete response. Three years later, following the placement of a phonatory

prosthesis, the patient had multiple hospital visits complaining of cervicalgia irradiating to the shoulder and right arm, with weakness and paresthesia in the right hand. MRI revealed spondylodiscitis (C7–D1 and D1–D2) with bone marrow edema, secondary to an ulcer in the posterior pharyngeal wall, with a small pre-vertebral collection at D1–D2 level (shown in Fig. 2). Surgery was not indicated at this time, and the patient underwent a 42-day course of IV antimicrobial therapy (ceftriaxone 2 g/day and metronidazole 500 mg q6h), and a nasogastric tube was placed. A control MRI 14 days later showed improving inflammatory changes in the right pre-vertebral soft tissues. Pre-vertebral and right paravertebral contrast enhancement remained at C6–C7 level, with only a small pre-vertebral collection facing C7 (shown in Fig. 3). The patient is still alive and in complete remission.

Patient 3

The final patient is a 52-year-old male former smoker, diagnosed with undifferentiated carcinoma of the nasopharynx (T1N2aM0). He underwent chemotherapy (3 cycles of epirubicin 90 mg/m² and cisplatin 100 mg/m² D1, q21d), followed by radiotherapy (70 Gy on the tumor), which ended 18 years ago. Six years later, he was submitted to hyperbaric oxygen therapy for radionecrosis of the skull base. The patient also suffered from peripheral facial paresis, secondary to radiation necrosis affecting the temporal bone. He underwent mastoidectomy and facial nerve decompression at this time. Subsequently, the patient experienced multiple episodes of skull-base infections (mastoiditis, otitis, and petrous apicitis), together with recurrent epistaxis episodes.

Thirteen years and 5 months after the primary treatment, the patient was hospitalized due to intractable cervicalgia and was diagnosed with C2–C3 spondylodiscitis secondary to an ulcer at the posterior wall of the hypopharynx. Surgery was not indicated due to the anatomic location, absence of neurological symptoms, and being in an already irradiated and necrotic area, also with increased risk of graft failure. After consultation with the infectious disease department, the patient completed 22 days of IV antimicrobial therapy (meropenem 1g q8h and vancomycin with a target serum concentration of 10–15 µg/mL).

An MRI of the cervical spine after completing antibiotics revealed discrete worsening of the epidural inflammatory component at C2–C3 and further obliteration of the ventral subarachnoid space, aggravated by a retrolisthesis of C2 over C3 that arose in the interval. It also showed significant bone marrow edema at C2–C3 level with involvement of the odontoid process, features overlapping with the previous scan. An extensive ulcer persisted on the posterior wall of the oropharynx in contiguity with this inflammatory/infectious process. Multidisciplinary otorhinolaryngology team suggested fistula closure with a free flap together with neurosurgical debridement and fusion at the same surgical time and/or hyperbaric oxygen therapy. As there is no neurosurgical department at our hospital, this procedure was not performed, and the patient remained under antibiotic therapy for an additional time of 57 days (meropenem plus vancomycin). He also took a course of 21 days of fluconazole (400 mg/day) to cover the possible existence of *Candida* spp. in the oropharyngeal microbiota). A third MRI after 6 weeks of antibiotics showed an improved pre-vertebral and epidural inflammatory component (negligible) and the appearance of a de novo depression fracture of the upper endplate of C3. The ulcer in the posterior wall of the hypopharynx remained stable, as did the fistulous tract between the airway and the body of C2 and the C2–C3 disc.

Following discussion with the infectious diseases department, it was decided to complete 8 weeks of antibiotic therapy. The fact that a fistulous tract remained between the ulcer and the body/disc of C2–C3 increased the risk of spondylodiscitis recurrence. Clinicians therefore recommended close neurological surveillance and patient education for alarm signs (novel neurological signs or infectious signs). He is still alive, with no more spondylodiscitis episodes.

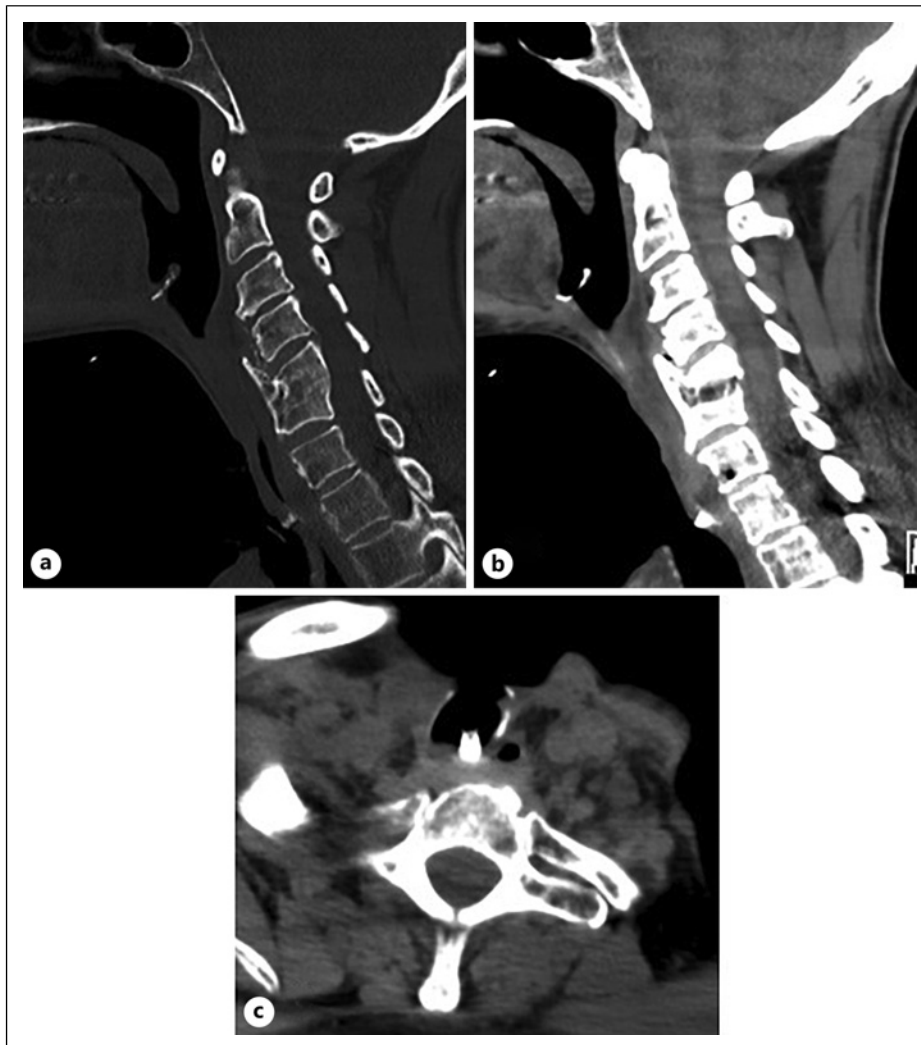


Fig. 2. CT of the cervical spine performed on May 13, 2022; reconstructions in the sagittal plan in bone (a) and soft tissue (b) windows; and axial section in soft tissue window (c) show the usual post-surgical changes of total laryngectomy with a phonatory prosthesis in normal position. Also noteworthy is the presence of a C5–C6 vertebral block and small posterior protrusions of the C4–C5 and C6–C7 discs.

Discussion

Spondylodiscitis is an infection of the vertebral endplates and intervertebral discs, typically caused by bacterial or fungal infections. The management of spondylodiscitis usually involves a multimodal approach comprising medical and surgical interventions [11]. Medical management involves the use of oral/intravenous antibiotics to treat the underlying infection, depending on the severity of the infection and the patient's overall health [11]. Surgical management of spondylodiscitis can be required if the infection does not respond to medical treatment or if there is significant structural damage to the spine [12]. Surgical options typically include debridement, spinal fusion, or instrumentation [12].

The above-described case series presenting at our institution highlights several important findings regarding cervical spondylodiscitis and its management, which could drive future optimized treatments for this condition. Most of the cases in this series presented with

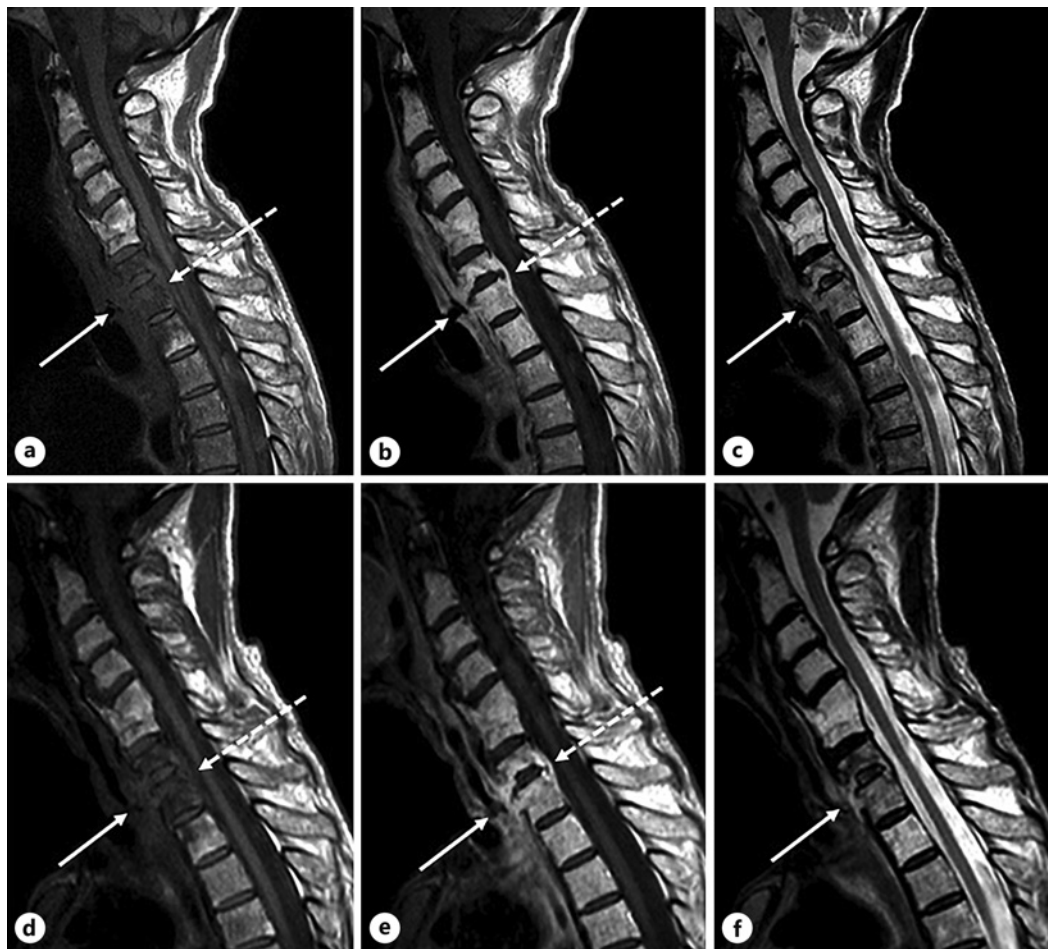


Fig. 3. MRI sequences of the cervical spine before (images **a** to **c**) and after (images **d** to **f**) antibiotic therapy. Sagittal T1-weighted sections before (**a**, **d**) and after (**b**, **e**) gadolinium administration, T2-weighted (**c**, **f**). The initial MRI study shows the interval appearance of a radiation ulcer on the posterior wall of the hypopharynx (arrow) extending deep into the pre-vertebral space and accompanied by spondylodiscitis changes centered on the C6–C7 intervertebral. The changes consist of an epidural soft tissue mass (dotted arrow) that shows enhancement after gadolinium administration and obliterates the ventral subarachnoid space with no signs of spinal cord distress. Erosive changes of the vertebral endplates and pronounced vertebral edema from C6 to D2 are also noted. After only 2 weeks of therapy, there was a slight reduction in the depth of the ulcer, in the thickness of the epidural and peri-vertebral inflammatory mass, and no conflict with the cervical spinal cord.

cervicalgia and were clinically interpreted as possible metastatic disease from the primary tumor. Consequently, it is important to raise awareness about differential diagnosis in this setting and reinforce the diagnosis by imaging and laboratory investigations [9].

Furthermore, a literature review of 70 cases of cervical spine complications following nasopharyngeal carcinoma treatment – including CRT – revealed multiple cases of spondylodiscitis, osteomyelitis, and osteonecrosis [13]. Our case series described a total of three head and neck cancer tumors requiring radiation therapy affecting the cervical spine. All such patients had ulcers of the posterior pharyngeal or hypopharyngeal wall, acting as the entry point for infection, as described in the available literature [4, 13]. This also highlights the importance of striking a balance when implementing CRT – between therapeutic efficacy and risk of unnecessary spinal irradiation – whereby all cases in the above-described series did

have such complications during the course of their disease. Interestingly, all patients in this case series were smokers, and 1 patient had diabetes-driven peripheral arterial disease, consequently compromising wound healing in such cases [12].

Regarding antimicrobial therapy for spondylodiscitis, the typical duration of antibiotic use is not standardized when the causative agent is not isolated. This consequently highlights the usefulness of bone biopsies with histopathological/tissue culturing analysis in the diagnosis of spondylodiscitis in order to deploy a bespoke antimicrobial (and not empirical) therapeutic strategy for the individual patient. Within this case series, none of the patients had isolated microbial agents in the bloodstream. In addition, antimicrobial courses typically lasted 6 to 8 weeks, with most cases undergoing a 42-day course of antibiotic agents, with an apparent lack of variation in patient outcomes.

Interestingly, surgical interventions to close the radiation-induced ulcerations in the posterior pharyngeal wall in such instances should not be disregarded, albeit it seems that typically – as also highlighted within this case series – surgical interventions were not deemed feasible. In addition, other measures – such as flap-based fistula closing and the use of hyperbaric oxygen therapy (for minimizing anaerobic infection development), should also be considered when managing cases of spondylodiscitis [4, 8].

In this case series, 2 patients recovered from spondylodiscitis, while 1 patient died from metastatic disease after tumor progression. Following our observations, together with previous literature, the authors firmly believe in the implementation of a severity code for spondylodiscitis, as described in the study by Homagk and colleagues [14], with specific attention given to cases of cervical spondylodiscitis, to increase standardization and streamlining of such cases and to obtain better patient outcomes.

Statement of Ethics

The review of patient data did not require ethical approval in accordance with national guidelines. Written informed consent has been obtained from the son of the deceased patient (case 1) for publication of this case report, details of their medical case, and any accompanying images. Written informed consent was obtained from the patients (cases 2 and 3) for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No financial support was obtained for this publication.

Author Contributions

Diana Pessoa, Inês Vicente, and Carolina Pereira drafted the manuscript. Ana Teresa Pina and Pedro Freitas helped collecting and analyzing the data of the patients. Alexandra Borges provided the images in this case report. Isabel Sargento was the patient's doctor in charge of all clinical information and directing patient care. All the authors participated in manuscript revision and approved the final version.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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