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Cervical Spine Infection as Serious Complication After Pharyngeal Surgery and Radiotherapy for Squamous Cell Carcinoma

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Abstract

We present a case of a 60-year-old man with osteomyelitis and spondylodiscitis of the cervical spine complicated with epidural abscess, severe cord compression, and consequential myelopathy developed three years after the surgery and radiotherapy of pharyngeal carcinoma. The patient presented with an acute onset of quadriplegia followed by three months of neck pain associated with vertigo. In his previous history, there were pharyngeal surgery and radiotherapy of squamous cell carcinoma on the posterior hypopharyngeal wall followed by three later performed excisions of ulceration at the treated place. MR imaging demonstrated spondylodiscitis at the level of the operation, osteomyelitis of related vertebral bodies, and a fluid collection in the epidural space with the compression of the dural sac associated with extensive myelopathy. The urgent decompressive neurosurgery showed pus within the epidural space. The following day, patient's clinical condition got worse with cardiorespiratory arrest and a fatal outcome.

Surgery followed by radiotherapy is established as a treatment for pharyngeal carcinoma in most cases of pharyngeal carcinoma. These procedures provide tumor removal and local control of neoplastic growth, but they can also cause damage of the peripheral lymphoid tissue and a consequent regional deficit in resistance to infection as well as a mucosal defect on the posterior pharyngeal wall as a road for the admission of infective organisms from the pharyngeal space to the cervical spine. Therefore, these patients should be considered as a risk group for cervical spine infections that can lead to serious consequences.

Key words: Spine Infection; Laryngopharyngeal Surgery; Radiotherapy; MRI;

Abbreviations:

MRI – Magnetic Resonance Imaging; CNS – Central Nervous System; OPSCC - Oropharyngeal Squamous Cell Carcinoma; HPV - Human Papillomavirus; ORN – Osteoradionecrosis; DWI -Diffusion Weighted Imaging; ADC - Apparent Diffusion Coefficient

Introduction:

Oropharyngeal squamous cell carcinoma (OPSCC) rates are 4-fold higher in men than women across ethnicities [1]. Historically, oropharyngeal carcinoma was primarily a disease of older individuals, with the highest incidence over the age of 70. However, these demographics have shifted due primarily to increased rates of tumors associated with the human papillomavirus (HPV). The last two decades have seen a steady increase in the rates of HPV-positive OPSCC among younger individuals, most notably white males between the ages of 50 and 70 [1].

Treatment of OPSCC includes surgery, radiation, and chemotherapy in different combinations and orders of application. Basically, the choice of treatment of carcinoma is stage related. The early stage of the disease may generally be treated with single-modality therapy, consisting of either surgery or definitive radiation. Either modality should include the management of both primary tumor site within the oropharynx and also at-risk cervical nodal basin. Treatment of cervical nodes is required even for early-stage (clinically N0) disease due to the elevated risk for the occult nodal metastasis associated with tumors of the oropharynx [1]. These procedures not only prevent neoplastic spreading but also diminish local tissue's ability for resistance to infection. On the

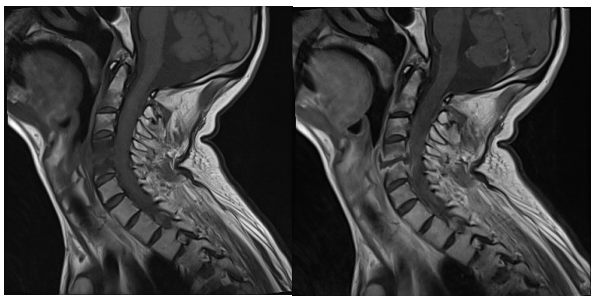
other hand, surgery and radiation procedures can cause a defect on the posterior pharyngeal wall and thus provide potential entering of infective organisms from the oropharyngeal space to the cervical spine region. Patients with previous radiotherapy or surgery for nasopharyngeal carcinoma carry a high risk of developing osteoradionecrosis and an infection due to the disruption of the cellular homeostasis and the breach of the lymphoid barrier with contamination by the nasopharyngeal flora [2].

Case report:

A 60-year old man was referred to our department due to a sudden onset of quadriplegia. He was an oncologic patient with a history of the squamous cell carcinoma of the posterior pharyngeal wall treated by surgery and radiotherapy three years ago. During the follow-up, the three endoscopic evaluations revealed ulceration at the treated place. Each time the performed excisions were followed with negative histopathology findings for carcinoma. The last two consecutive endoscopic examinations showed no evidence of local abnormality, the last one performed six months before his presentation to our department. In the period of three months prior to his presentation, the patient suffered from neck pain and occasional vertigo. His condition was considered as chronic pain that was a sequelae of radiotherapy and it was treated by a referred physician with painkillers. The day before his admission to our institution, the patient developed quadriplegia and after the consultative examination carried out by a neurologist, the MR exam was indicated.

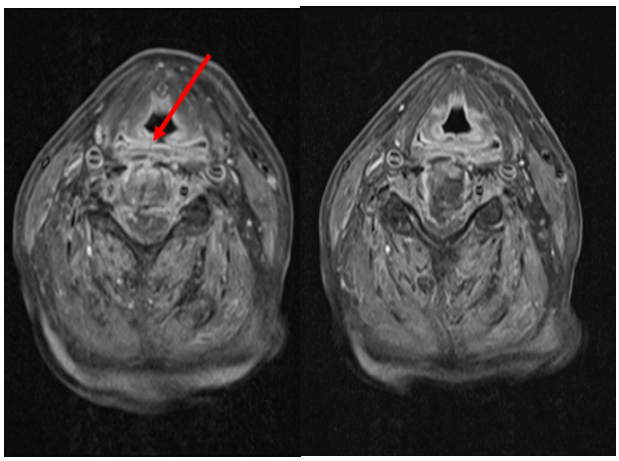
MR imaging of the cervical spine showed C4, C5 bodies of diffusely T1 low signal with irregular and blurred lines of the corresponding endplates, widened prevertebral space containing fluid collection which extends along the anterior aspect of the C4 body and C4/C5 level and propagates through the same disc space on the right side into the epidural space (Figure 1). At the same level, there was a subtle linear discontinuity of the dorsal pharyngeal wall on the right side associated with postcontrast enhancement of the regional retropharyngeal soft tissue, rim enhancement of the fluid collection, endplates enhancement as well as moderate enhancement of the C4, C5 vertebral bodies. On the post-contrast study, the severe compression of the dural sac with a mediosagittal diameter of the spinal canal of 2mm was well-shown (Figure 2). On T2 and STIR sequences, there was a signal abnormality within the spinal cord from the level C2/C3 to the level of the medial line of the C7 suggesting extensive myelopathy as a result of the compression. STIR hyperintensity within the C2 – C5 bodies was consistent with the altered bone marrow in terms of marrow edema, which suggested the radiation-induced osteonecrosis. DWI hyperintensity in the region of the fluid collection and postcontrast enhancement corresponding with ADC low signal additionally confirmed the process of infection.

We recommended emergency hospitalization and decompressive surgery was performed on the same day. The surgical finding described a significant amount of pus in the cervical epidural space. Further treatment continued in the intensive care unit with intravenous antibiotics and supportive therapy but, unfortunately, the patient failed to respond. The following day his clinical condition got worse with cardiorespiratory arrest and a fatal outcome.



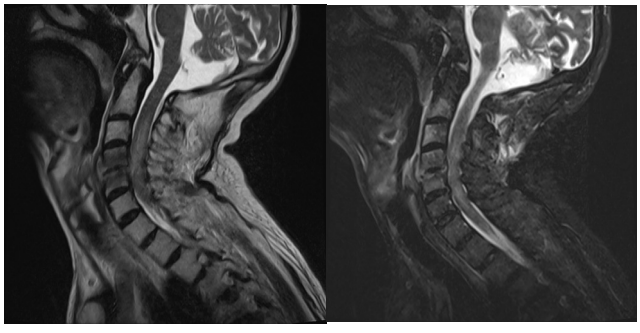
(a) (b)

Figure 1: T1W-weighted native (a) and post-contrast (b) sagittal images show extensive edema within the C4, C5 bodies, destruction of the endplates on the level in between and abscess collection in the prevertebral space that extends through the corresponding intervertebral level into the epidural space.



(a) (b)

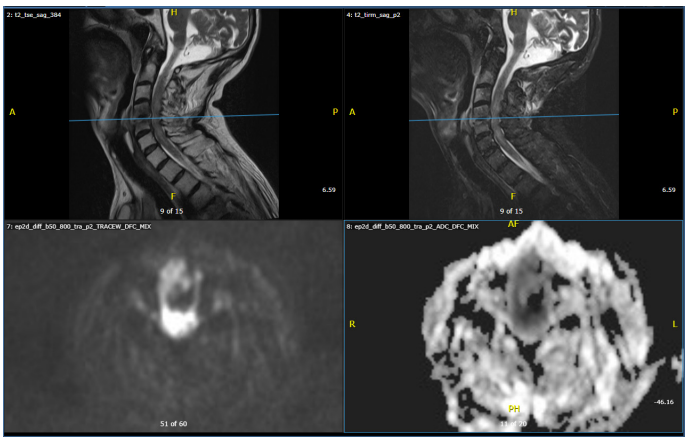
Figure 2: Post-contrast T1-weighted fat-suppressed axial images demonstrate the fissure of the posterior pharyngeal wall on the right side (a, arrowed), the enhancement of the retropharyngeal soft tissue, abscess collection and severe narrowing of the spinal canal (a,b).



(a) (b)

Figure 3: T2-weighted (a) and STIR sagittal images show myelopathy due to compression of the dural sac and bone marrow changes as a sign of the post-irradiation osteonecrosis.

(Images were taken from different slices in order to demonstrate the whole length of myelopathy of the curved spinal cord.)



(a) (b)

Figure 4: At the level of the most pronounced changes, high signal on DWI (a, low row) and low signal on ADC (b, low row) suggested an infection.

Discussion:

Anatomically, the pharynx is divided into three parts in terms of its connection to different anatomic regions: nasopharynx, oropharynx, and hypopharynx. Each of these parts has its specificity, not only in terms of distinct anatomic features and physiologic function but also typical phatology. Beside the differences of the particular regions of the pharynx, there are many common characteristics of all of its parts. From the aspect of morphology one of the mutual features are the same anatomical compartments positioned along the posterior wall: retropharingeal, „danger" and prevertebral space, respectively. The retropharyngeal compartment (also called the "retrovisceral" compartment of the visceral space) is a potential space between the buccopharyngeal fascia and alar fascia that contains fat and medial and lateral retropharyngeal nodes (between the prevertebral muscles and pharyngeal constrictor muscles) and extends from the base of the skull to T3. It is different than the "prevertebral" space that is limited posteriorly by the cervical vertebrae and anteriorly by the prevertebral fascia. The "danger" space is between the alar and prevertebral fascia and extends from skull base to posterior mediastinum [3]. These compartments separate the pharyngeal structures from the cervical spine structures but also can – in case of being affected by the pathologic changes – transfer the pathologic processes or pathological causative agents from the pharyngeal region to the cervical spine space, in the first place an infection.

The most frequently encountered neoplasm in the pharynx is squamous cell carcinoma [4]. Although rarely, minor salivary gland tumors, chordomas, soft tissue tumors and bone tumors may arise in the nasopharynx [4]. Lymphomas are often seen because of the abundance of lymphoid tissue in the oropharynx, which is a significant component of Waldeyer's ring [4]. In the hypopharynx, adenocarcinomas of minor salivary gland origin occur infrequently as well as melanomas, soft tissue tumors and occasional metastatic tumors [4].

Treatment possibilities depend on the stage and location of the disease, as well as patient factors and suitability for different treatment options. The three primary modalities of radical treatment are surgery, radiotherapy and chemotherapy. Another systemic option that is a current area of active research is immunotherapy [5]. The anticipated response to chemoradiation therapy is a key factor in the selection of initial definitive treatment. In general, early staged pharyngeal squamous cell carcinomas are responsive to radiation, with only a small proportion of patients requiring salvage surgery. Therefore, most of these cancers, and particularly those where the larynx is at risk, are currently treated with radiation or chemoradiation therapy. This approach is supported by several prospective trials and has become the standard of care [4]. Surgery remains the only effective option for salvage of patients who do not respond to initial nonsurgical treatment. The management of these patients is challenging, both from the perspective of the cancer and the patient. Tumors that are resistant to chemotherapy and radiation are biologically more aggressive than those that respond, leading to higher rates of recurrence even after complete surgical resection. In addition, chemoradiated tissues heal poorly, leading to increased risk for surgical complications [4].

Therefore, during the follow-up, the assessment of the control of the pharyngeal cancer is not the only subject of clinical investigation, but also the potential post-therapeutic complications. Close position of the pharynx to the cervical spine and thus to the central nervous system (CNS) is the anatomic predisposition on account of which the therapeutic procedures of pharynx carry the potential risk for the elements of the spine itself and for the CNS too.

Radiotherapy can lead to development of osteoradionecrosis (ORN), but can also cause adjacent soft-tissue complications [6]. Radiotherapy effects include inhibition of osteoblasts and osteoclasts, vascular damage and loss of cellular and metabolic balance leading to osteolysis and increased susceptibility to infection. ORN is a process of ischemic bone necrosis associated with soft-tissue necrosis in the absence of malignancy. Cervical spine infections can be related to ORN or manifest on its own. Ulceration of the pharyngeal mucosa or oral cavity can arise secondary to radiotherapy. This results in tissue breakdown and formation of a chronic non-healing wound, which can lead to fistula formation. Microorganisms could gain direct access to the cervical spine from these defects leading to cellulitis, osteomyelitis of the vertebra and/or pathological fracture. Radiotherapy and radical nasopharyngectomy can also destroy the lymphoid tissue surrounding the nasopharynx, predisposing to bony infection. In addition, radiotherapy can increase the permeability of the blood brain barrier leading to the spread of infection to the central nervous system [6]. The presentation of these complications may be delayed (>10–20 years) and the clinical signs and symptoms can be subtle [6]. One study (Zamparini at al., 2019) showed that the period between laryngectomy and diagnosis of cervical osteomyelitis was on average 3 years and 1 month and the male to female sex ratio was 9:1(2). Another study (Y. Cheung at al., 2012) demonstrated predominance of male patients (ratio 10:4) and average duration to diagnosis of the cervical complications after nasopharyngeal carcinoma treatment of 8,6 years (range 1-22)[6]. Cervical pain is the first sign to appear, sometimes 1 year before any other sign[2]. Unfortunately, this sign is not characteristic and can be – as in our case – underestimated and lead to misdiagnosis of chronic neck pain as a sequelae of radiotherapy.

In the case of our patient, all of the mentioned underlying factors for the development of complications existed. The MR exam revealed the osteonecrotic changes within cervical bodies that could be the complication as itself or – at the same time – the base for the further development of more severe complications. Although osteomyelits and discitis are not necessarily indicative of pre-existing ORN and may result from acute infection; the clinical history of these patients is highly suggestive of chronic ORN [7].

In the case of our patient, we could guess that the fistula at the posterior pharyngeal wall was either a postsurgical defect that didn't heal well, a radiation-induced damage, or result of both previously performed tharapeutic procedures. Finally, the post-treatment low local structures defense capacity is also an important aspect that must not be forgotten in such cases. The neck pain that our patient was suffering from was actually the sign of an active slowly progressive infection, not a post-procedural chronic condition. Unfortunately, it is highly likely that the negative endoscopic control exams in given patient contributed as well in wrong clinical assessment.

It is highly important to be familiar with all aspects of possible complications in the group of patients that were treated surgically and by irradiation for pharyngeal carcinoma. These patients should be taken as a group with a high risk of developing complications with a mortality rate of 40% [2]. Although the endoscopic local exam is nessesary for the follow-up, it should be combined with MR examination that can provide insight into the status of the whole cervical region.

We suggest the involvement of the cervical spine MR exam as a standard in the follow-up protocol in order to get information about potential changes within all structures that suffered from the performed therapeutic procedures too. Any changes in the clinical pictures in these patients must be taken seriously.

Additionally, we would like to clarify the usage of terms. Although each of the pharyngeal parts has its specificity and although the anatomical location of the carcinoma may affect prognosis and modality of treatment [5] - as previously mentioned – we think that all of the pharyngeal segments should be considered equally in terms of spinal infections as severe post-therapeutic complications. For this reason, we alternately used the terms: nasopharynx, oropharynx, or hypopharynx throughout the text of the article with regards to different sources from the literature focused only on one of the parts of the pharynx.

Conclusion:

It is of great importance to understand the patients with treated pharyngeal carcinoma of any segment as a risk group for cervical spine infections.

The timely performed MR exam can be essential.

Conflict of interest:

There are no conflicts of interest and no source of funding.

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