Pyogenic Spondylitis with Rapid Bone Destruction After Chemoradiotherapy for Tongue Cancer: A Case Report and Literature Review

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Radiation therapy is a frequently used effective treatment for head and neck cancer. It has several adverse effects of which osteomyelitis is a late complication of radiotherapy. Although uncommon, when it occurs in the vertebral body, it results in pyogenic spondylitis, which can be fatal.
We report a case of pyogenic spondylitis, observed 2 years and 5 months after chemoradiotherapy following surgery for the treatment of tongue cancer. The initial symptoms were fever and posterior cervical pain. Initial CT images showed no abnormality in the cervical spine. However, when CT and MRI were followed over time, bone destruction and abscess formation were observed at the C3 and C4 vertebral endplates. Hence, CT-guided puncture drainage was performed from the anterior neck. The collected pus was diagnosed as Class II pyogenic spondylitis by cytology and the culture test revealed the presence of *Streptococcus agalactiae*. The infection was successfully treated by drainage and antibacterial chemotherapy.

Key word: Cervical spine, pyogenic spondylitis, radiation therapy, *streptococcus agalactiae*, tongue cancer

INTRODUCTION

Pyogenic spondylitis commonly arises from the hematogenous spread of bacteria. Other causes include trauma, nerve block, and other medical procedures, and the spread of surrounding infections [1]. Although rare, pyogenic spondylitis might occur after radiation therapy for head and neck cancer. Most of these are cases of pharyngeal cancer, laryngeal cancer, and cancer of the base of the tongue whose primary tumor site is near the cervical spine [2–4].

We here report a patient with tongue cancer who underwent surgery and chemoradiotherapy, and 2 years and 5 months later developed pyogenic spondylitis. The clinical symptoms were fever and posterior cervical pain. There were no obvious abnormalities on computed tomography (CT) images at the time of onset. However, subsequent CT and magnetic resonance imaging (MRI) images showed rapid bone destruction at the site of C3 and C4 vertebral endplates and abscess formation between the vertebrae. The significance of this case is that it was followed up regularly on CT and MRI from the onset of pyogenic spondylitis until it healed.

CASE REPORT

A 32-year-old man was admitted for pain in the tongue and dysphagia to the Tokai University Hachioji Hospital, Department of Oral and Maxillofacial Surgery. He had no relevant past medical history and had been a smoker for more than 10 years, smoking 20 cigarettes a day. He was obese with a height of 170 cm and a weight of 90 kg. Intraoral findings revealed a large tumor located on the left side of the tongue that crossed the midline. Up on biopsy and a closer examination, a diagnosis of squamous cell carcinoma (7th UICC classification, cT4aN2cM0 stage IVA) on the left side of the tongue was made. Surgery was performed (bilateral functional neck dissection, total tongue resection, and free rectus abdominis myocutaneous flap reconstruction) and postoperative chemoradiotherapy (CDDP 100 mg/m2 × 2; total dose of 66 Gy) was administered. The field of irradiation covered the entire neck including the primary site (Fig. 1). Postoperatively, nutritional management was managed by both gastrostomy and oral administration.

No recurrence or metastasis of the tongue cancer was observed during the follow-up; however, compliance with nutritional management was poor and a necessary tube feeding was not provided. Therefore, 1 year and 1 month after the treatment, megaloblastic anemia developed due to deficiency of folic acid and vitamin B12, which required transfusion and intravenous hyperalimentation (IVH) therapy. At this stage, his weight was 58 kg, a decrease of 32 kg since his first visit. Subsequently, he did not develop anemia but continued to maintain an unbalanced diet.

Two years and 5 months after the treatment, he developed a fever of 38˚C and posterior neck pain. Investigations showed a white blood cell (WBC) level

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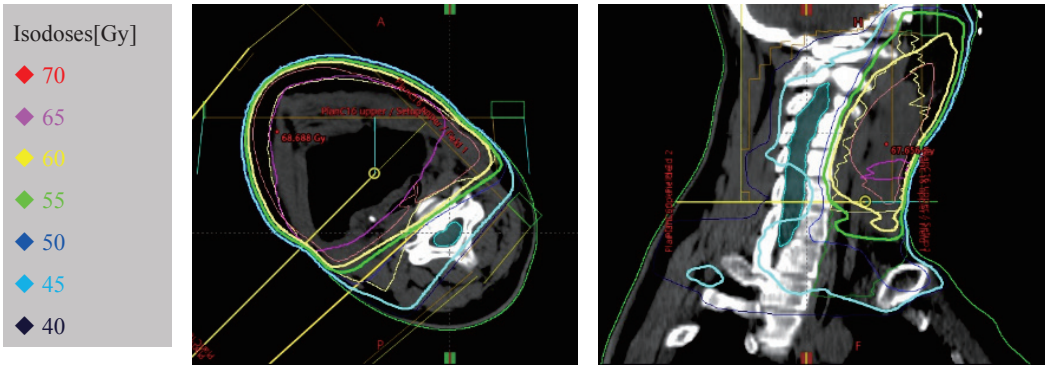

Fig. 1 The irradiation field of radiotherapy, including the entire neck and the primary site.

Fig. 2 CT image at the time of onset. No obvious abnormality was observed on CT images.

of 7.8 × 10 3 /μL, C-reactive protein (CRP) level of 2.6 mg/dL, erythrocyte sedimentation rate (ESR) level of 45 mm/h, and a mild inflammatory reaction. No obvious abnormality was observed on CT images; hence, non-steroidal anti-inflammatory drugs (NSAIDs) were administered and the patient was regularly followed up (Fig. 2). Since the symptoms did not improve, a cervical MRI, performed 17 days later, revealed hypointensity of the vertebral bodies C3 and C4 on T1 weighted sequences. In addition, the C3 and C4 intervertebral discs showed high-intensity areas on T2 weighted sequences. The dural sac appeared to be protruding from the front through osteophytes on the bodies of the vertebrae. Degeneration of the intervertebral disc was observed; however, there was no abnormality of the cervical cord (Fig. 3). Eighteen days later, another CT scan revealed bone destruction of the vertebral body end plate at C3 and C4 (Fig. 4). The 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) showed and accumulation in the C3 and C4 intervertebral regions, and the SUV value to be Max 6.9 (Fig. 5).

Based on these findings, vertebral body metastasis of tongue cancer, vertebral osteomyelitis, epidural abscess, and Crowned dens syndrome were considered among the differential diagnosis. Considering the possibility of spinal nerve palsy due to vertebral fracture, the patient was urgently hospitalized and a neck rest made of polyneck was provided. Antibacterial drugs (Sulbactam/Ampicillin, Vancomycin) were started as empiric therapy for the inflammation. Tissue biopsy was performed by puncturing the intervertebral disc between C3 and C4 from the anterior cervix under CT's guidance. The pus was drained using fine-needle aspiration and a tube drain was placed (Fig. 6). The cytology of the pus was Class II, and metastatic tumors were ruled out. *Streptococcus agalactiae* was detected in the bacterial culture of the pus. Hence, the antibacterial drug was changed to the sensitive benzylpenicillin, which was intravenously administered for 6 weeks, after which amoxicillin was orally administered for 10 weeks. The fever and neck pain subsided. Two months after the onset, a pathological fracture of C3 was observed on CT; however, bone resorption of C3 and C4 vertebral bodies was reduced and the callus formation and cortical bone line were visible on the CT 6 months after the onset (Fig. 7 A and B). To date, pyogenic spondylitis has not recurred, and there has been no recurrence or metastasis of the tongue cancer as of 6 years after the surgery.

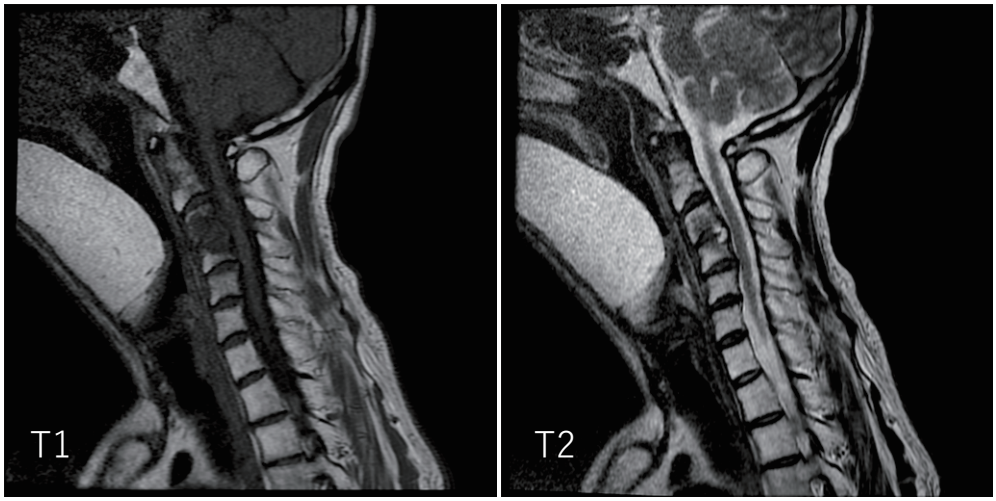

Fig. 3 MRI findings 17 days after onset. The vertebral bodies of C3 and C4 show hypointensity on the T1 weighted image. A high T2 weighted image site was found in the C3 and C4 discs. No abnormal signal was observed in the cervical spinal cord.

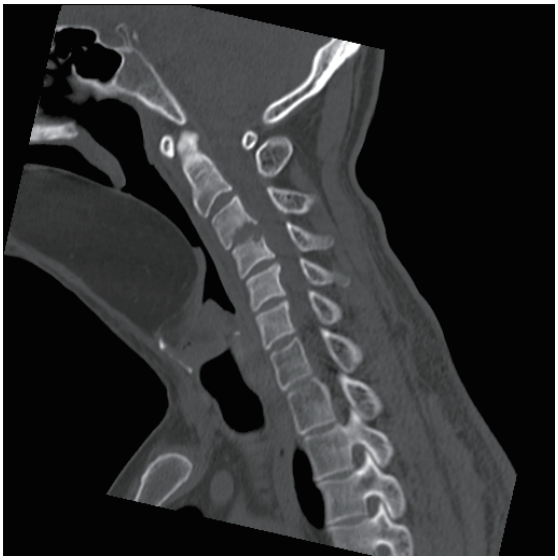

Fig. 4 CT image 18 days after onset. The bone destruction image of the end plate was observed in C3 and C4.

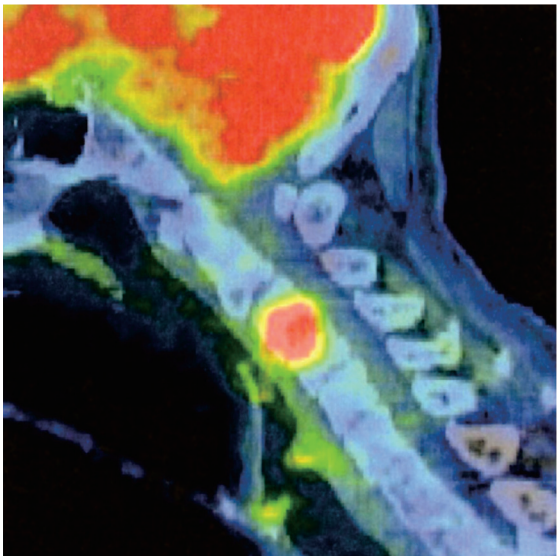

Fig. 5 Accumulation of SUV value MAX 6.9 observed in the intervertebral region of C3 and C4.

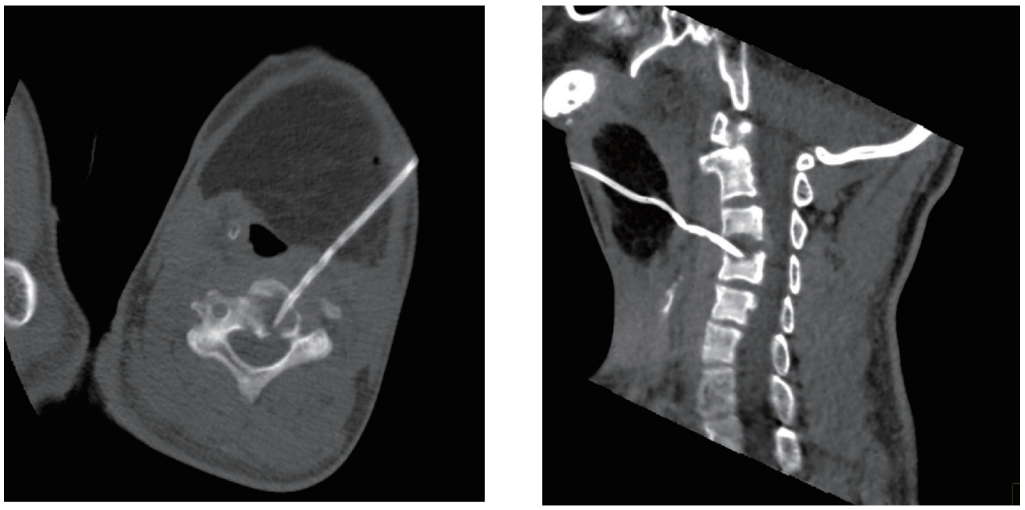

Fig. 6 The tissue biopsy was performed by puncturing the intervertebral disc of C3 and C4 from the anterior cervix under CT guidance. The pus was drained using fine-needle aspiration, and the tube drain was placed.

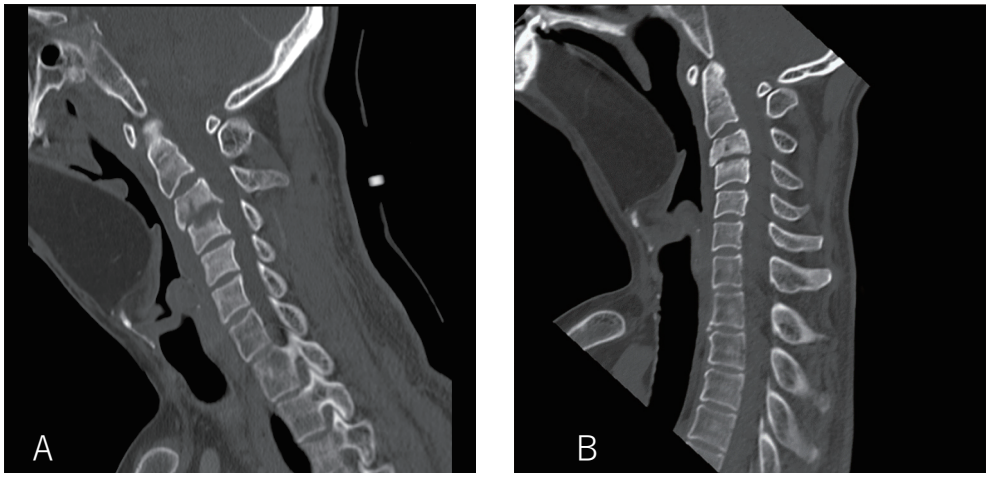

Fig. 7 A Two months after the onset, CT showed pathological fractures in C3; however, the bone resorption of C3 and C4 vertebral bodies was reduced.
B Six months after the onset, CT showed callus formation, and the line of cortical bone is visible.

DISCUSSION

Pyogenic spondylitis encompasses a broad range of clinical entities, including pyogenic spondylodiscitis, septic discitis, vertebral osteomyelitis, and epidural abscess [1]. Pyogenic spondylitis commonly arises from the hematogenous spread of bacteria [5]. The most common site of infection is the lumbar spine (45–50%), followed by the thoracic (35%), cervical (3–20%), and sacral regions [6]. However, pyogenic spondylitis of the cervical spine might occur in patients who have been treated with radiation for head and neck cancer [2–4]. This is because the mucosa of the posterior pharyngeal wall near the cervical spine develops an ulcer due to radiation therapy and causes a direct bacterial infection, or radiation-induced osteonecrosis, and the infection spreads through blood circulation. The primary tumors are usually cancers of the larynx and base of the tongue where the irradiation field is near the cervical spine; however, there are very few reports of tongue cancer [7]. A literature review of 32 cases with cervical spine complications after head and neck cancer treatment including radiotherapy revealed that nasopharyngeal cancer was the most frequently observed case with 18 cases followed by hypopharynx with 6 cases. In contrast, only one case of tongue cancer was observed (Table).

In this case, cancer had spread over a wide area and metastasized to the cervical lymph nodes on both sides. Therefore, the range of irradiation of radiotherapy was wide and a part of the vertebral body at C1–4 level was also included.

The onset of symptoms is usually insidious, with back or neck pain being the most common presenting complaint in more than 90% of the cases. Fever is typically not present and is observed in less than 20% of the patients [8]. Other symptoms include nausea, vomiting, anorexia, weight loss, lethargy, and confusion. Dysphagia might be present in pyogenic spondylitis of the neck. Neurological complications associated with pyogenic spondylitis have been reported in 29% of the cases [8].

According to the literature review, neck pain was most common and was observed in 19 of the 32 cases (60%). On the other hand, fever was only observed in 6 cases (20%).

In this case, a fever of 38°C and posterior neck pain were observed; however, there were no neurological symptoms nor any spinal cord invasion.

Useful laboratory tests are the ESR, CRP, and WBC tests. ESR is quite sensitive and is elevated in almost all cases of pyogenic spondylitis. It slowly declines after the infection is eradicated. CRP is also increased in 90% or more of the cases. It is found elevated within 6 hours of the bacterial infection and is more sensitive than ESR. The WBC count might not be elevated in patients with a spinal infection and, if so, the elevation is usually moderate. The WBC count is not particularly useful in the diagnosis of a spinal infection but should be part of an infection/fever workup as it may provide general insight into the response to treatment [9]. Blood culture is an important test for diagnosing pyogenic spondylitis and is positive in 50% of the cases; the bacteria can also be easily identified. In addition, urinalysis and urine culture, chest X-ray and sputum culture are essential [5].

Early changes in plain radiographs can be inconspicuous as it may develop slowly. The earliest signs are blurring of the endplates and decrease in the disc space, which develops 2 to 8 weeks after the onset of infection. After 8 to 12 weeks, bony destruction can be observed [1]. Radionuclide studies are more sensitive than radiographs in detecting early diseases. Three-phase technetium-99m bone scans are sensitive (sensitivity 90%) but nonspecific (specificity 78%) for spinal infections, particularly in older patients with some degree of spondylosis and degenerative changes in the disc [10]. Gallium-67 citrate scans have similar sensitivity (89%), specificity (85%), and accuracy (86%) as the technetium scans when evaluating pyogenic spinal infections [9]. MRI is the gold standard for imaging the spinal infections. It is particularly useful in the early stages of infection when other imaging modalities are still normal (radiography) or nonspecific (nuclear medicine). The sensitivity, specificity, and accuracy of MRI are reported to be 96%, 92%, and 94%, respectively [9].

Table Case studies with cervical spine complications after head and neck cancer treatment.

Author and year	Age/sex	Primary tumor	Radiotherapy (Total dose/Gy)	Ulceration of posterior pharyngeal wall	Infection site	bacteria	Elapsed time (y)	Sympton
Ng RL. [16] 2002	65/M	Posterior pharyngeal wall	70	+	C3-4	*staphylococcus aureus, candida albicans*	25	Neck pain
Donovan DJ. [17] 2005	62/M	unknown	80	+	C6-7	MRSA	25	Neck pain, Difficulty extending neck, Bilateral upperextremity paresthesias
	69/M	supraglottic larynx	59.4	NA	C5-7	MRSA	0.8	Dyspnea, Kyphosis, Bowel and bladder incontinence, Body weight loss, Left upper and lower extremity weakness.
	71/M	nasopharyngeal	125.4	+	Clivus, C1-2	NA	10	Neck pain, Dysgeusia, Dysphagia
Kosaka Y. [18] 2010	69/F	hypopharynx	76.8	-	C1-6	culture(-)	2.5	Dysphasia, Ascending paralysis
	75/M	oropharynx	76.8	+	C1-3	MRSA	2.3	Left occipital pain
	74/M	upper thoracic esophagus / hypopharyngeal	90	NA	C4-7	NA	2.3	Right upper limb neuropathy
Cheung JP. [4] 2013	55/M	nasopharyngeal	120	NA	C4-5	NA	1	Incidental finding on X-ray
	42/M	nasopharyngeal	NA	NA	C1	NA	2	Headache and fever
	45/M	nasopharyngeal	80	NA	C1-2	NA	3	Neck pain, stiffness, palm numbness
	56/F	nasopharyngeal	NA	NA	C1-2	NA	11	Neck pain, Fever
	49/F	nasopharyngeal	120	NA	C2-4	NA	2	Neck pain, no neurology
	58/F	nasopharyngeal	NA	NA	C2	NA	19	Neck pain, no neurology
	55/M	nasopharyngeal	136	NA	C7	NA	1	Neck pain, no neurology
	51/M	nasopharyngeal	NA	NA	C1-2	NA	22	Neck pain, no neurology
	51/F	nasopharyngeal	NA	NA	C2-4	NA	17	Incidental finding on MRI
	42/M	nasopharyngeal	NA	NA	C5-6	NA	11	Left C5-6 weakness
	52/M	nasopharyngeal	76	NA	C1-2	NA	8	Neck pain
	53/M	nasopharyngeal	NA	NA	C1-6	NA	1	Neck pain, Right upper limb weakness, Fever
	60/F	nasopharyngeal	NA	NA	C1-2	NA	11	Fever
	46/M	nasopharyngeal	NA	NA	C1-2	NA	11	Neck pain
Powell DK. [19] 2013	55/M	hypopharynx	NA	NA	C3-6	*Candida albicans, pseudomonas*	5	Neck pain, Dyspnea
Ueki Y. [20] 2014	68/M	hypopharynx	70	+	C4	culture(-)	0.5	Sore throat
Khorsandi AS. [3] 2015	53/M	pyriform sinus	129.6	NA	C4-5	*Candida albicans*	2.1	Neck pain, Odynophagia
	55/M	palatine tonsil/hypopharynx	85	NA	C3-6	*Veillonella and Staphylococci*	2.5	Neck pain, Inability to lift head, Paraesthesia and bilateral arm weakness, Cord edema
	71/M	base of tongue	72	NA	C3-5	NA	8	Neck pain, Inability to lift head
	68/F	base of tongue	>120.6	NA	C7-T1	NA	0.3	Neck pain, Difficulty swallowing
Lalani N. [21] 2017	54/M	oropharynx/hypopharynx	70	+	C2-3	NA	2	Neck pain
	53/F	nasopharyngeal	70	+	Petrous apices	NA	0.5	Rapidly progressive right-sided otitis externa, Facial pain and restricted neck flexion with torticollis
West JL. [7] 2019	42/M	nasopharyngeal	NA	-	Clivus, C1-2	NA	7	Neck pain
	63/M	tongue	NA	+	Clivus, C1-2	NA	9	Fever and dizziness
Lorna Ting KN. [22] 2019	57/M	nasopharyngeal	70	+	Clivus	*Actinomycetes*	0.5	Bilateral nasal discharge, Fever, Neck stiffness

NA, not available

A typical signal pattern of acute spinal infection on MRI is an increase in the fluid signal because of the marrow edema, with a signal decrease in T1-weighted sequences and a signal increase in T2-weighted sequences with contrast enhancement. In most cases, the infection starts in the anterolateral vertebral body near the endplate. Associated edema is typically pronounced and affects much of the vertebral body and inter-vertebral disc. Spinal neoplasms might also present with similar T1-weighted and T2-weighted findings on an MRI. However, the presence of disc space involvement helps in distinguishing infections from the neoplasms [1]. FDG-PET for the diagnosis of musculoskeletal infection has been reported for orthopedic diseases. The sensitivity and specificity in detecting disc-space infection were 100% and 100% for FDG-PET, respectively [11]. In this case, an accumulation was observed in the disc space between C3 and C4. These findings are important for diagnosing pyogenic spondylitis. However, the definitive diagnosis of pyogenic spondylitis can only be made on a microscopic or bacteriological examination and culture of the infected tissues [12]. Although this case was strongly suspected to be spondylitis based on imaging, a percutaneous biopsy was performed under CT guidance as no bacteria were detected in the blood culture and it could not be distinguished from the vertebral body metastasis of tongue cancer. Class II was detected using cytology and *Streptococcus agalactiae* was detected using a bacterial culture; pyogenic spondylitis was the final diagnosis.

Pyogenic spondylitis after radiotherapy is often caused by bacterial infection directly from the ulcer of the posterior pharyngeal wall, as was observed in this case; however, it was not confirmed within the visible range. Moreover, the diagnosis was incomplete due to the trismus associated with the surgery for tongue cancer and radiotherapy. In such cases, an examination should be performed using a Fiberscope [4]. The common organisms that cause pyogenic spondylitis are Staphylococcus aureus and streptococcus species, which account for more than 50% of the cases [13].

In the literature review, 10 cases of the pathogenic bacterium were described with *Streptococcus aureus* affecting half of these cases (5), and of which 3 cases were MRSA. In addition, *Candida albicans* was observed in 3 cases suggesting that it was immunocompromised.

The *Streptococcus agalactiae* detected in this case generally resides in the intestine and vagina, and is rarely detected in the oral cavity and pharynx.

Diabetes mellitus, malnutrition, substance abuse, HIV, malignant tumors, long-term steroids, chronic renal failure (CRF), liver cirrhosis (LC), and sepsis are the predisposing factors for pyogenic spondylitis and infection [14]. In this case, oral feeding and gastrostomy were used for postoperative nutritional management; however, the patient's compliance was poor. As a result, there were several episodes of temporary deficit of folic acid and vitamin B12, leading to megaloblastic anemia. In addition, weight loss was more prominent compared to the initial examination, and the patient appeared undernourished. Hence, he was considered to be in a compromised condition.

Although the exact route of infection could not be determined, the weakening of the pharyngeal mucosa by radiation therapy may have caused a blood circulation infection of *Streptococcus agalactiae* and thereby pyogenic spondylitis.

Currently, intensity-modulated radiotherapy (IMRT) is the norm, and there are fewer side effects compared to conventional methods [15]. This patient did not receive IMRT as he was unable to lie supine due to the postoperative scar contracture and pain. Furthermore, it was difficult for him to be completely immobile during the treatment. As a result, there was a possibility of dose variations and unnecessary irradiation of the spine.

CONCLUSION

Radiation therapy is frequently used to treat head and neck cancer; however, late complications may develop. We report a patient that developed pyogenic spondylitis in the cervical spine, two and a half years after the treatment. The clinical symptoms were mild with only fever and posterior cervical pain; however, imaging findings showed rapid destruction of the cervical spine and abscess formation. This case is of significance as we demonstrate the image changes over time for the disease.

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