

A rare late complication after concomitant chemoradiation of an oropharyngeal tumor: cervical necrotizing fasciitis

Eş zamanlı orofarenks tümör kemoradyoterapisi sonrasında gelişen nadir bir komplikasyon: Servikal nekrotizan fasiit

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Chemoradiation is increasingly being used to treat locally advanced head and neck carcinomas. Possible rare complications of this treatment modality have begun to appear, as the number of treated patients increase. In this report, we present a case who underwent chemoradiation due to T₃N₃M₀ tonsil cancer and developed necrotizing fasciitis of the neck at seven months following treatment. The patient recovered fully after treatment with surgical debridement with pectoralis major flap reconstruction and intravenous antibiotherapy.

Key Words: Cervical necrotizing fasciitis; chemoradiation; complication; head and neck cancer.

Lokal olarak ilerlemiş baş ve boyun tümörlerinin tedavisinde kemoradyoterapinin yeri giderek artmaktadır. Bu tedaviyi gören hastaların sayısı arttıkça, tedavinin nadir muhtemel komplikasyonları da görülmeye başlanmıştır. Bu makalede, T₃N₃M₀ tonsil kanseri nedeniyle kemoradyoterapi gören ve tedaviden yedi ay sonra boynunda nekrotizan fasiit gelişen bir hasta sunuldu. Hasta cerrahi debridman, pektoralis majör flep rekonstrüksiyonu ve intravenöz antibiyoterapi sonrası tamamen iyileşti.

Anahtar Sözcükler: Servikal nekrotizan fasiit; kemoradyoterapi; komplikasyon; baş ve boyun kanseri.

Necrotizing fasciitis is an infection of the subcutaneous tissues that leads to progressive destruction of fascia and fat. It most commonly affects the abdominal wall, perineum and extremities.^[1,2] It rarely affects the head and neck region. When necrotizing fasciitis does affect the cervical region it is known mostly as a complication of a pharyngeal or a dental infection or as a complication of trauma or surgery.^[1,2] The causative bacteria are a mix of aerobes (e.g. *Streptococcus spp.* and *Staphylococcus spp.*) and anaerobes. Conditions that impair the healing process such as diabetes mellitus and substance abuse are reported to be

risk factors.^[1,2] Chemoradiation therapy (CRT) of the head and neck area, which became the standard of care especially for advanced stage oropharyngeal cancers,^[3-5] could also be a risk factor. Concomitant CRT is reported to have more severe toxicity compared to radiation.^[6,7] Impaired tissue healing is listed as one of the consequences of CRT, which modified salvage surgery principles to utilizing flap reconstructions to bring non-radiated tissue to the operation field. Even with this approach higher pharyngocutaneous fistula rates are reported when salvage surgery follows chemoradiation.^[8] The current report describes such a patient who

went through a treatment track including CRT and salvage surgery and developed cervical necrotizing fasciitis seven months after CRT and three months after salvage neck dissection.

CASE REPORT

A 63-year-old male patient was diagnosed with T₃N₃ tonsil cancer and treated with concomitant CRT, which consisted of 70 Gy in 35 fractions over seven weeks and three infusions of cisplatin intravenously at a dose of 100 mg/m². According to the treatment protocol at our institution post-treatment evaluation by magnetic resonance imaging (MRI) and ultrasound (US) guided fine needle aspiration (FNA) biopsy, took place three months after the completion of CRT, which showed complete remission at the primary site, and -although no malignant cells were identified by FNA- a persistent necrotic node in level 2 of the right neck. The persistent lymph node was removed four months after treatment by a super-selective neck dissection. During this procedure a panendoscopy was performed and biopsies were taken from a de-epithelialized area at the right tonsil. The histopathology of the residual lymph node and the biopsy from the tonsil showed necrosis, and no vital tumor cells. Postoperatively, the patient developed pain and trismus due to epithelial defects at the right tonsil. These

defects were attributed to impaired tissue healing after CRT and managed conservatively with 10 sessions of hyperbaric oxygen therapy. Three months after the salvage surgery the patient was admitted with general malaise, fever, pain in the right oral cavity and neck, trismus and no oral intake since one week. Physical examination revealed foetor ex ore, subfebrile temperature of 37.8 °C and a diffusely erythematous, warm, swollen neck with two necrotic skin lesions with purulent discharge. Laboratory values showed a CRP of 140 mg/L and white blood cell count of 20.6*10E9/L. Computed tomography (CT) scan of the neck revealed a subcutaneous gas formation from the right side of the neck extending to the retropharyngeal space, and 3.5 cm cavity filled with fluid on the right side of the neck in close contact with the common carotid artery (Figure 1a, b). Based on the physical examination and the findings of the radiological evaluation the diagnosis of necrotizing fasciitis was established. The patient was brought to the operating room, where extensive necrotic tissue debridement took place. The tissue was unidentifiable. The carotid artery, vagal and hypoglossal nerves were identified and spared. The rest of the neck tissues up to the level of the oral cavity were removed including the overlying skin and necrotic parts of the deep cervical muscles. After placement

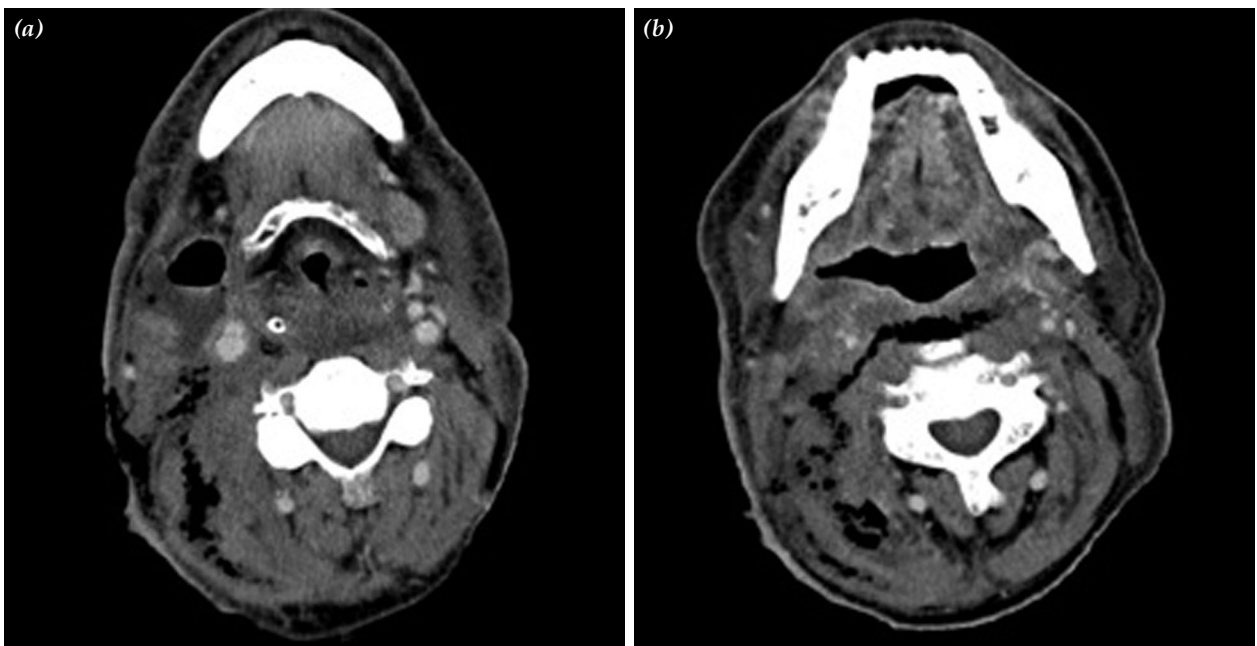


Figure 1. (a) Shows a 3.5 cm cavity filled with fluid on the right side of the neck in close contact with the common carotid artery. (b) Shows subcutaneous gas formation from the right side of the neck extending to the retropharyngeal space and fistula formation with the pharynx.

of two drains, the defect was covered with a pectoralis major muscle flap (PMMF) and left to secondary healing. Histopathology of the fibrous and muscle tissue showed necrosis and signs of active chronic inflammation. Postoperatively the patient received gentamycin and penicillin that was later switched to clindamycin because of a beta hemolytic group F *Streptococcus* in the wound culture. The wound culture in addition grew mixed anaerobes. The wound was twice daily irrigated with diluted iodine solution through the drains. The patient improved gradually; the drains were removed after three weeks and the PMMF was covered with a split thickness skin graft from the thigh. The patient was discharged after four weeks. At follow-up six months after discharge the patient had a completely healed neck, but still had trismus and swallowing dysfunction for which he was dependent on gastrostomy tube feeding.

DISCUSSION

The potential link between necrotizing fasciitis and chemoradiotherapy is not yet well documented. In the head and neck region Maluf et al.^[9] described a case of cervical necrotizing fasciitis nine months after completing treatment with neoadjuvant and concurrent chemotherapy with radiotherapy for an oropharyngeal tumor. Cavel et al.^[10] described a patient with AIDS that developed necrotizing fasciitis of the skull base and neck one week after chemotherapy treatment with Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisone (CHOP) for a non-hodgkin lymphoma. Miyagawa et al.,^[11] presented a case where necrotizing fasciitis of the penile skin occurred seven years after treatment with chemotherapy and radiotherapy for a relapsed seminoma. Mortimore et al.^[12] report two cases of cervical necrotizing fasciitis years after radiotherapy for head and neck malignancy.

The isolated case reports are not strong evidence to list cervical necrotizing fasciitis as one of the complications of CRT. However impaired tissue healing is one of the predisposing factors and this phenomenon is well documented. Long-term effects of radiotherapy include skin atrophy, soft tissue fibrosis, lymphatic and microvascular damage leading to a higher risk of wound healing problems, even decades after radiotherapy treatment.^[13] Physicians following patients who were treated with CRT should

be alert to infection entry points such as non-healing oral ulcers, tissue defects and dental infections. In the current case the long period between neck surgery and infection implies that the non-healing defects in the oral mucosa are the potential entry point of this serious infectious condition. The preferred management of such an infection entry point is wound care and -although controversial- hyperbaric oxygen treatment.^[14] The improvement in tissue healing is proposed to come from the increased level of tissue oxygen, which is necessary for many cellular functions. For example it increases white cell function and stimulation of collagen synthesis by fibroblasts.^[14]

In the current patient hyperbaric oxygen treatment was not able to contain the oral infection and prevent it from spreading to the fascial planes of the neck. Complete surgical debridement and regular irrigation of the infection site is the standard of care. It is preferential to leave the wound bed open for sufficient irrigation, however when the carotid artery is exposed such as in the current case bringing healthy tissue to the wound bed becomes essential.

In conclusion, cervical necrotizing fasciitis is a manageable condition if recognized in the early stages. Alertness to the risk in patients who have received CRT to the head and neck area, especially in the presence of a non-healing oral/pharyngeal defect could establish early diagnosis and management.

REFERENCES

1. Bahu SJ, Shibuya TY, Meleca RJ, Mathog RH, Yoo GH, Stachler RJ, et al. Craniocervical necrotizing fasciitis: an 11-year experience. *Otolaryngol Head Neck Surg* 2001;125:245-52.
2. Chattar-Cora D, Tulsyan N, Cudjoe EA, Onime GD, Pyo DJ, Weinstein L. Necrotizing fasciitis of the head and neck: a report of two patients and review. *Head Neck* 2002;24:497-501.
3. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. The Department of Veterans Affairs Laryngeal Cancer Study Group. *N Engl J Med* 1991;324:1685-90.
4. Weber RS, Berkey BA, Forastiere A, Cooper J, Maor M, Goepfert H, et al. Outcome of salvage total laryngectomy following organ preservation therapy: the Radiation Therapy Oncology Group trial 91-11. *Arch Otolaryngol Head Neck Surg* 2003;129:44-9.
5. Pignon JP, le Maître A, Maillard E, Bourhis J; MACH-NC Collaborative Group. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93

- randomised trials and 17,346 patients. *Radiother Oncol* 2009;92:4-14.
6. Bhide SA, Newbold KL, Harrington KJ, Nutting CM. Combined chemotherapy and intensity-modulated radiotherapy for the treatment of head and neck cancers. *Expert Rev Anticancer Ther* 2010;10:297-300.
 7. Ang KK, Harris J, Garden AS, Trotti A, Jones CU, Carrascosa L, et al. Concomitant boost radiation plus concurrent cisplatin for advanced head and neck carcinomas: radiation therapy oncology group phase II trial 99-14. *J Clin Oncol* 2005;23:3008-15.
 8. Taki S, Homma A, Oridate N, Suzuki S, Suzuki F, Sakashita T, et al. Salvage surgery for local recurrence after chemoradiotherapy or radiotherapy in hypopharyngeal cancer patients. *Eur Arch Otorhinolaryngol* 2010;267:1765-9.
 9. Maluf FC, William WN Jr, Rigato O, Menon AD, Parise O Jr, Docema MF. Necrotizing fasciitis as a late complication of multimodal treatment for locally advanced head and neck cancer: a case report. *Head Neck* 2007;29:700-4.
 10. Cavel O, Gil Z, Khafif A, Leider-Trejo L, Segev Y, Werner B, et al. Necrotizing Fasciitis of the Skull Base and Neck in a Patient with AIDS and Non-Hodgkin's Lymphoma. *Skull Base* 2006;16:201-5.
 11. Miyagawa T, Kawai K, Onozawa M, Hattori K, Shimazui T, Akaza H. Unusual presentation of necrotizing fasciitis in a patient who had achieved long-term remission after irradiation for testicular cancer. *Int J Urol* 2005;12:332-4.
 12. Mortimore S, Thorp M. Cervical necrotizing fasciitis and radiotherapy: a report of two cases. *J Laryngol Otol* 1998;112:298-300.
 13. Dormand EL, Banwell PE, Goodacre TE. Radiotherapy and wound healing. *Int Wound J* 2005;2:112-27.
 14. Jallali N, Withey S, Butler PE. Hyperbaric oxygen as adjuvant therapy in the management of necrotizing fasciitis. *Am J Surg* 2005;189:462-6.