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## **Cervical osteomyelitis: A new identity of dreaded complication following pharyngeal cancer treatment**

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22 **RUNNING HEAD:** ‘Cervical osteomyelitis following pharyngeal cancer treatment with chemoradiotherapy and  
23 laryngectomy’

24 **AUTHORS’ CONTRIBUTIONS**

25 • Dr Emmanuel Zamparini (MD): 1<sup>st</sup> author, clinical data collection; involved in drafting and revising  
26 the manuscript.

- 27 • Dr Piseth Seng (MD, PhD): 2<sup>nd</sup> and corresponding author; involved in drafting and revising the  
28 manuscript.
- 29 • Dr Matthieu Bardou (MD): 3<sup>rd</sup> author, involved in clinical data verification, revising the manuscript.
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- 35 • Pr Patrick Dessi (MD, PhD): 7<sup>th</sup> author, involved in clinical data verification, revising the manuscript.
- 36 • Pr Andreas Stein (MD, PhD): last author approved the final version to be published
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#### 38 **ETHICS**

39 This study was approved by the institutional research ethics board, and a written informed consent form was  
40 signed by the patients.

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46 this manuscript once it was ready for submission.

47 **KEYWORDS:** Cervical osteomyelitis; Laryngectomy; Larynx carcinoma; cervical cancer; Infection

48

49 **ABSTRACT**

50 **Background.** Cervical osteomyelitis following pharyngeal cancer treatment with chemoradiotherapy and  
51 laryngectomy is poorly reported.

52 **Methods.** We herein report the cases of six cases over a one-year period and we also reviewed the four cases  
53 reported in literature.

54 **Results.** Among the ten cases, the average age was 58.7 years, the period between laryngectomy and diagnosis  
55 of cervical osteomyelitis was 3 years and 1 month and the sex ratio was 9 men /1 woman. Two patients had a  
56 history of cervical fistula with an esophageal prosthesis, one had a spontaneous cervical fistula, one had a  
57 pharyngeal cutaneous fistula and one had an esophageal prosthesis without any fistula. At the time of diagnosis,  
58 seven had a history of cervical pain (70%) and nine had a neurological deficiency (90%). Seven patients (70%)  
59 underwent surgery; one (10%) was contraindicated for a general anesthetic, two (20%) died before any  
60 intervention. The indications for surgery were: a neurological deficit for six patients (60%) and two (20%)  
61 needed a lavage and debridement. Average length of antimicrobial treatment was of 12.7 weeks. The outcome  
62 was favorable for 6 patients. Four patients died.

63 **Conclusions.** Cervical osteomyelitis is a serious but rarely reported complication following pharyngeal cancer  
64 treatment with chemoradiotherapy and laryngectomy. Cervical pain was the first sign to appear, sometimes one  
65 year before any other sign. Physicians should be aware of this dreaded complication which is probably  
66 underdiagnosed and which is related to an increased mortality rate.

67

68 **1 Introduction**

69 Cervical osteomyelitis following pharyngeal cancer treatment with laryngectomy, radiotherapy and  
70 chemotherapy is poorly reported (1,2,3). We herein report the cases of six patients treated by laryngectomy for  
71 laryngeal or pharyngeal cancer, with chemoradiotherapy complicated by cervical osteomyelitis and review 4  
72 more cases of literature (4,5,6).

73 **2 Materials and methods**

74 Our center is the referral center for bone and joint infections in south of France located in the Marseille  
75 university hospital. This study design was approved by the review board of our institute. We retrospectively  
76 reviewed the 6 cases of vertebral osteomyelitis with positive culture following pharyngeal cancer treatment with  
77 chemoradiotherapy and laryngectomy managed between January 2015 and December 2017. We also reviewed  
78 the 4 cases of literature.

79 The diagnosis of vertebral osteomyelitis was based on patient's medical history, including clinical evidence of  
80 infection based on biological and radiological data, with  $\geq 2$  positive blood cultures or  $\geq 2$  positive cultures from  
81 deep samples from surgical or percutaneous biopsy to exclude contaminating bacteria.

82 After incubation, the bacteria species was identified through conventional phenotypic identification or MALDI-  
83 TOF MS (Brüker Daltonik). A complete 16S rRNA gene sequencing and real-time PCR assays targeting  
84 *Staphylococcus aureus* performed on bacteria colony for the unknown bacteria identified through MALDI-TOF  
85 MS and on deep samples which were negative at culture.

86 We evaluated each patient's medical history, assessing factors such as demographic characteristics,  
87 comorbidities, and clinical. We reviewed the antimicrobial and/or surgical treatment approaches used in each  
88 case and the outcome.

89 **3 Results**

90 **3.1. Clinical characteristics**

91 Among the ten cases, the average age was 58.7 years, the period between laryngectomy and diagnosis of cervical  
92 osteomyelitis was 3 years and 1 month and the sex ratio was 9 men /1 woman. Two patients had a history of  
93 cervical fistula with an esophageal prosthesis, one had a spontaneous cervical fistula, one had a pharyngeal  
94 cutaneous fistula and one had an esophageal prosthesis without any fistula. At the time of diagnosis, seven had a  
95 history of cervical pain (70%) and nine had a neurological deficiency (90%).

96 **3.2. Microbiological characteristics**

97 Surgical bone cultures were positive in 90 % of cases. Blood cultures were positive for three out of seven  
98 patients (42.8%). Surprisingly, pathogens detected did not belong to the oropharyngeal flora: *Streptococcus*  
99 *constellatus* (3 patients), *Enterobacter cloacae* (1 patient), *Escherichia coli* (1 patient), *Pseudomonas aeruginosa*  
100 (2 patients), *Enterococcus faecalis* (1 patient), *S. epidermidis* (1 patient), Mucormycosis (1 patient),  
101 *Enterococcus faecium* (1 patient), coagulase negative staphylococci (1 patient), *Staphylococcus aureus* (1  
102 patient). Infection was monomicrobial for six patients, polymicrobial for three patients, and culture negative for  
103 one.

104 **3.3 Medical and surgical treatment**

105 All patients underwent antimicrobial therapy excepted two who died before any treatment. Average length of  
106 treatment was of 12.7 weeks [4 weeks – 24 weeks]. Antimicrobial therapy are show in table 1. Seven patients  
107 (70%) underwent surgery; one (10%) was contraindicated for a general anesthetic, two (20%) died before any  
108 intervention. The indications for surgery were: a neurological deficit for six patients (60%) and two (20%)  
109 needed a lavage and bacteriological documentation because the patient's condition were worsening. The six  
110 patients (60%) who underwent an operation had a posterior arthrodesis, five patients (50%) had a local bone  
111 biopsy (two patients, two times), one patient (10%) underwent two lavages, and another patient (10%) had a  
112 simple needle aspiration.

113 **3.4 Clinical outcome**

114 The outcome was favorable for 4 patients, and one patient who had a follow-up for a long period didn't show  
115 any sign of recurrence. One died after 3 months of care, of an uncontrolled infection further complicated by  
116 Lemierre's syndrome. One patient presented a hypertensive cerebral hemorrhage, one month after being  
117 discharged. One died of septic shock few days after admittance. Another died of hypoxemia arrest one month  
118 after discharge. One died of complication of his neurological involvement.

119 **4 Discussion**

120 Cervical vertebral osteomyelitis is rarely reported but a serious complication following the treatment of pharynx  
121 carcinoma treated with chemoradiotherapy and laryngectomy. To the best of our knowledge, only four cases of  
122 this disease have been previously reported in adults. In this paper, we report six new cases over a one year  
123 period. In the context of laryngeal or pharyngeal cancer treatment with chemoradiotherapy and pharyngo-  
124 laryngectomy, cervical pain, fever or neurological signs should lead to early imaging to confirm the diagnosis.

125 Cervical pain was the first sign to appear, sometimes one year before any other sign. In addition, esophageal  
126 prosthesis could be a risk factor of cervical infection; osteomyelitis after this kind of surgery has been previously  
127 reported (7). Unlike some other team's, we did not retain patients with cervical osteomyelitis after a second  
128 invasive procedure (8). Treatment in a neurological surgery center seems compulsory, in order to stabilize the  
129 spine while documenting the infection. In this context of pharyngeal cancer with previous radiotherapy and  
130 surgery, we recommend posterior arthrodesis only. Microbial documentation is necessary to guide antimicrobial  
131 therapy. We recommend to do blood culture, surgical or percutaneous biopsies (five samples) with aerobic,  
132 anaerobic and fungal cultures. If cultures are negatives, we recommended molecular biology with 16S rRNA  
133 gene sequencing and real-time PCR assays targeting *Staphylococcus aureus*. Antimicrobial therapy should be  
134 adapted to polymicrobial infections and maintained over several weeks in order to obtain a definitive cure. We  
135 recommended initial antimicrobial therapy with piperacillin, tazobactam and vancomycin for two weeks and  
136 after identification, two oral antimicrobial therapy if it's possible. If identification it's not possible, we  
137 recommended antimicrobial therapy focus on oral streptococci and negative bacilli such as Cotrimoxazol and  
138 clindamycin. The duration of therapy should be 6 weeks without any surgical device or 3 months if arthrodesis  
139 had been performed. All of these recommendations are consistent with those of Infectious Diseases Society  
140 America (9). Physicians should be aware of this dreaded complication which is probably underdiagnosed (we  
141 diagnosed six cases over a year in our center) and which is related to a high mortality (40%). It seems that early  
142 diagnosis and management improve the fatal issue, but more extensive studies are requested to confirm this  
143 finding.

## 144 5 Conclusion

145 In the context of laryngeal or pharyngeal cancer treatment with laryngectomy, cervical pain, fever or  
146 neurological signs should lead to early imaging to confirm the diagnosis. Cervical pain was the first sign to  
147 appear, sometimes one year before any other sign. In addition, esophageal prosthesis could be a risk factor of  
148 cervical infection. Treatment in a neurological surgery center seems compulsory, in order to stabilize the spine  
149 while documenting the infection. Precise microbial documentation is a crucial step in the management of those  
150 infections because bacteria found are not those from oropharyngeal flora. Antimicrobial therapy should be  
151 adapted to polymicrobial infections and maintained over several weeks in order to obtain a definitive cure.  
152 Physicians should be aware of this dreaded complication which is probably underdiagnosed and which is related  
153 to a high mortality (40%). It seems that early diagnosis and management improve the fatal issue.

154

155 CONFLICT OF INTEREST

156 The authors declare that they have no conflict of interest.

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160 or conflict with the subject matter or materials discussed in the manuscript. A native English speaker polished

161 this manuscript once it was ready for submission.

162

163 ETHICS

164 This study was approved by the institutional research ethics board, and a written informed consent form was

165 signed by the patients.

166 **6 References**

167 1. Skaf GS, Domloj NT, Fehlings MG, Bouclaous CH, Sabbagh AS, Kanafani ZA, et al. Pyogenic  
168 spondylodiscitis: an overview. *J Infect Public Health*. 2010;3(1):5-16.

169 2. Prasad KC, Prasad SC, Mouli N, Agarwal S. Osteomyelitis in the head and neck. *Acta Otolaryngol*. feb  
170 2007;127(2):194-205.

171 3. Kremers HM, Nwojo ME, Ransom JE, Wood-Wentz CM et al. Trends in the epidemiology of  
172 osteomyelitis: a population-based study, 1969 to 2009. *J Bone Joint Surg Am*. 2015; 97(10):837-45.

173 4. Biller HF, Ogura JH, Rontal M, Ehrlich C. Cervical osteomyelitis complicating pharyngeal resection.  
174 *Arch Otolaryngol Chic Ill* 1960 1971; 94: 165-8.

175

176 5. Buruma OJ, Craane H, Kunst MW. Vertebral osteomyelitis and epidural abcess due to mucormycosis, a  
177 case report. *Clin Neurol Neurosurg* 1979; 81: 39-44.

178

179 6. Ell SR, Parker AJ, Limb D, Clegg RT. Osteomyelitis of the cervical spine following laryngectomy. *J*  
180 *Laryngol Otol*. 1992; 106: 1096-7.

181

182 7. Mullen TD, Sharma AK, Varma AK. Cervical osteomyelitis after placement of a self-expanding plastic  
183 stent for palliation of dysphagia associated with chemoradiation-induced esophageal strictures. *Head Neck*. Jun  
184 2013;35(6):E197-201.

185 8. Espitalier F, de Keating-Hart A, Morinière S, Badet J-M, Asseray N, Ferron C, et al. Cervical  
186 spondylodiscitis following an invasive procedure on the neopharynx after circumferential  
187 pharyngolaryngectomy: a retrospective case series. *Eur Spine J*. 2016;25(12):3894-901.

188 9. Berbari EF, Kanj SS, Kowalski TJ, Darouiche RO, et al. 2015 Infectious Diseases Society of America  
189 (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in  
190 Adults. *Clin Infect Dis*. Sep 2015; 61(6):859-63.

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Table 1. Demographic characteristics, clinical features, treatment and outcomes of the 10 patients with cervical osteomyelitis following pharyngeal cancer treatment with chemoradiotherapy and laryngectomy.

Cases number	Ages (years), Sex	Comorbidities	Localization	TNM Classification	Treatment of cancer	Time to diagnosis	Clinical signs	Localization	Pathogens	Surgical Treatment	AT duration (weeks)	Outcomes
Our 1st case	63, M	Smoking, alcohol	Tonsillar PS, Palate	n. k.	LRG, RTH, CTH	5 years	Fever, cervical pain	C3-C4	<i>S. constellatus</i> <i>S. epidermidis</i> <i>E. cloacae</i>	LD, PA, laminectomy LD x 2	24	Deceased
Our 2nd case	53, F	Smoking, alcohol	Hypopharynx	T4N0M0	LRG, RTH, CTH	4 years	Fever, syncope, quadriparesis	C3-C5	None	LD, PA, laminectomy	8	Cured, fistula
Our 3rd case	55, M	Smoking	Hypopharynx	N. K.	LRG, RTH, CTH	4 months	Cervical pain, fever, quadriplegia	C7-T2	<i>S. constellatus</i>	LD, PA, laminectomy	13.5	Cured, paresthesia
Our 4th case	65, M	Pulmonary tuberculosis, cirrhosis, Smoking	Hypopharynx	T4N2c	LRG, RTH, CTH, ER	2 years	Paresthesia, cervical pain	C5-T1	<i>P. aeruginosa</i> <i>E. faecalis</i>	LD, PA, laminectomy	6	Cured
Our 5th case	67, M	Smoking, alcohol, HBP	Hypopharynx	T4aN1M0	LRG, RTH, CTH, EP	2 years	Fever	C5-C6	<i>S. epidermidis</i>	CI	On going	Being treated, no relapse
Our 6th case	62, M	Smoking, alcohol	Hypopharynx	T4N0M0	RTH, LRG	6 years	Swallow disorder, cervical pain, paresthesia	C6-C7	<i>E. faecium</i>	LD, PA, laminectomy	12	Deceased
Buruma et al. (1979)	60, M	Tuberculous lymphadenopathy	Hypopharynx	n. k.	RTH, LRG	11 years	Horner syndrome, quadriparesis, cervical pain, fever	C3-C4	<i>Mucormycose</i> (post-mortem)	None	None	Deceased
Ell et al. (1992)	51, M	HBP, Smoking	RVF	T2N0M0	RTH, LRG	4 months	Fever, cervical pain, paresthesia (left arm)	C6-C7	CNS <i>E. coli</i>	LD, PA, laminectomy, bone graft (iliac crest), 6 weeks of traction	n. k.	Cured
Biller et al. (1971) case-1	59, M	n. k.	Right lateral PS	n. k.	RTH, Skin graft reconstruction and Negus stent	1 month	Swallow disorder, cervical pain, paresthesia	C6-C7	<i>S. aureus</i>	Needle aspiration, Cruchfield tongs (1 M), Four-poster brace (1 Y)	n. k.	Cured
Biller et al. (1971) case-2	52, M	n. k.	Palate Hypopharynx Right PS	n. k.	RTH Partial pharyngectomy	2 months	Fever, hemiparesis	C5-C7	<i>P. aeruginosa</i>	Refused by patient	None	Deceased

n. k.: not known, RTH: Radiotherapy, CTH: Chemotherapy, LRG: laryngectomy, EP: Esophageal prosthesis, ER: Esophageal reconstruction, HBP: high blood pressure, PLP: partial laryngopharyngectomy, CNS: Coagulase negative staphylococci, LD: lavage and debridement, PA: posterior arthrodesis, CI: contraindicated, AT: antimicrobial therapy