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Classification of craniofacial osteoradionecrosis: The addition of 'end stage disease'

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Craniofacial Osteoradionecrosis (ORN) represents a late complication of radiotherapy (RT) for head and neck cancer. Traditionally, mandibular ORN refers to the RT-related mandible necrosis and subsequent exposure of the bone for at least 3 months in the absence of recurrence (1). We now have increasing evidence of long-term tissue damage from chemo-radiation (2,3). Most of cases are diagnosed between 1 to 2 years following RT but there is lifelong risk (2). Caparroti et al recently reported that the actuarial rate of ORN of the mandible was 3% at 1 year, 5% at 3 years, and 7% at 5 years in 1196 patients who were diagnosed with squamous cell carcinoma of the oropharynx and treated with curative-intent radiotherapy, with or without concomitant systemic treatment, from January 2005 to December 2014. As the proportion of HPV- related oropharyngeal cancer treated with chemo- RT is soaring, and it mainly affects young non- smoker individuals, 'at risk' population has significantly increased necessitating better understanding, and management of the disease (5).

ORN is characterized by hypoxic, hypocellular and hypovascular tissue, followed by tissue breakdown secondary to radiation-induced activation and dysregulation of the fibroblastic activity that caused vascular fibrosis and thrombosis. The mandible is more susceptible to ORN as it is solely supplied by the paired inferior alveolar arteries; therefore, the obliteration of its nutrient vessels causes an ischemic necrosis in irradiated atrophic tissue. Due to this relatively poor vascularization and the absence of collateral blood supply, the mandible, especially buccal cortex of premolar, molar and retromolar regions, is at greater risk of necrosis (3).

It has been suggested that post-RT dental extractions, especially of posterior lower teeth, or dental implant placement are the main culprits (although we are lacking level I evidence), but ORN can also occur spontaneously. The recommended dose constraint is a maximum dose of 70Gy. However, it is generally accepted that the risk of ORN is high at dose >60 Gy, moderate between 40 and 60 Gy, and null <40 Gy, and that there is a dimension-dose correlation: lesions >2 cm occurred at doses>60 Gy, whereas lesions <2 cm in size are related to doses <60 Gy (3).

The clinical spectrum of disease ranges from the asymptomatic exposure to debilitating pain, extra-oral fistulae and pathological fracture. In line with the onset and severity of clinical symptoms and radiological findings several classification systems have been proposed, and treatment varies from clinical surveillance to major reconstructive surgery with composite free flaps.

As mentioned above, several ORN classification systems have proposed. Shaw et al. recently reviewed 16 ORN classifications and considered Notani classification with the addition of

minor bone spicules as the most reliable and consistent in terms of reporting ORN for prospective clinical trials (5,6). In addition, Notani et al proposed treatment based on the height of mandible that is affected (Table 1).

Most clinicians and researchers will use the Notani classification for communicating a patient's condition and for the reporting in clinical trials. Indeed, this is a step forwards but can also be misleading implying that the mandible is the primary and exclusive site of ORN. Nonetheless, a group of patients are now emerging, with a history of chemo-radiation for head and neck cancer with mandibular ORN and additional involvement of adjacent craniofacial skeleton and its underlying structures. In this context temporal or frontal bone ORN with TMJ destruction, extra-intraparenchymal brain collections, middle ear otitis/mastoiditis and facial palsy can be encountered. These patients are difficult to classify using the Notani or other available classifications (Picture 1).

Patients with isolated mandibular ORN are often challenging pertained to their reconstructive problems, but overall their aesthetics and function can be restored with free tissue transfer resulting in an acceptable health related quality of life (HRQOL). In contrast the patient with mandibular ORN in addition to the sites described above often have dismal prognosis and invariably have signs and symptoms that are very difficult to manage; often are not amenable to surgery and may succumb to their complications. We recommend the addition of ''end stage disease'', to include cases with Notani stage III and additional regional involvement as per Table 2.

Table 1. The Notani classification for mandibular ORN

Stage I	ORN confined to the alveolar bone.
Stage II	ORN limited to the alveolar bone and/or the mandible above the level of the mandibular alveolar canal.
Stage III	ORN that extended to the mandible under the level of the mandibular alveolar canal and ORN with a skin fistula and/or a pathologic fracture.

Table 2. Features of 'end-stage' ORN

End stage ORN	**Mandibular Notani III plus any of the following:** • Fronto-Zygomatic-Orbital Complex involvement • Skull base bone destruction with middle ear involvement (with or without VIIth or other cranial nerve involvement) or TMJ involvement with destruction of fossa and temporal bone • Extradural abscess, Subdural Empyema or Brain abscess

Conflict of interest: The authors have no conflict of interest to report

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Figure 1. Extensive ORN involving the mandible and base of skull (please see arrow)

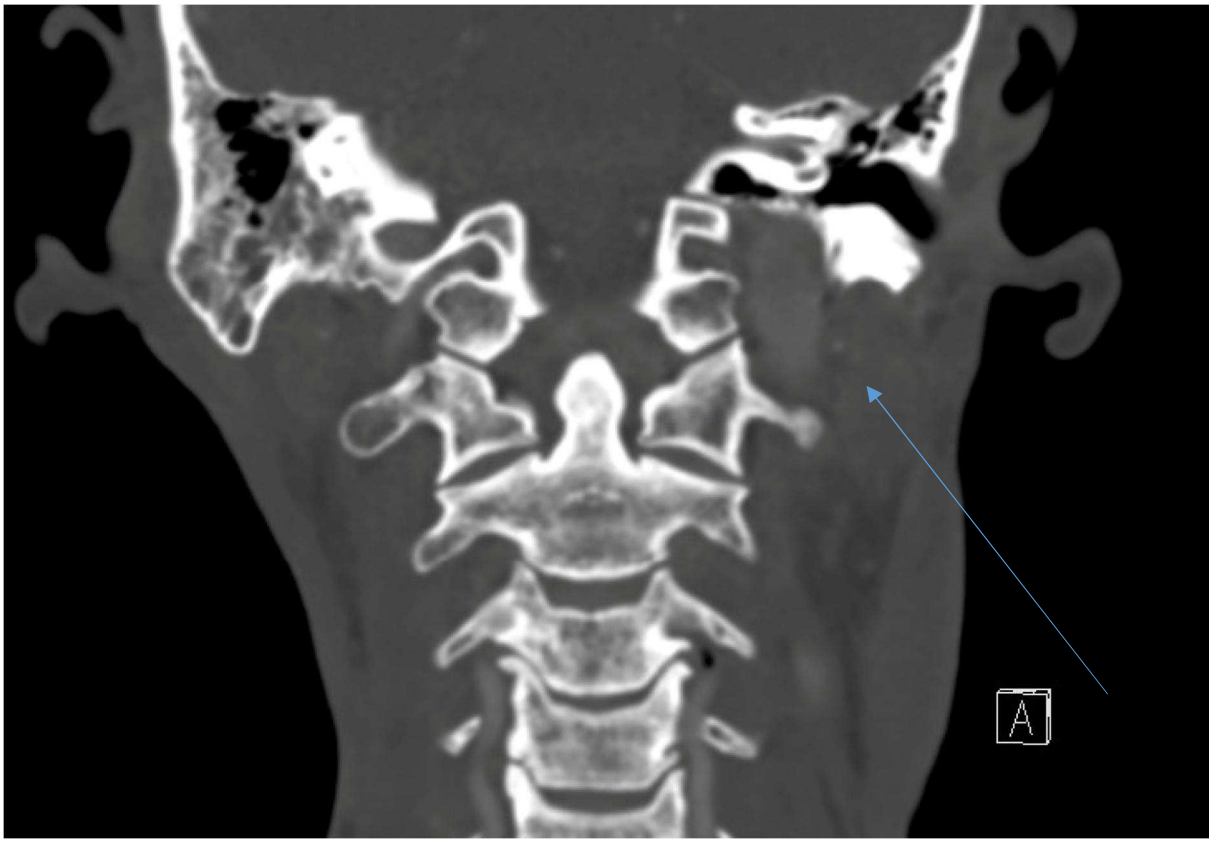

Figure 2. Extensive ORN involving the mandible and temporal bone and subdural collection (please see arrow)