Extended survival after chemotherapy and conservative radiotherapy for HPV-16 positive stage IVB oropharyngeal carcinoma

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To the Editor,

Stage IVB head and neck cancer represents an unresectable disease with some chance of cure. Treatment of this extensive malignant tumor using a combination of chemotherapy and radiotherapy has resulted in complete tumor response rates of 40–71%, with survival at three years seen in approximately one third of cases (and up to 56% with

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(Received 15 January 2013; accepted 24 January 2013)

ISSN 0284-186X print/ISSN 1651-226X online © 2013 Informa Healthcare
DOI: 10.3109/0284186X.2013.770922

follow-up of 29–45 months) and grade 2 or 3 toxicity experienced by 36–89% of patients [1–3]. People with human papillomavirus (HPV) positive oropharyngeal squamous cell carcinomas (OPSCC) have a significantly better response and improved survival after aggressive therapy compared to those with HPV-negative OPSCC [4–6]. We report a case of stage IVB HPV-positive OPSCC which exhibited a sustained response to induction and then concurrent chemotherapy with conservative, de-escalated dose radiotherapy (ICCR).

Case report

A 49-year-old man was referred in July 2001 for management of histologically-proven OPSCC (the diagnosis was established a month prior). The patient's medical history showed that he was not a smoker or an alcoholic. Physical examination revealed a reddish tumor in the right tonsil extending into the nasopharynx, ipsilateral pyriform sinus and lateral pharyngeal wall; a 0.5 cm level II lymph node was palpable in the right side of the neck. HPV-16 status was positive (Figure 1) after evaluation of the formalin-fixed, paraffin-embedded tumor specimens by the in situ hybridization-catalyzed signal-amplification method for biotinylated probes (GenPoint, Dako [7]). A chest radiograph was normal. The multidisciplinary tumor board at our institution staged the HPV-16 positive OPSCC as IVB (T4bN1M0) and recommended ICCR with a curative intent. Combined therapy was administered in the manner akin to that mentioned in a previous report except that the employed total dose for gross disease was 60 Gy given in 30 fractions, and for subclinical disease, 50 Gy in 25 fractions [8]. Treatment was well tolerated and a complete response was achieved. The patient was alive and free of cancer at the time of the last follow-up in March 2012.

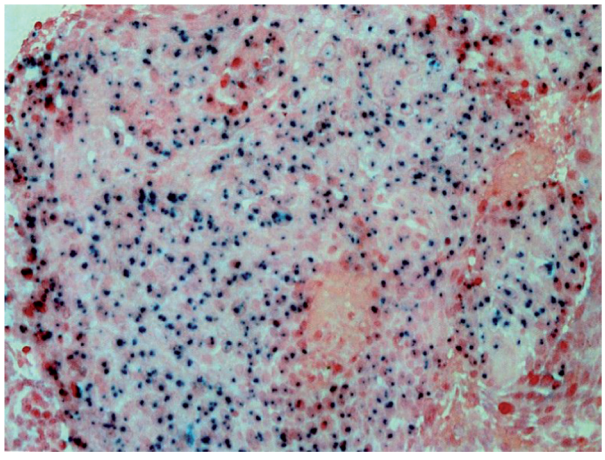

Figure 1. Human papillomavirus-16 positive tumor defined by punctate hybridization signals localized to the tumor cell nuclei.

Discussion

The reported incidence of stage IVB head and neck cancer is 4–27% [9,10]. In our institution, we observed such locally advanced, HPV-positive OPSCC in an individual who remains disease free for more than 10 years after ICCR. A review of the literature about HPV-positive OPSCC and its management by chemoradiation did not reveal a case of similar disease stage. More importantly, due to clinician preference, our administered dose (way below the standard prescription of 70 Gy) to the primary tumor was 60 Gy. This dose selection was based on the impression that chemoradiotherapy alters the potential for late effects of treatment, and the use of chemotherapy adds a biologic equivalent dose of 12 Gy [11].

The reasons for the generally observed good outcome in patients with HPV-16 positive OPSCCs are not clearly known, but the various postulations include patient-related factors such as: young age, infrequent presence of co-morbidity, and limited exposure to tobacco and alcohol, the absence of field cancerization, enhanced local immunity to the viral antigen, and the theories that HPV-positive tumors are apparently less hypoxic and can be more easily induced to undergo apoptosis after chemoradiation [12–15].

Appropriate selection of patients is essential to ensure that they are neither under- nor over-treated. Besides the higher cost, the use of aggressive chemoradiotherapy is associated with a greater risk of significant toxicity and smaller benefit compared to radiotherapy alone [16]. HPV-16 positive OPSCCs in patients without a history of tobacco or alcohol abuse may be biologically different and more amenable to cure [17]. This consideration can, perhaps, be ascribed to the hypothesis that tumors in this category do not develop as many mutations to undergo malignant transformation as a result of the viral-induced molecular changes. Very little in the way of a treatment recommendation can be drawn from this single case report. Nonetheless, under the perspective of the observed good outcome, decreasing the treatment intensity for these neoplasms which are believed to be less hypoxic, might result in lesser toxicity through reduction of treatment-associated morbidity, a more complete and durable response, and an ultimately favorable impact on long-term survival. Clinical investigations designed to identify the precise role of chemotherapy with de-intensified radiotherapy for HPV-16 positive OPSCCs are currently in progress.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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