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Original article

Three-year results after radiotherapy for locally advanced sinonasal adenoid cystic carcinoma, using highly conformational radiotherapy techniques proton therapy and/or Tomotherapy

Résultats à trois ans d'une association de tomothérapie et/ou de protonthérapie pour les carcinomes adénoïdes kystiques nasosinusiens de la base du crâne

A. Dautruche[a,*], S. Bolle[b], L. Feuvret[c], C. Le Tourneau[a], T. Jouffroy[d], F. Goudjil[e], S. Zefkili[a], C. Nauraye[e], J. Rodriguez[d], P. Herman[f], V. Calugaru[a]

[a] *Radiotherapy Department, institut Curie, 26, rue d'Ulm, 75005 Paris, France*
[b] *Radiotherapy Department, Gustave-Roussy Cancer campus, 114, rue Édouard-Vaillant, 94800 Villejuif, France*
[c] *Radiotherapy Department, hôpital La Pitié-Salpêtrière, 47–83, boulevard de l'Hôpital, 75013 Paris, France*
[d] *Head and Neck Surgery Department, institut Curie, 26, rue d'Ulm, 75005 Paris, France*
[e] *Medical Physics Department, institut Curie, 15, rue Georges-Clémenceau, 91400 Orsay, France*
[f] *Head & Neck Surgery Department, hôpital Lariboisière, 2, rue Ambroise-Paré, 75010 Paris, France*

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ABSTRACT

Purpose. – We report the patient outcomes of a treatment combining proton therapy and Tomotherapy in sinonasal adenoid cystic carcinoma involving skull base.
Materials and methods. – We included patients treated at Curie Institute, Paris, France, between March 2010 and February 2014 for an advanced adenoid cystic carcinoma involving skull base. Patients received Tomotherapy, proton therapy or both. We evaluated treatment toxicity (according to CTCAE V4), local control, distant metastasis-free survival and overall survival.
Results. – Thirteen patients were included, with a median follow-up of 34 months. Radiation therapy followed surgery for 77% of the patients and margins were positive in all those cases. Median dose was 73.8 Gy. Local control, distant metastasis-free survival and overall survival at 3 years were respectively 60%, 48% and 60%. One-sided grade 3 hearing impairment occurred in 46% of the patients.
Conclusion. – Combining high-dose proton therapy and Tomotherapy is effective and has moderate toxicity in the treatment of T4 sinonasal adenoid cystic carcinoma involving skull base.

Mots clés :
Carcinome adénoïde kystique
Protonthérapie
Tomothérapie: Réirradiation
Radiothérapie

RÉSUMÉ

Objectif de l'étude. – Nous avons réalisé une étude retrospective sur les résultats à trois ans d'une prise en charge par tomothérapie et/ou protonthérapie pour les carcinomes adénoïdes kystiques nasosinusiens atteignant la base du crâne.
Matériel et méthodes. – Nous avons inclus les patients traités à l'institut Curie, Paris, France, entre mars 2010 et février 2014 pour un carcinome adénoïde kystique nasosinusal atteignant la base du crâne. Les patients ont été pris en charge par une tomothérapie, une protonthérapie ou une association des deux techniques. Les réirradiations étaient permises. Nous avons évalué la tolérance du traitement, le contrôle local, la survie sans métastase et la survie globale.
Résultats. – Treize patients ont été inclus, avec un suivi médian de 34 mois. La radiothérapie intervenant après une intervention chirurgicale chez 77 % des patients. Les berges opératoires étaient atteintes chez tous les patients opérés. La dose médiane était de 73,8 Gy. À 3 ans, le taux de contrôle local était de 60 %, celui de survie sans métastase de 48 % et celui de survie globale de 60 %. Une hypoacousie tardive de grade 3 était présente parmi 46 % des patients.

* Corresponding author. Radiotherapy Department, institut Curie, 26, rue d'Ulm, 75005 Paris, France.
E-mail address: Antoine.Dautruche@gmail.com (A. Dautruche).

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Conclusion. – L'association de tomothérapie et de protonthérapie permet une irradiation à haute dose, efficace et bien tolérée; dans le traitement des carcinomes adénoïdes kystiques sinonasaux de stade T4 atteignant la base du crâne.

1. Introduction

Adenoid cystic carcinoma, first named cylindroma for its histologic appearance, is mostly known for its salivary gland localization, where it appeals for 10% of the neoplasms [1]. This histology can also be found in the nasal or oral cavity, larynx or pharynx and makes for 1% of all head and neck tumours [2,30]. These tumours, although having a slow growth rate, are prompt to perineural involvement, distant metastasis (mostly lung and liver), and have ability to recur over a long period after a satisfying surgical treatment.

Sinonasal tumours can be challenging to treat, as they can grow without causing symptoms until they reach the orbit or the skull base and are associated with worst outcomes than salivary glands or oral cavity adenoid cystic carcinoma [2,3]. Furthermore, negative oncologic margins are difficult to obtain surgically as they are located in functionally critical sites, making radiotherapy mandatory [4].

Despite the lack of large randomized study, most authors suggest that conventional treatment for head and neck adenoid cystic carcinoma should be in most cases surgery followed by radiotherapy, even for small tumours with negative margins [5–7]. Doses superior to 64 Gy are required to obtain local control [5], which can be difficult to achieve in this region as this may lead to severe early (mucositis, denutrition, eye disorders) and late (osteoradionecrosis, brain necrosis, blindness, hearing impairment) side effects. The frequent perineural invasions may be difficult to include, even with multimodal imaging, and often lead to complex clinical target volumes requiring highly conformational radiation therapy techniques.

Proton therapy is known to be safe and efficient, even at the high doses required for other face neoplasms such as chordomas, chondrosarcomas, neuroendocrine tumours, nasopharyngeal carcinoma and skull base adenoid cystic carcinoma [8–12]. It shares unique physical properties with other particles such as carbon ions that allow preservation of organs at risk, with a very fast dose decrease behind the "Bragg peak", where the maximum dose is given, and a moderate entry dose. It is indicated for well-limited tumours, such as meningioma, chordomas and eye melanomas. Proton therapy is already known for providing an acceptable local control rate in locally advanced sinonasal adenoid cystic carcinoma (50% at 5-year disease-free survival) [13].

Photon therapy using intensity-modulated irradiation, or dose modulation, is also known to be efficient and safe for the treatment of face, skull base and sinonasal tumours [14] and the combination of proton and photon therapy may be used to combine the advantage of both techniques, usually using proton therapy for dose-escalation purposes [12].

The purpose of this study is to evaluate the results, in terms of global survival and local control as well as side effects, of proton therapy and/or photon therapy on advanced sinonasal cavities adenoid cystic carcinoma involving skull base.

2. Material and methods

2.1. Patient selection

We reviewed retrospectively the patients treated at institut Curie, France, between March 2010 and February 2014 who had a confirmed locally advanced sinonasal adenoid cystic carcinoma. The patients were treated using Tomotherapy, proton therapy, or a combination of both techniques.

Inclusion criteria were a histologically confirmed advanced adenoid sinonasal carcinoma with incomplete surgical resection (R1 or R2), or non-operated. The tumour had to be a large T4b tumour involving skull base. Metastatic tumours at the time of treatment were excluded from this study.

2.2. Treatment

Radiotherapy was performed with Tomotherapy, proton therapy or a mix of both. Unless the patient had previously been treated, the prescribed radiation dose was at least 70 Gy. Conventional fractionation was used, with 1.8 Gy to 2 Gy per fraction. The technique used for protons was double-scattering. Three-dimensional proton therapy was performed using a 201MeV proton beam at the Curie institute protontherapy centre of Orsay, France (ICPO). Relative biological effectiveness of protons was 1.1 Gy. Tomotherapy was given at Curie institute, Paris, France. Image-guided radiotherapy was used for both techniques. Reirradiation and concomitant chemotherapy was allowed.

For immobilization purposes, a thick custom-made thermoplastic mask was used throughout the entire treatment program. Proton treatment procedure included the implantation under local anaesthesia of four to five radiopaque gold fiducial markers in the outer skull. The fiducial markers were used for the proton part to determine required translational and angular corrections using an original computer program developed at ICPO (Rotaplus). Then, a 3D virtual simulation based on a contrast CT scan with 1 and 2 mm thick slices and contrast 3D MRI (T2, T1 with and without gadolinium sequences) with 1.5 mm thick slices was performed with the patient in a supine position.

Target volumes and organs at risk were defined on MRI. Gross tumour volume was defined as the visible tumour on MRI. A margin of 0.3–0.5 cm was added to the gross tumour volume to define the high risk clinical target volume (CTV3 HR), depending on proximity of the organs at risk and bone structures. An intermediate risk clinical target volume (CTV2 IR) was defined as the preoperative tumour volume expended to the operatory bed and ipsilateral sinus. A low risk clinical target volume (CTV1 BR) was defined as CTV2 IR plus the ipsilateral cavernous sinus and a 1.5 at 2 cm extension to the trajectory of the involved nerfs. A high risk planning target volume (PTV3 HR) was defined as the CTV3 HR with a surrounding margin of 5 mm for the Tomotherapy plan and 1 mm for the protons. An intermediate risk planning target volume (PTV2 IR) was defined as

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