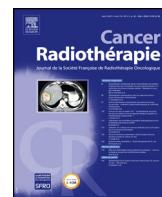




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Original article

Analysis of rare periparotid recurrence after parotid gland-sparing intensity-modulated radiotherapy for nasopharyngeal carcinoma



Analyse des rares récidives périparotidiennes après radiothérapie conformationnelle avec modulation d'intensité avec épargne parotidienne des carcinomes nasopharyngés

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ABSTRACT

Purpose. – Periparotid recurrence is an uncommon phenomenon after intensity-modulated radiotherapy (IMRT) for nasopharyngeal carcinoma. This study aimed to discuss the clinical characteristics, reasonable causes and feasible therapeutic modalities of patients with nasopharyngeal carcinoma and periparotid recurrence.

Patients and methods. – The medical records of 1852 patients with non-metastatic nasopharyngeal carcinoma treated with initial IMRT between January 2008 and December 2012 were retrospectively reviewed, and nine patients were finally found to have developed periparotid recurrence after IMRT. After periparotid failure, four received radiotherapy and chemotherapy, two had surgery, two had surgery and adjuvant radiotherapy or chemotherapy, and one received radiotherapy alone.

Result. – The incidence rate of periparotid recurrence was 4.9%. According to pretreatment magnetic resonance imaging (MRI) scans, all patients had both ipsilateral retropharyngeal lymph nodes metastasis with 66.7% of extracapsular spread and level II lymphadenopathy with all extracapsular spread. The median time interval to periparotid failure was 14.8 months, and six patients were found to have a relapse in the primary sites of unsuspicious parotid nodules. After a median follow-up of 46.4 months, five patients developed distant metastasis, three of them developed local failure. In addition, one developed regional failure, one developed locoregional recurrence, and only one was alive without evidence of disease at the last follow-up.

Conclusion. – Periparotid recurrences are rare after definitive IMRT for nasopharyngeal carcinoma. However, patients with ipsilateral retropharyngeal lymph nodes or level II nodal extracapsular spread on pretreatment MRI could be suspicious of metastatic periparotid nodules. Distant metastases were the main treatment failure despite a combination of several salvage treatment of periparotid recurrence. More effective chemotherapy should be explored.

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RÉSUMÉ

Mots clés :

Carcinome nasopharyngé
Récidives périparotidiennes
Radiothérapie avec modulation d'intensité
Métastases à distance
Chimiothérapie

Objectif de l'étude. – La récidive périparotidienne est un phénomène rare après la radiothérapie conformatrice avec modulation d'intensité (RCMI) des carcinomes nasopharyngés. Cette étude visait à examiner les caractéristiques cliniques, les causes potentielles et les modalités thérapeutiques possibles pour la prise en charge des carcinomes nasopharyngés avec récidive périparotidienne.

Patients et méthodes. – Les dossiers de 1852 patients atteints de carcinome nasopharyngé non métastatiques, pris en charge par RCMI entre janvier 2008 et décembre 2012, ont été rétrospectivement revus. Neuf patients ont vu se développer une récidive périparotidienne. Parmi ces patients, quatre ont été pris en charge par radiothérapie et chimiothérapie, deux par chirurgie, deux par chirurgie et radiothérapie adjuvante ou chimiothérapie, et un exclusivement par radiothérapie.

Résultat. – Le taux de récidive périparotidienne était de 4,9 %. Sur les IRM faites avant le traitement, tous les patients étaient atteints à la fois de métastases ganglionnaires rétropharyngées homolatérales (dont 66,7 % avec envahissement extracapsulaire) et dans l'aire II, avec envahissement extracapsulaire. L'intervalle de temps médian jusqu'à la récidive périparotidienne était de 14,8 mois, et six patients avaient été atteints de récidives dans des nodules parotidiens présents initialement et considérés comme non suspect. Après un suivi médian de 46,4 mois, cinq patients ont vu se développer des métastases à distance, trois de ces patients étaient atteints de récidive locale. Par ailleurs, un patient était atteint de récidive régionale et un de récidive locorégionale. Seulement un était en vie sans signe de maladie au dernier suivi.

Conclusion. – Les récidives périparotidiennes de carcinome nasopharyngé sont rares après une RCMI. Cependant, les patients atteints de métastases ganglionnaires rétropharyngées homolatérales ou dans l'aire II homolatérale avec envahissement extracapsulaire sur l'IRM faite avant le traitement pourraient être atteints de nodules métastatiques périparotidiens. Les métastases à distance étaient la principale cause d'échec du traitement malgré la conjugaison de plusieurs traitements de sauvetage des récidives périparotidiennes. L'utilisation de chimiothérapies plus efficaces devrait être explorée.

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1. Introduction

Nasopharyngeal carcinoma is characterized by unique histologic types and highly sensitive to irradiation [1]. Therefore, radiotherapy has become the mainstream therapeutic approach in non-metastatic nasopharyngeal carcinoma. However, when treating patients with conventional radiotherapy, co-irradiation of parotid glands and subsequent xerostomia is unavoidable. With the prevalence of parotid gland-sparing intensive-modulated radiotherapy (IMRT), significant improvements in salivary function have been confirmed in a number of randomized controlled trials [2,3]. Nevertheless, a concern with parotid-sparing modality is that overprotection of parotids might result in marginal failure [4–7].

In 2008, Cannon and Lee first reported on two nasopharyngeal carcinoma patients who developed marginal failure in spared parotids in IMRT era [4]. In the subsequent study, Lin et al. retrospectively reviewed the records of three patients with nasopharyngeal carcinoma who developed periparotid recurrences after definitive IMRT, suggesting that advanced stage of disease, preexisting metastasis in periparotid region and overprotection of the parotid gland may contribute to periparotid failure [5]. However, the above two studies were confined to sporadic case reports; concrete reasons for periparotid failure need further systematic exploration.

Recently, a comprehensive study with a larger number of cases was published by Cao et al. for the purpose of discussing the clinical characteristics and reporting on survival outcomes of periparotid recurrence [6]. The author considered that the involvement of retropharyngeal lymph nodes was one of the major contributions to periparotid failure, while 69.4% of patients with nasopharyngeal carcinoma presented with retropharyngeal lymphadenopathy at diagnosis [8]. At present, it is still difficult for clinicians to identify suspect cases and carry out individual treatments to avoid periparotid failure. In addition, despite multidisciplinary salvage protocols, the optimal treatment modalities could not be established. Therefore, it is imperative to make a thorough analysis of

the exact causes of the rare recurrence, and make an exploration of the feasible treatment modalities.

In the present study, very rare patients with nasopharyngeal carcinoma (nine out of 1852 cases) were also found to develop peri-parotid recurrence after definitive IMRT. Therefore, the aim of the current study is to depict clinical characteristics and discuss the reasonable causes and feasible therapeutic modalities for periparotid recurrence, and to give a reference for the clinicians to prevent and treat them.

2. Patients and methods

2.1. Patients

This retrospective study was approved by the institutional review board of Fujian provincial cancer hospital. We performed a retrospective review of the medical records of 1852 patients with histologically proven and newly diagnosed non-metastatic nasopharyngeal carcinoma treated by definitive intensity-modulated radiation in our institution from January 2008 to December 2012. The pretreatment evaluation of all patients was completed based on our institutional protocol [9], and the disease staging was accomplished according to the 7th edition of the International Union Against Cancer/American Joint Committee on Cancer (UICC/AJCC) for nasopharyngeal carcinoma [10,11]. None of these patients had previously undergone surgery or radiotherapy of the head and neck.

Amongst these 1852 patients with nasopharyngeal carcinoma, nine were finally found to have developed periparotid recurrence after radical radiotherapy, as detailed in Table 1. Indeed, patients with periparotid recurrences were initially identified based on routine MRI follow-up at nasopharynx and neck after the completion of IMRT, and MRI diagnostic criteria for periparotid recurrence was indicated by our previous study [12]. After initial evaluation of MRI follow-up, a suspicious parotid lesion was finally confirmed by

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