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Clinical Study

Late-onset radiation-induced optic neuropathy after radiotherapy for nasopharyngeal carcinoma

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ABSTRACT

Radiation-induced optic neuropathy (RION) is a rare but devastating late complication of radiotherapy, usually manifesting months to years after cancer treatment of the head and neck, resulting in rapidly progressive blindness in one or both eyes. The incidence of radiation-induced complications following radiotherapy, especially RION, is correlated with survival time of patients. Nasopharyngeal carcinoma (NPC), the most common type of cancer in southern China, has been primarily treated with radiotherapy, with associated neural injuries. To our knowledge, there are few reports of RION among patients with NPC who have undergone radiotherapy. To study this further, we reviewed nine patients with NPC and RION after radiotherapy and examined the clinical manifestations of RION, characteristics of the ophthalmologic examination, MRI results and the treatments used. Of the nine patients with RION, the most frequent clinical presentation was a decline of vision with visual field defects in one or both eyes. Ophthalmologic examinations showed flame hemorrhages in the retina, optic nerve atrophy and cotton wool spots. T1-weighted enhanced MRI showed enhancement of the optic nerve and optic chiasm in six patients. Treatment with corticosteroids, anticoagulation and hyperbaric oxygen (HBO) treatment did not reduce visual loss or blindness in patients.

1. Introduction

Nasopharyngeal carcinoma (NPC) in the Guangdong province of southeastern China constitutes approximately 32% of all cancers, making it the most common type of cancer in the province. The incidence of NPC in Guangdong province is more than 20 per 100,000 people every year among males[1] and is, to our knowledge, the highest in the world.[2] Owing to the special pathological features of NPC, radiotherapy is the first, and sometimes the only, effective treatment for the disease.[3] However, radiation exposure to normal brain tissue during radiotherapy may cause severe side effects. Radiation-induced brain injury, especially to the bilateral inferior temporal lobes, is the most common sequela of radiotherapy and can lead to progressive deterioration of hippocampal-associated learning and memory function.[4]

Radiation-induced optic neuropathy (RION) is a rare but usually devastating side effect of radiotherapy, with iatrogenic radiation damage in patients who have had radiotherapy for tumors in sites near the visual apparatus, such as the choroid plexus, orbit, paranasal sinuses, nasal cavity and cranial fossae.[5–8] RION usually begins after a latency months to years following radiation exposure and typically presents with acute, painless, irreversible visual loss in one or both eyes.[9–12] Although RION has been documented for almost 100 years, no proven effective treatment has emerged to reverse or halt the visual function once visual loss has begun,[13] which can be especially devastating to patients and caregivers.

With improvements in treatment techniques, patients with cancers now have longer survival times. However, these treatment improvements mean more attention needs to be given to RION, despite the fact that it is a rare complication of radiotherapy. Other studies have also reported RION in patients with NPC.[14–18] In the current study we report data obtained in a retrospective chart review of patients with NPC who suffered visual failure after receiving radiotherapy. Studying the characteristics of this side effect may lead to future research into effective methods for preventing RION in patients with NPC who receive radiotherapy.

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2. Materials and methods

2.1. Patients

Between January 2007 and December 2011, 238 patients at Sun Yat-sen Memorial Hospital of Sun Yat-sen University displayed various radiation-associated complications after undergoing radiotherapy for NPC. These patients were periodically evaluated in outpatient visits or by telephone interview after they were discharged from hospital. Six patients (2.5%) could not be contacted and were excluded from the study. We performed a retrospective chart review of the files of the other 232 patients to collect all available data on the course of the illness during their stay in our hospital. During the review, we found nine patients who suffered from RION. The goal of the current study was to examine the characteristics of RION in these nine patients.

2.2. Diagnostic criterion of RION

In patients with NPC who had previously received radiotherapy, a diagnosis of RION was based on clinical characteristics. The diagnostic criterion for RION is evidence of an irreversible visual dysfunction (impaired visual function with loss of visual acuity and/or visual field defect) in the absence of other causes, making it a diagnosis of exclusion.

2.3. Methods

In this retrospective descriptive study, we used data from a chart review. Certified neurologists and oculists performed the follow-up neurological and ophthalmologic examinations. Descriptive statistics were used to summarize the clinical profiles of eligible patients.

2.4. Outcomes assessment

The vision decline of each patient was measured as a global functional assessment of the change in the ophthalmologic condition: blindness, light perception (LP), hand movement (HM), and varying degrees of vision decline.

The classification of the severity of visual impairment was based on the Chinese diagnostic criteria for radiation-induced nervous system disease published by the Ministry of Health of the People's Republic of China in 2009 [in Chinese]: I° (color vision decline), II° (blurred vision, color discrimination loss), III° (severe visual impairment, visual field defect with central vision loss affecting daily activities), and IV° (blindness).

A CT scan rarely shows changes in the optic chiasm and nerve and thus is usually inconclusive in diagnosing RION. However, the use of MRI has improved the diagnosis of RION, and can also distinguish RION from other types of cancers.[11] Therefore, all nine patients received MRI examinations.

3. Results

3.1. Patient profiles

We reviewed the charts of nine patients who were recruited with their signed consent (Table 1). The nine patients had undergone radiotherapy after a diagnosis of NPC. Clinical manifestations of these patients fulfilled the diagnostic criteria for RION. The male-to-female ratio was 5:4. The age range on admission to hospital was 41 years to 67 years (mean ± standard deviation: 53.5 ± 2.8 years), and first onset of clinical manifestation of RION ranged from 39 years to 63 years of age (48.1 ± 2.6 years).

3.2. Clinical characteristics of NPC

Each patient was diagnosed with NPC by nasoendoscopy and biopsy. Five patients had stage T2, three had stage T3 and one had stage T4 NPC. Nodal involvement was N1 in three patients, N2 in three patients and N3 in three patients, and there were no distant metastases. The pathological subtypes included three keratinizing squamous cell carcinomas, four non-keratinizing carcinomas (including three undifferentiated non-keratinizing carcinoma, one differentiated non-keratinizing carcinoma), one adenosquamous carcinomas and one mucoepidermoid carcinoma. Individual patient data are listed in Table 1.

3.3. Therapeutic process for NPC

Every patient received definitive radiotherapy after being diagnosed with NPC with the intent for cure. The radiotherapy method used was conventional fractionated radiotherapy (1.8–2 Gy per treatment each day, 5 days per week), and the accumulated irradiation doses ranged from 59.4 Gy to 70 Gy (65.5 ± 1.5 Gy). The irradiation fields were chosen based on the clinical and imaging features of the NPC and included the nasopharynx, oropharynx, neck, cranial base, parapharyngeal space, pterygopalatine fossa, and sphenoid sinus. The six patients with stage T3–T4 or N2–N3 NPC also received at least two cycles of neoadjuvant chemotherapy, a platinum-based chemotherapy regimen.

3.4. Clinical characteristics

The time interval between the onset of RION and irradiation was 2 to 8 years (5.4 ± 0.7 years). Although all patients received active treatment, including corticosteroids, anticoagulation and hyperbaric oxygen (HBO) therapy as soon as the symptoms appeared, their visual acuity failed to reverse or halt once it began to appear. In fact, many of the patients developed rapidly progressive visual loss reaching total blindness within 2 to 12 weeks in one or both eyes (6.5 ± 1.2 weeks). Oculus uterque (OU) were implicated in RION in eight patients, and only one patient had oculus dexter (OD). In the course of their visual deterioration, none of the patients felt eye-pain or had eye swelling.

3.5. Ophthalmologic examination

All nine patients received thorough ophthalmologic examinations showing varying levels of vision decline, ranging from poor vision (between 6/60 to 6/12) to LP, HM or blindness in one or both eyes. With respect to the radiation-induced nervous system disease classification, two patients were classified as IV°, five as III° and two as II°. The results of the eye examination of each patient can be found in Table 1. In addition, the patients had varying degrees of visual field defect demonstrated by sparse vascularity and flame hemorrhages in the retina, optic nerve atrophy and cotton wool spots (Fig. 1).

Six patients underwent fundus fluorescein angiography (FFA) examinations. The early-phase FFA angiography showed segmental narrowing of retinal arteries, scattered punctuate hemorrhages and retinal microaneurysms. Late-phase FFA showed capillary non-perfusion, telangiectasia, leakage of fluorescein dye from the abnormal perifoveal capillaries, hemorrhage, macular edema and stained disc (Fig. 2).

3.6. MRI examination

T1-weighted MRI enhanced images showed enhancement of the optic nerve, optic chiasm, and optic tracts in six patients. Tortuous optic nerves and rough edges were observed in four patients. In