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Nasopharyngeal Adenoid Cystic Carcinoma: Report of Five Cases and Treatment Outcome

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Abstract

Background: The present study aimed to report the characteristics and treatment outcomes of five patients with nasopharyngeal adenoid cystic carcinoma and a literature review.

Methods: Between 2000 and 2009, five consecutive patients (4 men, 1 woman) were diagnosed with nasopharyngeal adenoid cystic carcinoma and treated at our institution. Three patients had stage IVa (T4N0M0) and two patients had stage III (T3N0M0) cancer. Primary treatment consisted of concurrent chemoradiation in three patients and radiotherapy alone in two patients. Surgery was limited to endoscopic biopsy for histological diagnosis.

Results: Four patients achieved complete response during or after completion of treatment and remained free of disease for a median of 27 months. Four patients developed local recurrence 8-30 months after initial treatment. The fifth patient is alive and free of disease.

Conclusion: The findings of the present study and literature review suggest that local failure is a major problem in adenoid cystic carcinoma of the nasopharynx.

Keywords: Nasopharyngeal adenoid cystic carcinoma, Radiotherapy, Surgery, Skull base

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Introduction

Adenoid cystic carcinoma is an uncommon epithelial malignant tumor that accounts for less than 1% of all head and neck malignancies and about 10-22% of all salivary

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gland tumors.[1,2] This neoplasm is characterized by its prolonged clinical course, tendency for perineural spread, infrequent lymphatic invasion, multiple local recurrence and delayed distant failures. Despite a good five-year survival rate, adenoid cystic carcinoma tends to have a fatal outcome at 10 to 20 years of follow up.[1]

The minor salivary glands of the oral cavity and the sinonasal tract, and the major salivary glands are the most common primary sites for this neoplasm.[1-3] The nasopharynx is a rare location for this tumor and accounts for less than 4% of all head and neck adenoid cystic carcinomas.[4] Nasopharyngeal adenoid cystic carcinoma occurs more often in women than men, and the male-to-female ratio is approximately 1 to 1.3 in most reported series, with a peak incidence in the fifth and sixth decades of life.[5,6]

Nasopharyngeal adenoid cystic carcinoma tends to present at a locally advanced stage, with a high frequency of local failure and poor outcome.[7] Involvement of the skull base, sinus cavernous and cranial nerves are common findings in these patients at presentation. Epistaxis, nasal obstruction, hearing loss, tinnitus, headache and diplopia are the most frequent symptoms.[5,8,9] The five-year local control is 49%, disease-free rate is 30% and overall survival rate is 55%.[5]

The present study aims to report the characteristics and treatment outcome of five patients with nasopharyngeal adenoid cystic carcinoma and a literature review with special focus on the critical role of surgery in the combined modality therapy of these patients.

Patients and Methods

This retrospective study was performed by reviewing patients' records from our departmental computer databases or from patients' handwritten files. Five consecutive patients with histopathologically proven diagnoses of primary nasopharyngeal adenoid cystic carcinoma treated and followed in our institution between 2000 and 2009 were selected for the present study. Clinical investigations included history and physical examination, complete blood count, renal function tests, serum electrolytes, liver function tests, chest X-rays, and computed tomography (CT) or magnetic resonance imaging (MRI) of the nasopharynx and neck. Panendoscopy of the upper aerodigestive tract was performed for all patients.

Patients were staged according to the seventh edition of the American Joint Committee on Cancer staging classification. Clinical and pathological tumor responses were assessed one

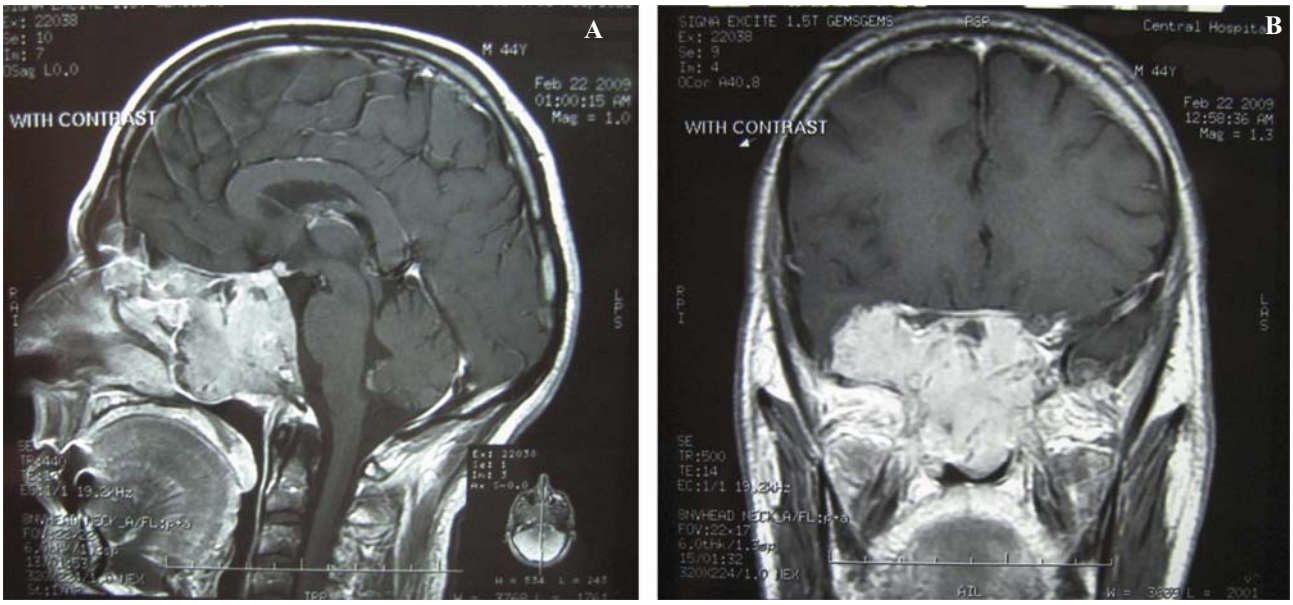

Figure 1. Contrast-enhanced sagittal (A) and coronal (B) view of T1-weighted MRI of the nasopharynx and skull base showing locally advanced nasopharyngeal adenoid cystic carcinoma invading the skull base, sphenoid sinus, sinuous cavernous, with extension to the intracranial fossa. (Case 5)

Table 1. Clinical characteristics, treatment and outcomes of five patients with nasopharyngeal adenoid cystic carcinoma.

Patients	Age	Sex	TNM stage	Treatment modality	Response to therapy	Relapse	Time to relapse (months)	Last clinical status	Last follow-up after treatment (months)
1	75	Male	T4N0M0	RT alone (70 Gy)	Complete remission	Local	27	DOD	31
2	45	Male	T3N0M0	Chemoradiation (70 Gy)	Complete remission	-	56	ANED	56
3	52	Male	T3N0M0	RT alone (70 Gy)	Complete remission	Local	15	DOD	37
4	45	Female	T4N0M0	Chemoradiation (70 Gy)	Complete remission	Local	30	AWD	52
5	44	Male	T4N0M0	Chemoradiation (70 Gy)	Partial remission	Local + distant	0	DOD	21

RT: Radiotherapy; DOD: Dead of disease; AWD: Alive with disease; ANED: Alive with no evidence of disease.

month after treatment completion by findings from the CT scans and MRIs, and confirmed by pathological examination through direct nasopharyngoscopies and biopsies.

A literature review of PubMed using the search terms "adenoid cystic carcinoma" and "nasopharynx" or "nasopharyngeal" was performed for the references of the present study.

Results

There were four men and one woman included in this study. The age at presentation was 44-75 years (median: 45 years; mean: 52 years). All patients had locally advanced disease at presentation. Three patients had stage IVa (T4N0M0) and two patients had stage III (T3N0M0) disease. Headache, nasal obstruction, otalgia, hearing loss, epistaxis and diplopia were the most frequent presenting symptoms.

Primary treatment consisted of concurrent chemoradiation in three patients and radiotherapy alone in two patients. Surgery was limited to endoscopic biopsy for histological diagnosis with or without tumor debulking. Extensive involvements of the skull base, internal carotid artery, sinus cavernous, sphenoid sinus, or intracranial extension were the causes for a non-surgical approach in our patients (Figures 1 A and B).

External-beam radiation therapy was delivered by megavoltage photons of Cobalt-60 units or linear accelerator to the primary site. The nasopharynx and skull base (with or without sinonasal region) were treated through anterior portal and lateral parallel-opposed fields. In general, the tumor dose to the primary site ranged from 60 to 70 Gy, with a median dose of 70 Gy (mean: 66 Gy), delivered at a rate of 1.8-2 Gy per fraction over 6-7 weeks at doses of 9-10 Gy/week.

Concurrent chemotherapy regimen consisted of weekly cisplatin (40 mg/m^2) from the first day of radiation therapy up to 7 cycles. Four patients achieved complete response during or up to four weeks after completion of treatment and remained free of disease for 15-40 (median: 27) months. Four patients developed local recurrence 8-30 months after initial treatment. All patients with local recurrent disease received multiple cycles of palliative chemotherapy that included regimens of PF (Cisplatin and 5-FU), TPF (Docetaxel, Cisplatin and 5-FU), CG (Cisplatin and Gemcytabine), oral Capecitabine and oral Imatinib; however, no objective response was observed in any patient. In addition, two patients underwent endoscopic debulking surgery of their local recurrent disease. One patient was treated with gamma knife radiosurgery for his skull base recurrent disease. After a median follow-up of 37 months (range: 17-49 months), one patient was alive and without disease, one is alive with disease and the three remaining patients died due to disease progression.

Discussion

Malignant nasopharyngeal neoplasms differ from other head and neck malignancies in many

aspects. These tumors are located in proximity to the critical neurovascular structures, have a tendency to locally involve the internal carotid artery, and cranial nerves III, IV, and V, invade the cavernous sinus, and erode through the skull base.[8,10] Radical surgical resection of nasopharyngeal tumors is a complex otolaryngological and neurosurgical challenge and may be associated with significant morbidity and mortality.[8,9]

Nasopharyngeal carcinoma and lymphomas constitute the vast majority of malignant neoplasms of the nasopharynx.[11,12] They are chemosensitive and radiosensitive hitologies and combined chemoradiation is considered the treatment of choice for these neoplasms. Surgery plays a limited role in the primary treatment of nasopharyngeal carcinoma and lymphoma. It is restricted to obtaining a biopsy and nasopharyngeal inspection.[11,12] However, surgery is an important treatment option in recurrent nasopharyngeal carcinoma following primary chemoradiation.[11] In addition, surgery plays an essential role in the primary treatment of minor salivary gland tumors such as adenoid cystic carcinoma, which are relatively radiosensitive, as well as chemoresistant neoplasms.[5,6,11]

In the literature review, we have found that radical surgical resection and postoperative radiotherapy is considered the treatment of choice for locoregional nasopharyngeal adenoid cystic carcinoma, although complete excision is not possible in most cases due to the diffuse neurovascular or skull base tumor infiltration.[5,6,8,9,13]

In our patients, surgical resection was not performed due to extensive involvement of the skull base, sinus cavernous or internal carotid artery and/or intracranial tumor extension. The findings of the present study confirmed the results of previous reported series in which most patients with nasopharyngeal adenoid cystic carcinoma had locally advanced unresectable disease at presentation and radiotherapy constituted the cornerstone of local therapy. In addition, patients treated with non-surgical managements had poorer local control and lower survival compared to surgical management.[5,6,8,14] Recent data has indicated a promising local control rate of 93% at five years with the use of high-dose conformal proton beam radiotherapy in patients with adenoid cystic carcinoma of the skull base.[15]

Adenoid cystic carcinoma is generally a chemoresistant tumor, although recent studies suggest Imatinib mesylate, a potent inhibitor of KIT tyrosine kinase, may be an effective systemic treatment for metastatic and unresectable disease.[16]

Conclusion

The findings of the present study and the literature review indicate that local failure is a major problem in adenoid cystic carcinoma of the nasopharynx. Therefore, more effective local treatment by using combined surgical resection and/or novel radiotherapy techniques such as high-dose conformal proton beam radiotherapy is highly recommended for improving local control and overall survival in these patients.

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