Nasopharyngeal Malignancies Causing Abducens Palsy

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Abstract

Four patients with nasopharyngeal malignancies were reported. The main symptom was diplopia due to abducens palsy in all patients; it was unilateral in three patients and bilateral in one. Skull tomographic evaluation was valuable for detecting nasopharyngeal malignancies. Histological examination of biopsy specimens from the nasopharynx confirmed these lesions to be squamous cell carcinoma in three patients and poorly differentiated carcinoma in the fourth. Radiation therapy (5,225–7,250 rads) was employed in combination with chemotherapy consisting of cyclophosphamide or 5-fluorouracil. In three patients, the survival time from the onset of diplopia to death ranged from seven months to three years and three months. One patient is still alive and in good condition, four years and 10 months after the onset of diplopia.

Key words: nasopharynx, carcinoma, abducens palsy

Introduction

That malignant neoplasms arising from the nasopharynx occasionally involve a variety of cranial nerves is well documented. However, because of the relative inaccessibility of the nasopharynx to routine examination, their diagnosis is difficult even upon full radiological evaluation. Especially when these conditions present with only cranial nerve involvement in the absence of primary nasal symptoms, and when neoplastic infiltration to the skull base produces only minimal mucosal thickening, tumors in the nasopharynx may frequently escape early recognition.

We encountered four patients with nasopharyngeal malignancies who manifested diplopia due to abducens palsy as their main clinical symptom. Their clinical features, radiological findings, treatment, and results are discussed.

Case Reports

Case 1: A 48-year-old man was admitted on January 10, 1966 with a one-month history of diplopia accom-
metastases developed on the right side and subsequently on the left. These were extirpated each time and cobalt-60 irradiation was given to each side of the neck (each side about 3,000 rads for 3–4 weeks).

Three years later, a bloody nasal discharge occurred. Radiological examination revealed an ulceration of the nasopharynx and opacification by multiple lung metastases. Subsequently, without the further appearance of any neurological abnormalities, his general condition deteriorated insidiously and he died three years and three months after the onset of the initial symptom.

Case 2: A 41-year-old man was admitted on November 13, 1967 for further evaluation of diplopia which had developed 18 months earlier and was accompanied by nasal discharge and slight epistaxis. One month prior to admission, he developed numbness in his left cheek. Neurological examination disclosed left abducens palsy, some hearing loss on the left side, and hypesthesia in the region of the 2nd branch of the left trigeminal nerve. A plain film and tomogram of the skull demonstrated bony destruction of the posterior half of the sella turcica including the clivus and a large, ill-defined soft tissue mass involving the nasopharynx as well as the sella turcica (Fig. 2). Bilateral carotid metastases developed on the right side and subsequently on the left. These were extirpated each time and cobalt-60 irradiation was given to each side of the neck (each side about 3,000 rads for 3–4 weeks).

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Fig. 1 Case 1. A: Plain film of the skull shows cloudiness of the sphenoid sinus. B: Tomogram reveals a nasopharyngeal soft tissue mass extending into the sphenoid sinus and bone destruction. The bony structure of the sella turcica is atrophic.

Fig. 2 Case 2. A: Lateral roentgenogram of the skull shows bony destruction of the sella turcica and clivus. B: A large, ill-defined soft tissue tumor in the sphenoid sinus region is seen to encroach the nasopharyngeal air shadow. C: On the post-irradiation plain film, the sella turcica appears almost normal.

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angiograms showed no abnormalities. Nasopharyngeal examination revealed a reddish bulge in the vault; upon histological examination of a biopsy specimen from the bulge, a diagnosis of undifferentiated squamous cell carcinoma was made.

The lesion was irradiated with 6,270 rads of cobalt-60 over a 46-day period and chemotherapy was started (cyclophosphamide, 100 mg per day for two months). Upon completion of the irradiation treatment, hypesthesia in the cheek improved though the diplopia persisted unchanged. A plain skull film obtained six months after the completion of irradiation therapy showed nearly normal configuration and bone density of the sella turcica, which before treatment appeared to have been destroyed (Fig. 2C).

One year later, the patient developed severe headache and pain in the left cheek. Due to the recurrence of the nasopharyngeal tumor, he received further cobalt-60 irradiation to the nasopharynx (3,200 rads for a 19-day period). He tolerated this therapy well and the headache and facial pain decreased markedly. Two weeks after finishing the second radiation treatment, massive arterial hemorrhage from the nasopharynx occurred suddenly; the bleeding could not be controlled and the patient died two years and nine months after the appearance of diplopia.

**Case 3:** A 32-year-old woman was hospitalized on October 21, 1968 because of diplopia and headache of three-month duration. A few months prior to admission, she had occasionally experienced nasal obstruction and a bloody nasal discharge. Neurological examination revealed bilateral abducens palsy, hypesthesia, and pain in the left cheek. A lateral X-ray film and tomogram of the skull showed a large, indefinite nasopharyngeal soft tissue mass with extensive bony destruction of the skull base (Fig. 3). On bilateral carotid angiogram, the carotid siphon was displaced upwards and the ganglial portion was stretched with posterior displacement (Fig. 3C, D). Nasopharyngeal examination showed an irregular, small protuberance on the vault. Histological examination of a biopsy specimen evidenced poorly differentiated carcinoma.

Cobalt-60 therapy (5,225 rads for 46 days) was administered to the nasopharyngeal and sellar region.

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Fig. 3 Case 3. A: Skull radiogram demonstrates extensive bony destruction including the sella turcica and clivus. B: Note the nasopharyngeal soft tissue tumor projecting into the nasopharyngeal air shadow. C, D: Bilateral carotid angiograms show marked upward displacement of the carotid siphon and stretching of the ganglial portion with posterior displacement.
however, no beneficial effect was obtained. Thereafter, her general condition deteriorated insidiously and there was radiological evidence of bone metastases affecting the cranial vault, the 5th thoracic vertebra, and the right 8th rib. The patient died seven months after experiencing the initial symptom.

**Case 4:** A 72-year-old man was admitted on January 8, 1978 with a three-month history of diplopia (first admission). Neurological abnormalities were limited to left 6th nerve palsy. Radiological evaluations included skull tomography, carotid angiography, and computed tomography (CT), but all failed to demonstrate any abnormality. The nasopharynx appeared to be intact; a blind biopsy showed chronic inflammatory changes without evidence suggesting the presence of neoplasms. The patient was discharged after diagnosis of transient abducens palsy of undetermined origin and was followed up without the administration of any treatment.

Follow-up neurological examination performed one year and nine months after the development of diplopia revealed the persistence of left abducens palsy, hypesthesia in the region of the 2nd branch of the left trigeminal nerve, and acoustic nerve impairment on the left side (second admission). A lateral laminogram of the skull showed posterior thickening of the nasopharynx and prominence of the posterior wall encroaching on the nasopharyngeal air shadow (Fig. 4). No bony destructive changes were noted. CT scan showed no abnormalities. Carotid and vertebral angiographic findings were essentially normal. Nasopharyngeal examination disclosed the posterior wall to be edematous and congestive; its friable surface bled easily. Histological examination of a biopsy specimen from the posterior wall revealed the presence of squamous cell carcinoma.

The patient was treated with cobalt-60 irradiation to the skull base (5,695 rads over 48 days) and chemotherapy was started (5-fluorouracil, 250 mg per day for 30 days). Hypesthesia of the left cheek decreased though the abducens palsy and hearing disturbance remained unchanged. At present, four years and ten months after the onset of diplopia, the patient is pursuing his normal activities. His general condition is good and while neurological dysfunctions persist, there are no signs suggestive of tumor recurrence or distant metastases.

**Discussion**

Nasopharyngeal malignancies are relatively rare in Japanese, Koreans, and Caucasians of Europe and America, while they are common in the Chinese of South East China. Sawaki et al. reported that the incidence among Chinese was more than 30 times higher than in Japanese. In general, more males than females are affected, with a sex ratio of 2–3:1. The age of patients with these malignancies ranges from childhood to senility, with a peak incidence in persons in the fifth and sixth decades.

Most nasopharyngeal tumors may remain asymptomatic for several months. The predominant symptoms are enlarged cervical nodes, bloody nasal discharge or nasal obstruction, tinnitus, hearing impairment, headache, and neck pain. Cranial nerve symptoms may also be present. Frequently, a cervical metastatic mass is the initial sign. According to Thomas and Waltz, in about 30% of patients with nasopharyngeal malignancies there are neurological abnormalities attributable to these lesions. The nerves most frequently affected are the abducens, trigeminal, and glossopharyngeal nerves, often with simultaneous involvement of the abducens and trigeminal nerves. These malignant neoplasms usually spread in two directions. Extension through the foramen lacerum into the middle cranial fossa and the cavernous sinus may affect the 3rd, 4th, 5th, and 6th cranial nerves, while spreading to the parapharyngeal space may involve the last cranial nerves. In most patients, such neurological manifestations appear late in the course of the disease though they may infrequently be the earliest recognizable abnormalities or the only clinical manifestations in early, or even in advanced, tumors.

Three of our patients (Cases 1, 2, and 4) initially presented with diplopia due to abducens palsy. In Case 3, nasal symptoms developed first, followed by diplopia and facial numbness as the bilateral abducens and the left trigeminal nerves were affected. In Case 2 and 4,
unilateral abducens palsy appeared suddenly without any antecedent or associated symptoms and persisted for 18 and 24 months, respectively, in the absence of any sign of a primary lesion. During this period, no additional neurological signs appeared. The cause of actual 6th nerve palsy varies and it may be localized or non-localized.\(^5\) The nerve may be affected by various lesions at any level from the brain stem to the cavernous sinus and orbit. Neoplasms, localized inflammation, carotid-cavernous sinus fistulae, cavernous carotid artery aneurysms, petrosal sinus thrombosis, and arteriosclerosis of the branches of the basilar artery may lead to 6th nerve palsy, while non-localized inducers may include increased intracranial pressure, diabetes, and cranial arteritis. In addition, a 6th nerve palsy of undetermined origin can often be benign and transient.\(^5\) Among neoplasms, nasopharyngeal tumors are an important cause of producing 6th nerve palsy. However, in the absence of symptoms secondary to an existing lesion, it may be difficult to determine the cause of 6th nerve palsy of long duration, as was in Cases 2 and 4.

Early diagnosis of nasopharyngeal malignancies is difficult. Despite the presence of signs, most patients are diagnosed in the advanced stage, resulting in poor prognosis. This can be attributed to the anatomical peculiarities of these malignancies, their insidious manner of growth, and the lack of specificity of their clinical manifestations. Skull tomography is frequently of value in their recognition; two significant abnormalities are the presence of a soft tissue mass in the nasopharynx and bony destruction of the skull base. Kasell\(^6\) emphasized that nasopharyngography, thin section tomography, and Eustachian tube clearance study were valuable in identifying the minute changes induced by nasopharyngeal malignancies. According to Biller et al.\(^1\) early radiological evaluation using CT may be valuable in assessing the location and extension of these lesions. However, occult lesions infiltrating throughout the nasopharyngeal submucosa often fail to demonstrate any abnormality upon various types of radiological evaluation. As these occult lesions, which account for 30% of all lesions in nasopharyngeal malignancies,\(^8\) may not be noticed even upon nasopharyngeal inspection, only a biopsy from the nasopharynx may reveal the presence of neoplasms.\(^12\) Therefore, all suspicious lesions should be biopsied. If the biopsy does not demonstrate the presence of a malignancy, it should be repeated as long as there is any suspicion of a malignancy.\(^10\) The first examination of Case 4 performed three months after the onset of diplopia showed no evidence of the presence of nasopharyngeal neoplasms. The nasopharynx appeared to be normal upon direct inspection and upon blind biopsy and no findings suggestive of neoplasms were obtained. Even a blind repeat biopsy should have been performed considering that 18 months later, the second biopsy confirmed the presence of squamous cell carcinoma.

Radiation therapy is commonly employed as the primary procedure or in combination with other procedures in the treatment of nasopharyngeal malignancies. At high-dose irradiation, overall five-year survival rates of 24 to 57% have been reported.\(^2,7,13–15\) Some investigators\(^8,15\) noted a significant improvement in the survival rate with early treatment. In patients with early lesions confined to the primary site, the survival rate is about 70%. It dropped precipitously to less than 20% in patients with advanced lesions extending beyond the nasopharynx with bony invasion and/or cranial nerve involvement. Hoppe et al.\(^7\) reported that patients with cranial nerve dysfunctions had a poor prognosis, but that there were a few long-term survivors after radiation therapy among them. In the early stage, some nasopharyngeal malignancies may be radiocurable.\(^7,14\) Early diagnosis will insure improved prognosis. In individuals with unexplained cranial nerve dysfunctions, especially with the simultaneous presence of facial numbness and diplopia, the possibility of nasopharyngeal malignancies must be considered.

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