Malignant Schwannomas of the Ethmoid Sinus and the Larynx

—Case Report and Review of Literatures—

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The incidence of malignant schwannoma in the head and neck is extremely rare. Most tumors appear as a rapidly expanding nonpainful mass and the symptoms are usually attributable to local expansion of the mass. About one half occurs in association with von Recklinghausen's disease.

Wide surgical excision is generally recommended as a primary treatment. Recently, there has been a trend to include postoperative radiation therapy as a primary modality.

Prognosis of head and neck malignant schwannoma has been reported as particularly poor. However, recent authors advocate that prolonged survival is possible after adequate therapy including postoperative radiation therapy.

We present our experience with these tumors on very rare locations such as the ethmoid sinus and the larynx, with the review of literatures.

Key Words: Malignant schwannoma, Ethmoid sinus, Larynx, Radiation therapy

INTRODUCTION

Among the 471 patients of head and neck malignancy who were treated in the department of radiation oncology of KUH from Feb. 1981 to Dec. 1991, only 3 patients (0.36%) were diagnosed as malignant schwannoma. Out of the all patients of malignant schwannoma (6 patients) of the same period, 3 patients had the disease in the head and neck area. One of them had the disease in the right side of neck. Malignant schwannoma comprises approximately 10%[1] of all soft tissue sarcomas. Only 8% to 14%[2~4] of these tumors arise in the head and neck. There are only a few case reports of the disease of the paranasal sinuses or the larynx.

Robitaille et al.[5] and Shugar et al.[6] reviewed the American and European literatures of nerve sheath tumors dating back to 1810. And they found only 5 cases of malignant schwannoma in the paranasal sinuses.

The incidence of nonepithelial laryngeal malignancies is extremely low. Thomas[7] reported that it was less than 1%. Krajina[8] reviewed over 6000 malignant laryngeal tumors and reported the incidence of sarcoma to be 0.32%. The first case of an intrinsic laryngeal malignant schwannoma was reported by DeLozier HL[9] in 1982.

We present our experience with two patients of malignant schwannoma of the very rare locations such as the ethmoid sinus and the true vocal cord who underwent postoperative radiation therapy, with the review of literatures.

CASE REPORT

1. Case 1

A 35-year-old woman with 1-year history of nasal obstruction admitted to department of ENT, Korea Unievrsity hospital in Nov. 1990. Two months prior to the admission, she visited local hospital and under the impression of nasal polyp, she received polypectomy. At that time, a diagnosis of malignant schwannoma was established. Then she was referred to Korea university hospital.

Physical examination revealed unremarkable findings except postoperative scar and crust in right nasal cavity, and there was no findings compatible with von Recklinghausen's disease.

Routine sinus roentgenograms showed soft tissue mass density in the right ethmoid sinus and sphenoid sinus. The MRI demonstrated homogenous gadolinium enhancing high signal intensity mass on the right ethmoid sinus and nasal cavity. The tumor mass extended into the right ethmomaxillary plate, and displaced the midline septum to the left side. There was the invasion of the anterior part of the sphenoid sinus and suspicious bony erosion

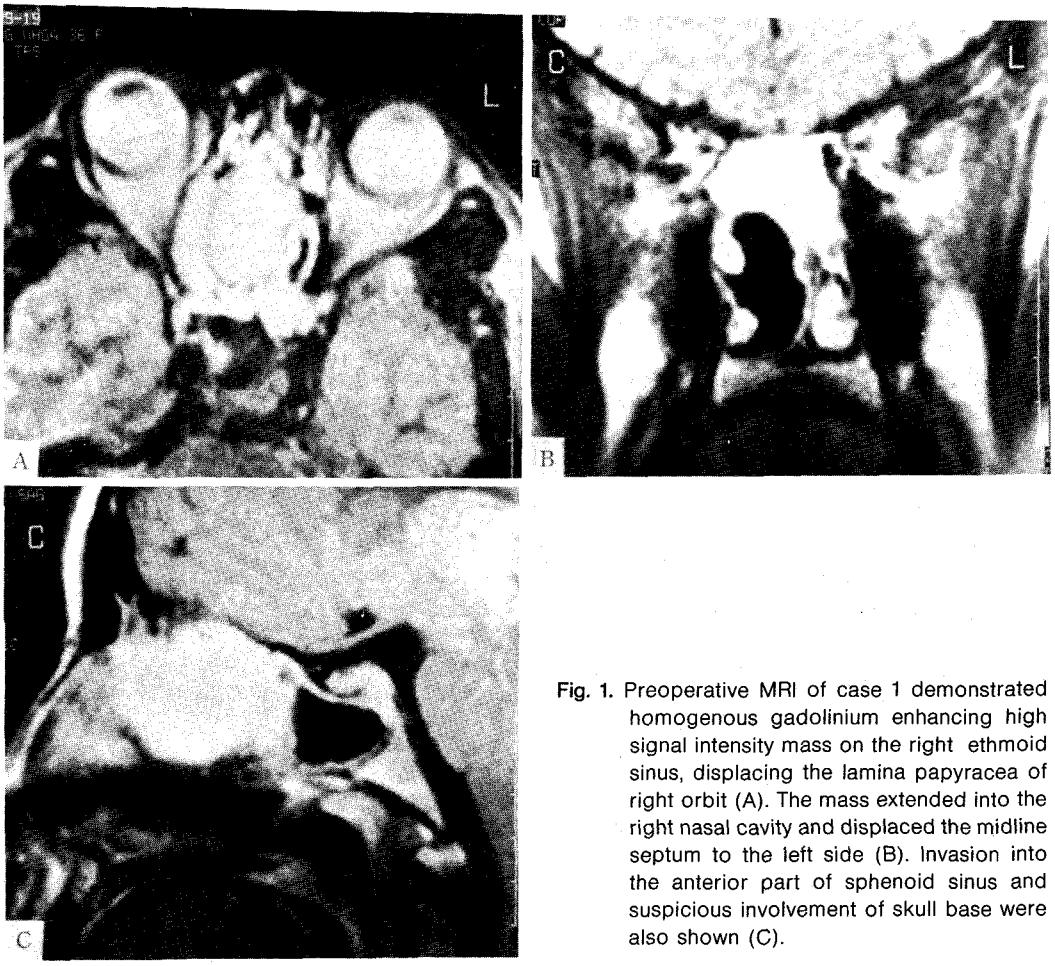

Fig. 1. Preoperative MRI of case 1 demonstrated homogenous gadolinium enhancing high signal intensity mass on the right ethmoid sinus, displacing the lamina papyracea of right orbit (A). The mass extended into the right nasal cavity and displaced the midline septum to the left side (B). Invasion into the anterior part of sphenoid sinus and suspicious involvement of skull base were also shown (C).

of the anterior skull base (Fig. 1).

The patient underwent a fronto-ethmoido-sphenoidectomy. At the surgery, the tumor seemed to be originated from right middle turbinate or ethmoid sinus. It extended into frontal sinus, cribriform plate, olfactory fissure, and right nasal cavity.

Light microscopy of the resected specimen revealed fascicles of spindle cells with oval to enlongated wavy nuclei(Fig. 2.). Some of them were multinucleated and pleomorphic. Occasional mitotic figures less than 5/10 HPF were found (Fig. 3). At the periphery, benign neurofibromatous lesion was also shown.

Immunohistochemical staining was performed. Most of the tumor cells were focally positive for S -100 protein and moderately positive for neuron specific enolase (Fig. 4). GFAP and neurofilament

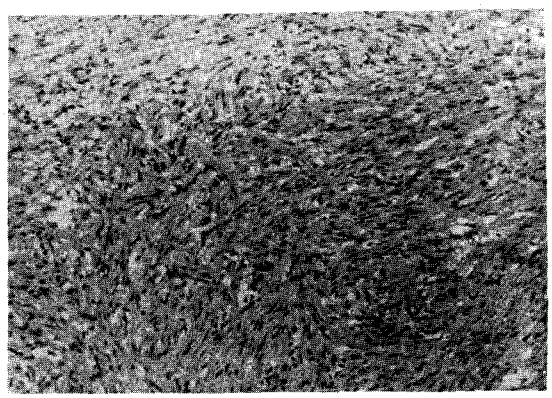

Fig. 2. Light microscopic examination of case 1 revealed that the tumor was made up of fascicles of spindle cells with wavy nuclei (H&E, × 100).

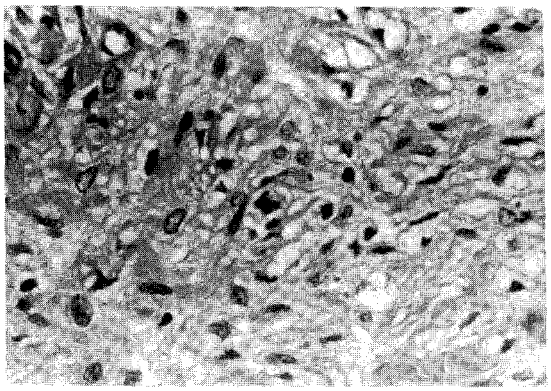

Fig. 3. In high magnification, the prominant mitotic figures were found (H&E, ×400).

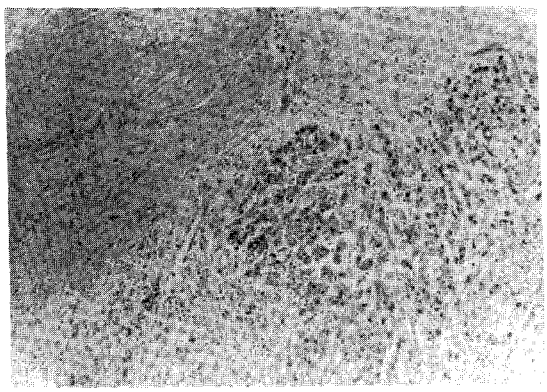

Fig. 4. In the immunohistochemical staining, the tumor demonstrated focal positive reaction for S-100 protein (ABC, ×100).

stainings demonstrated negative reaction. These findings were consistent with malignant schwannoma.

Four weeks after the surgery, post-operative radiation therapy was given with Co-60 teletherapy unit. We used the parallel opposing both lateral portals with field size of 6×6 cm. The treatment field included the anterior skull base superiorly (Fig. 5). At the tumor dose of 5040 cGy/28F/$5^1/_2$ wks, treatment planning CT scan showed no residual mass. Boost dose of 1600 cGy/8 fractions via anterior port was given. Total dose of 6640 cGy was given in 8 weeks.

Ten months after the completion of radiotherapy, follow up PNS CT scan was obtained. There was no evidence of recurrence (Fig. 6). Her chest roentgenogram at that time was normal.

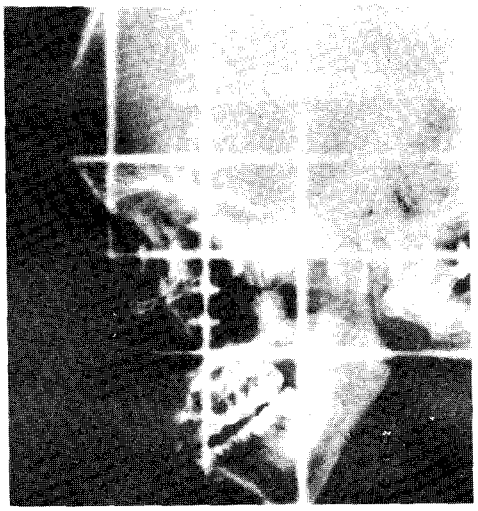

Fig. 5. Treatment portal of case 1. the treatment field included the anterior skull base superiorly, with the field size of 6×6 cm. We used the parallel opposing both lateral portals.

2. Case 2

A 36-year-old woman with 1-year history of hoarseness visited department of ENT, Korea university hospital in Feb. 1991. Two and a half months ago, the patient underwent removal of the right laryngeal mass at a local clinic. The initial pathologic diagnosis was a vascular vocal cord polyp. After the surgery, however, her symptom was not improved.

On physical examination, a papillomatous mass on the right true vocal cord was found but the cord motility was good. The laryngogram showed thickening of the right true vocal cord compared to left side and incomplete filling of contrast in the right ventricle (Fig. 7). The neck CT scan demonstrated a 1 cm sized mass on the right true vocal cord (Fig. 8). Direct laryngoscopy under the general anesthesia disclosed a papillomatous and easily bleeding mass on the right true vocal cord (Fig. 9). The pathologic diagnosis was malignant schwannoma (Fig. 10). Therefore, right cordectomy was done. A 1×1 cm sized tumor was located in the mid 1/3 of right true vocal cord. The pathological examination revealed microscopic infiltration of the tumor into laryngeal muscle layer.

Four weeks after the surgery, post-operative radiation therapy was started. The total tumor dose of 6800 cGy/34F/7wks delivered via Co-60 teletherapy unit.

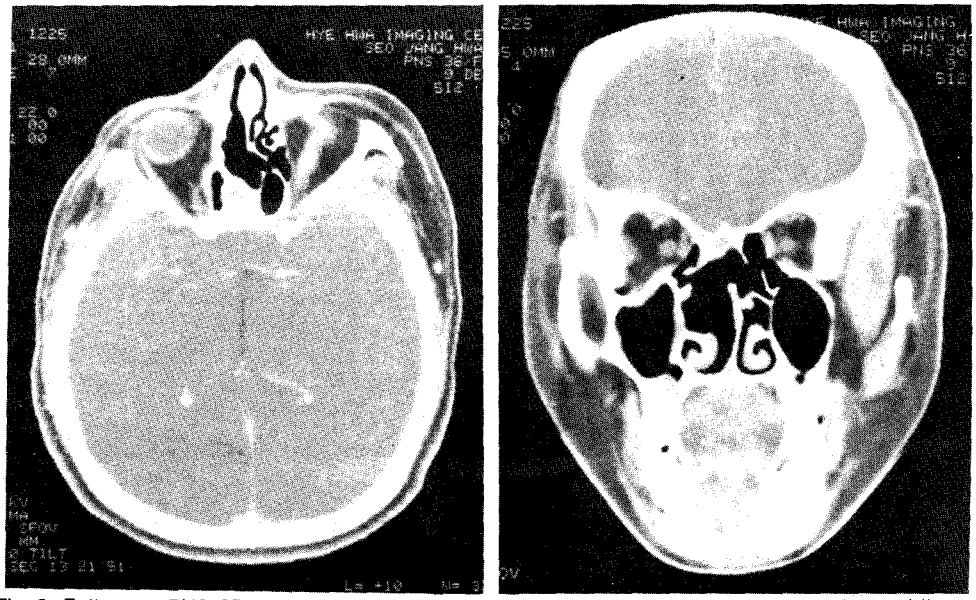

Fig. 6. Follow-up PNS CT scan after 10 months of postoperative radiotherapy revealed no evidience of recurrence.

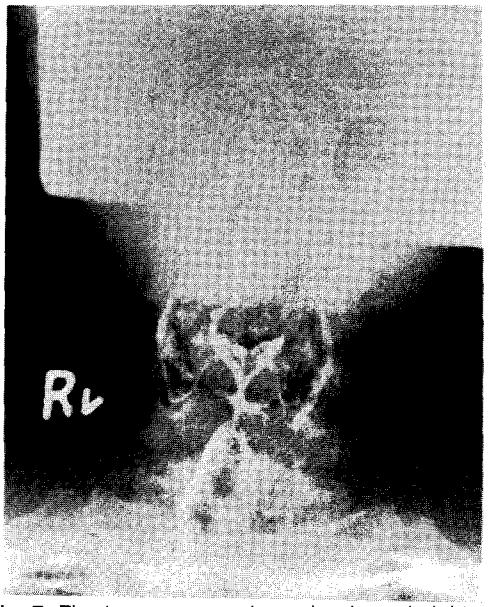

Fig. 7. The laryngogram showed enlarged right true vocal cord compared to left one and incomplete filling of the contrast in the right ventricle.

She has been followed up for 6 Months without any evidence of recurrence or metastasis.

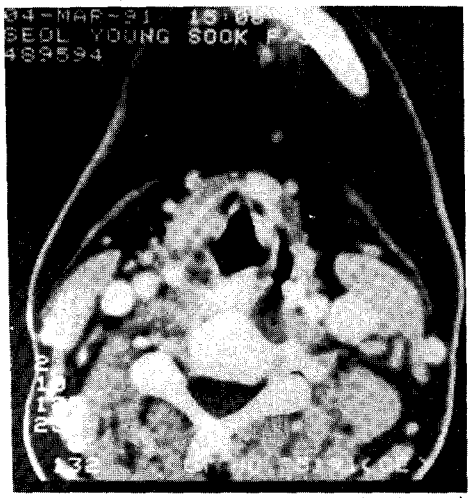

Fig. 8. The neck CT scan demonstrated a 1 cm sized mass on the right true vocal cord.

DISCUSSION

The malignant schwannoma is the principle malignancy of peripheral nerve, comprising approximately 10%[1] of all soft tissue sarcomas. This tumor may have diverse origins including Schwann cells, perineural cells, and fibroblasts of the nerve sheath. Therefore, the term "malignant peripheral nerve sheath tumor" has gained recent

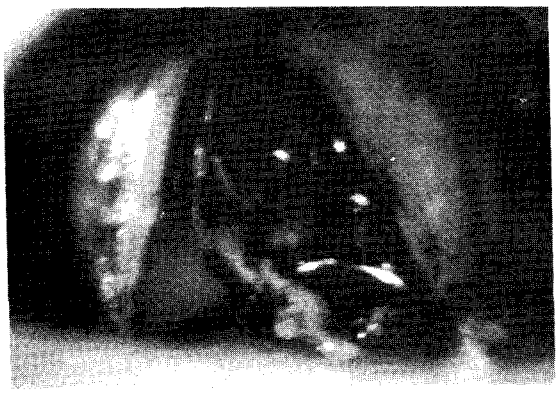

Fig. 9. Direct laryngoscopic examination of patient 2 disclosed a papillomatous and easily bleeding mass on the right ture vocal cord.

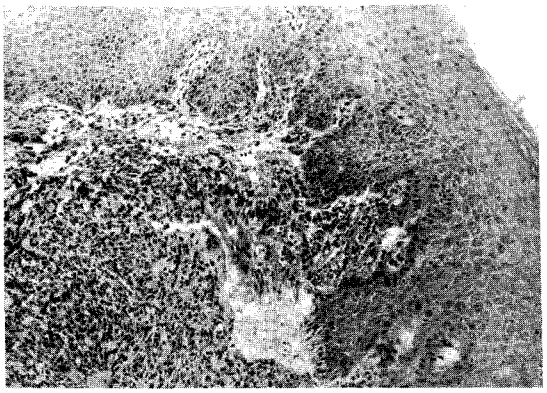

Fig. 10. The submucosa of the larynx showed irregular spindle appearance of tumor cells with hyperchromatic nuclei and enlongated cytoplasm (H&E, ×100).

popularity[1,15].

About 50% of these tumors occur in association with von Recklinghausen's disease varing from 26%[4] to 66%[16]. Patients with neurofibromatosis are clearly at increased risk to develop these tumors. By current study about 4% of patients with von Recklinghausen's disease develop malignant schwannoma[17]. Eight[18] to eleven[19] percent of patients of malignant schwannoma has the therapeutic or occupational irradiation history with the mean latency period of over 15 years[19].

Most malignant schwannomas arise in association with major nerve trunks including the sciatic nerve, brachial plexus, and sacral plexus. Consequently the most common anatomical sites include the proximal portions of the upper and lower extrimities and trunk. Only 8% to 14% of these tumors arise in the head and neck[2~4]. In the head and neck, they originate most often from the brachial plexus, the sympathetic chain, and the main trunk or branches of the cranial nerves (especially of trigeminal nerve)[10].

Clinically, these tumors generally present as a progressively enlarging painless mass[1,15]. The symptoms are usually attributable to local expansion of the mass, and the sensory and motor symptoms including projected pain, paresthesias, secondary muscular atrophy and weakness rarely antedate the detection of a mass. This tumor has the wide age distribution but predominantly occur in patients between 20 and 50 years of age[11~14]. There is no sex predilection[1,3,4,15]. The tumor mass is usually circumscribed and frequently extensively invade the surrounding tissues. Lymphatic spread is extremely rare[2]. Sordillo PP. et al.[18] reported only 2 cases of lymph node metastases out of 165 patients. However distant metastasis via hematogenous route is common. The most common site is lung; ranging from 35%[16] to 43%[17]. Bone, liver, and subcutaneous tissue follow in the order.

Histologically, malignant schwannomas are comprised of spindle cells with various degrees of pleomorphism. The spindle cells have makedly irregular contours, and arranged in sweeping fascicles. Their nuclei are wavy, buckled, or comma shaped. Nuclear palisadings may also be present. The mitotic rate is usually low, with greater than 5 mitoses/10 HPF representing a high grade of malignancy[20]. Myxoid zones, hyaline bands and nodules could also be found. Many authors found the focal divergent differenciation in about 15%[14,21] of malignant schwannomas. In order of frequency, rhabdomyosarcoma, chondrosarcoma, osteosarcoma, and angiosarcoma were reported. But epithelial components were quite rare. These findings may also aid in differential diagnosis of malignant schwannoma from other sarcomas. Ducatman BS. et al[14,21] advocated that such divergent differentitations do not seem to affect the prognosis.

General agreements of diagnostic criteria for malignant schwannomas are[12,14]; 1) tumor origin for a nerve. 2) association with a contiguous neurofibroma. Electron microscopic features of Schwann cells and inmmunohistochemical staining for S-100 protein may also aid in differential diagnosis.

Interestingly, Malignant tumors are not thought to arise in pre-existing benign schwannomas[4,11,13,18].

Once the diagnosis is confirmed, wide surgical excision is the treatment of choice[1,10,15]. Involved major nerves should be followed proximally, attempting to obtain clear margins. This may be particularly difficult at the base of the skull. In our case 1, the base of the skull was invaded by the tumor and clear resection margin was uncertain. In case 2, resection margin was involved by the tumor too. Regional lymphadenectomy is not necessary unless there is suspicious lymphadenopathy. In our cases, node dissection was not performed as a routine.

In the past, radiation therapy has been felt to be ineffective[12]. However recently, planned postoperative radiation therapy has been recommended in combination with surgical excision. Goepfert et al.[22] found that combind therapy significantly reduced the incidence of local recurrene of soft tissue sarcomas-including malignant schwannomas-in the adult head and neck. Hutcherson et al.[10] also recommended planned postoperative radiotherapy, to help the control and possible prevention of local recurrences.

Recurrences and pulmonary metastases may also be managed by radiation therapy. Survival time is significantly prolonged[8,15]. There is an succesful case report for the retreatment of a large recurrent malignant schwannoma in the retroperitoneum using interstitial ^{125}I implantation[23]. The patient is well, without disease 2 years later.

The role of chemotherapy is so far not been clearly defined. Some authors reported lower local recurrence rate after combination chemotherapy including adriamycin as an adjuvant therapy with surgery and/or radiotherapy.

The prognosis of malignant schwannomas has generally been described as poor to dismal. The over all 5-and 10-year survival rate were 34% and 22%, respectively.[14] For the patients with the disease in the head and neck, the prognosis has been described particularly poor[12,16] with death usually resulting from persistant or locally recurrent disease. In White's series[16], 9 of 15 patients died within 20 months of diagnosis, including both patients with head and neck. In Hutcherson et al.[10] series of seven patients with head and neck tumors, four died within 5 years of treatment, and one patient was living with disease.

In contrast, Goepfert et al[22] reported on seven patients treated with combined therapy and all were alive without disease from 2 to 7 years later. Radiation therapy was given within six weeks after the surgical procedure and consisted of a tumor dose of 6,000 cGy in six weeks to the site of primary and adjacent areas of potential tumor extension. Regional lymphatics were electively irradiated with a given dose of 5,000 cGy in five weeks for the patients with potential regional lymphatic spread. Hoffmann et al.[15] reported that 5 patients out of 9 patients (55%) were alive without disease from 9 months to 11 years after combined treatment. they used the total tumor dose of ranging from 5,940 cGy to 6,600 cGy.

In conclusion, malignant schwannomas are uncommon in the head and neck, especially in the PNS and larynx. Regional lymphatic metastases are rare but hematogenous metastases to lung are common. Recommended treatment is wide surgical excision, followed by postoperative radiation therapy. Radiotherapy is helpful in the local control and possible prevention of local recurrences. Prognosis is not necessarily dismal, particularly in those patients without neurofibromatosis. Prolonged survival is possible after adequate therapy. For the PNS and larynx, malignant schwannoma is extremely rare and prognosis is unknow. A review of the literature revealed few cases of the disease in these region. Though follow up periods are short, we report our cases because the incidence of malignant schwannoma in the PNS and larynx is extremely rare. We will continuously follow them up to obtain long-term results.

REFERENCES

1. **Enzinger FM, Weiss SW:** Malignant tumors of peripheral nerves In: Soft Tissue Tumors 2nd Ed, Missouri, Mosby, 1988, pp.781-815
2. **Russell WO. Cohen J, Enzinger F, et al:** A clinical and pathological staging system for soft tissue sarcomas. Cancer 40:1562-1570, 1977
3. **Das Gupta TK, Brasfield RD:** Solitary malignant schwannoma. Ann Surg 171:419-428, 1970
4. **Ghosh BC, Ghosh L, Huvos AG, Fortner JG:** Malignant schwannoma: A clinicopathologic study. Cancer 31:184-190, 1973
5. **Robitaille Y, Seemayer T, El Deiry A:** Peripheral nerve tumors involving paranasal sinuses. A case report and review of the literature. Cancer 35: 1254-1258, 1975
6. **Shugar JM, Som PM, Biller HF, Som LM, Krespi YP:** Peripheral nerve sheath tumors of the paranasal sinuses. Head Neck Surg 4:72-76, 1981
7. **Thomas RL:** Non-epithelial tumors of the larynx. J Laryngol Otol 93:1131-1141, 1979
8. **Krajina Z:** Laryngeal sarcoma. Can J Otolarygol 4: 303-306, 1975

9. **DeLozier HL:** Intrinsic Malignant schwannoma of the larynx: a case report. Ann Otol Rhinol Laryngol 91:336-338, 1982
10. **Hutcherson RW, Jenkins HA, Canalis FR, Handler SD, Eichel BS:** Neurogenic sarcoma of the head and neck. Arch Otolarngol Head Neck Surg 105: 267-270, 1979
11. **Bojsen-Moller M, Myrhe-Jensen O:** A consecutive series of 30 malignant schwannomas: Survival in relation to clinicopathological parameters and treatment. Acta Pathol Microbiol Scan (Sect A) 92: 147, 1984
12. **D'Agostino AN, Soule EH, Miller RH:** Primary malignant neoplasm of nerves (malignant neurilemomas) in patients without manifestations of multiple neurofibromatosis (von Recklinghausen's disease). Cancer 16:1003-1014, 1963
13. **D'Agostino AN, Soule EH, Miller RH:** Sarcomas of the peripheral nerves and somatic soft tissues associated with multiple neurofibromatosis (von Recklinghausen's disease). Cancer 16:1015-1027, 1963
14. **Ducatman BS, Scheithauer BW, Piepgras DG:** Malignant peripheral nerve sheath tumors: A clinicopathologic study of 120 cases. Cancer 57: 2006-2021, 1986
15. **Hoffmann DF, Everts EC, Smith JD, et al:** Malignant nerve sheath tumors of the Head and neck. Otolaryngol Head Neck Surg 99:309-314, 1988
16. **White HR Jr:** Survival in malignant schwannoma: An 18-year study. Cancer 27:720-729, 1971
17. **Sorensen SA, Mulvihill JJ, Nielsen A:** Long-term follow up of von Recklinghausen neurofibromatosis. N Engl J Med 305:1617, 1981
18. **Sordillo PP, Helson L, Hajdu SI, et al:** Malignant schwannoma: Clinical characteristics, survival, and response to therapy. Cancer 47:2503-2509, 1981
19. **Ducatman BS, Scheithauer BW:** Post-irradiation ueurofibrosarcoma. Cancer 51:1028-1033, 1983
20. **Hajdu S:** Tumors of the peripheral nerves. In: Pathology of soft tissue tumors. Philadelphia, Lea and Febiger, 1979, pp. 427-482
21. **Ducatman BS, Scheithauer BW:** Malignant peripheral nerve sheath tumor with divergent differentiation. Cancer 54:1049-1057, 1984
22. **Goepfert H, Lindberg RC, Sinkovics JG, Ayala AG:** Soft tissue sarcoma of the head and neck after puberty: treatment by surgery and postoperative radiation therapy. Arch Otolaryngol Head Neck Surg 103:365-368, 1977
23. **Kumar PP, Good RR:** Interstitial ^{125}I implantation in the retreatment of retroperitoneal soft tissue sarcoma. Acta Radiologica Oncology 25:37-39. 1986

= 국문초록 =

사골동과 후두에 발생한 악성신경초종

고려대학교 의과대학 치료방사선과학교실

이 규 찬 · 최 명 선

악성 신경초종의 두경부 영역에서의 발생은 극히 드물다. 대부분의 종양은 급속도로 커져가는 무통성 종물로서 발견되며, 그 증상은 대개 종물의 국소적 팽윤에 기인한다. 약 반수의 경우에서 본 레클링하우젠씨 병과 동반된다.

광범위한 외과적 절제술이 일반적으로 권장되는 일차 치료법이며, 최근 수술후 방사선치료를 이에 포함시키고 있다.

두경부 영역에서 발생한 악성 신경초종의 예후는 특히 나쁜 것으로 보고되어 왔으나, 최근에는 수술후 방사선 치료를 포함한 적절한 치료를 시행함으로써 생존율의 증가가 가능하게 되었다.

저자들은 사골동과 후두 등 희귀한 위치에 발생한 악성 신경초종 2례를 문헌 고찰과 함께 보고 하는 바이다.