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A Case of Multiple Schwannomas of the Trigeminal Nerves, Acoustic Nerves, Lower Cranial Nerves, Brachial Plexuses and Spinal Canal: Schwannomatosis or Neurofibromatosis?

Jung Yong Ahn[1], Seong Oh Kwon[1], Moon Soo Shin[1], Jeong Yun Shim[2], and Ok-Joon Kim[3]

Departments of [1]Neurosurgery, [2]Patholgy, and [3]Neurology, Pundang CHA Hospital, Pochon CHA University, Sungnam, Korea.

In most cases, while schwannoma is sporadically manifested as a single benign neoplasm, the presence of multiple schwannomas in one patient is usually indicative of neurofibromatosis 2. However, several recent reports have suggested that schwannomatosis itself may also be a distinct clinical entity. This study examines an extremely rare case of probable schwannomatosis associated with intracranial, intraspinal and peripheral involvements. A 63-year-old woman presented with a seven-year history of palpable lumps on both sides of the supraclavicular area and hearing impairment in both ears. On physical examination, no skin manifestations were evident. Facial sensory change, deafness in the left ear and decreased gag reflex were revealed by neurological examination. Magnetic resonance imaging revealed multiple lesions of the trigeminal nerves, acoustic nerves, lower cranial nerves, spinal accessory nerve, brachial plexuses, and spinal nerves. Pathological examination of tumors from the bilateral brachial plexuses, the spinal nerve in the T8 spinal position and the neck mass revealed benign schwannomas. Following is this patient case report of multiple schwannomas presenting with no skin manifestations of neurofibromatosis.

Key Words: Schwannoma, schwannomatosis, neurofibromatosis

INTRODUCTION

Typically, schwannoma presents frequently as a single benign neoplasm of the nervous system originating in the neural sheath. Occasionally it presents in multiple form or simultaneously arises from several points along the peripheral nervous system, including cranial nerves, spinal roots, the brachial and lumbosacral plexuses, or major peripheral nerves.

Several syndromes, including the well-known neurofibromatoses, are associated with an increased frequency of schwannomas.[1,2] The defining feature of neurofibromatosis 2 (NF2) is the presence of bilateral vestibular schwannomas.[3]

Recent reports have suggested that some patients develop multiple schwannomas without any other associated stigmata of neurofibromatosis and that schwannomatosis may thus be regarded as a distinct clinical entity.[4,5] We here present a case of probable schwannomatosis with intracranial, intraspinal, and peripheral involvement.

CASE REPORT

A 63-year-old woman presented with a seven-year history of palpable lumps on both sides of the supraclavicular area and hearing impairments in both ears. Ten years earlier, she had visited another hospital for evaluation of hearing difficulty of the right ear, but the results of this examination were not available. The hearing of the left ear had begun to decrease seven years prior to presentation, from which time she had used a hearing aid. An abdominal mass had been excised 6 years ago. The bilateral

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Reprint address: requests to Dr. Jung Yong Ahn, Department of Neurosurgery, Pundang CHA Hospital, Pochon CHA University College of Medicine, 351, Yatap-Dong, Pundang-Gu, Sungnam, 463-070, Korea. Tel: 82-31-780-5262, Fax: 82-31-780-5259, E-mail: jyahn@cha.ac.kr

lesions on the supraclavicular area had been enlarged and she had felt paresthesia on the skin overlying the masses. There was no family history of neurologic disturbances, cafe-au-lait spots, or tumors of the skin or central nervous system.

Upon admission, her physical examination was remarkable for the presence of multiple masses located on both sides of the supraclavicular area and an anterior triangle area of the left neck. There were no cafe-au-lait spots or auxiliary freckles. No Lisch nodules were evident on ophthalmologic examination. Pure tone audiometry detected a high-tone sensorineural hearing loss of 30 dB in the left ear. The right ear was completely deaf. The findings of neurologic and mental status evaluations were normal except for a sensory change evident on the right face of the second trigeminal area. The patient and her family did not undergo molecular genetic analysis.

Magnetic resonance imaging (MRI) of the thoracolumbar spine demonstrated an extradural mass at the T8 position as well as multiple masses in the intradural sac of the lumbar spinal canal (Fig. 1). MRI of the brachial plexus showed two enhancing masses at the bilateral brachial plexus and one small mass located behind the jugular vein (Fig. 2). Axial MRI of the brain revealed multiple lesions in the bilateral cerebellopontine angles. These masses originated from the bilateral trigeminal, acoustic, and lower cranial nerves (Fig. 3).

First, right hemilaminectomy of the T8 spine was performed with the patient in the prone position and a tumor mass causing compression and deformation of the dural sac and costal surface was observed. A branch of the dorsal root at T8 was sacrificed to achieve complete resection of the tumor. Next, the patient was placed in the supine position and the tumors on the bilateral brachial plexuses were removed utilizing the intracapsular approach with electrophysiologic monitoring. After the almost complete removal of the tumor, the capsule was carefully dissected from the brachial plexus. Masses were found to have arisen from the nerve fascicles in the upper portions of the brachial plexus and these were completely dissected. Lastly, the neck mass was removed by the careful dissection of the neck.

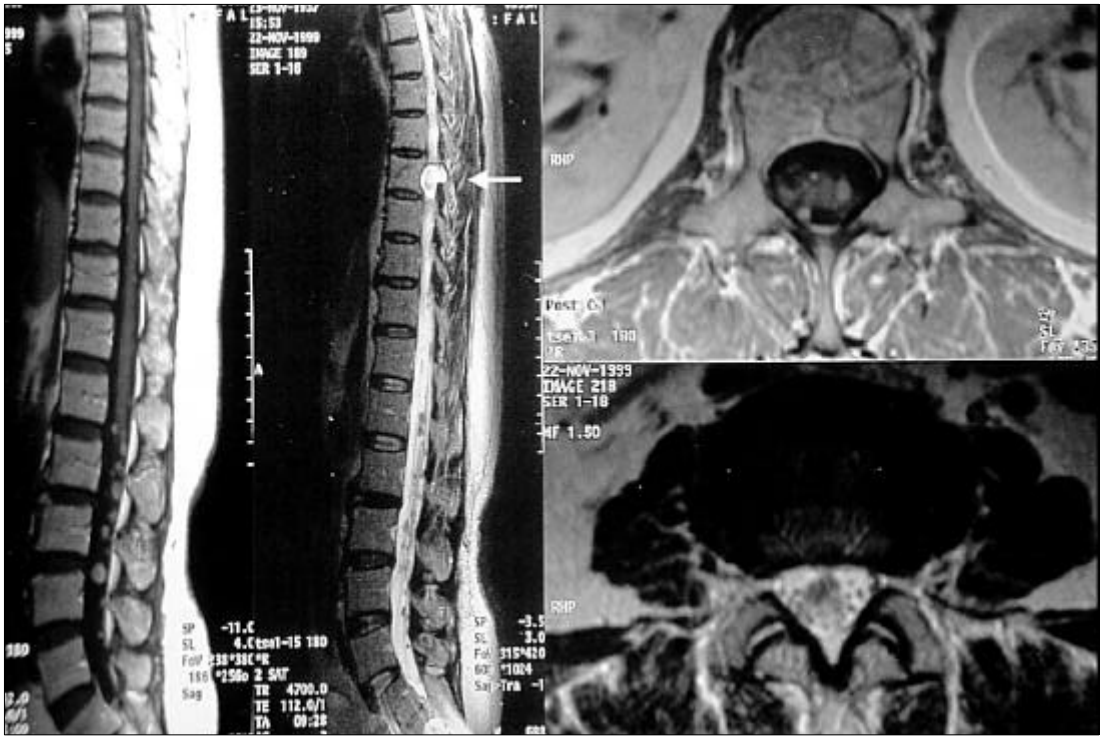

Fig. 1. Magnetic resonance imaging of the thoracolumbar spine demonstrating an extradural mass (arrow) at T8 and multiple masses in the intradural sac at the lumbar spinal canal.

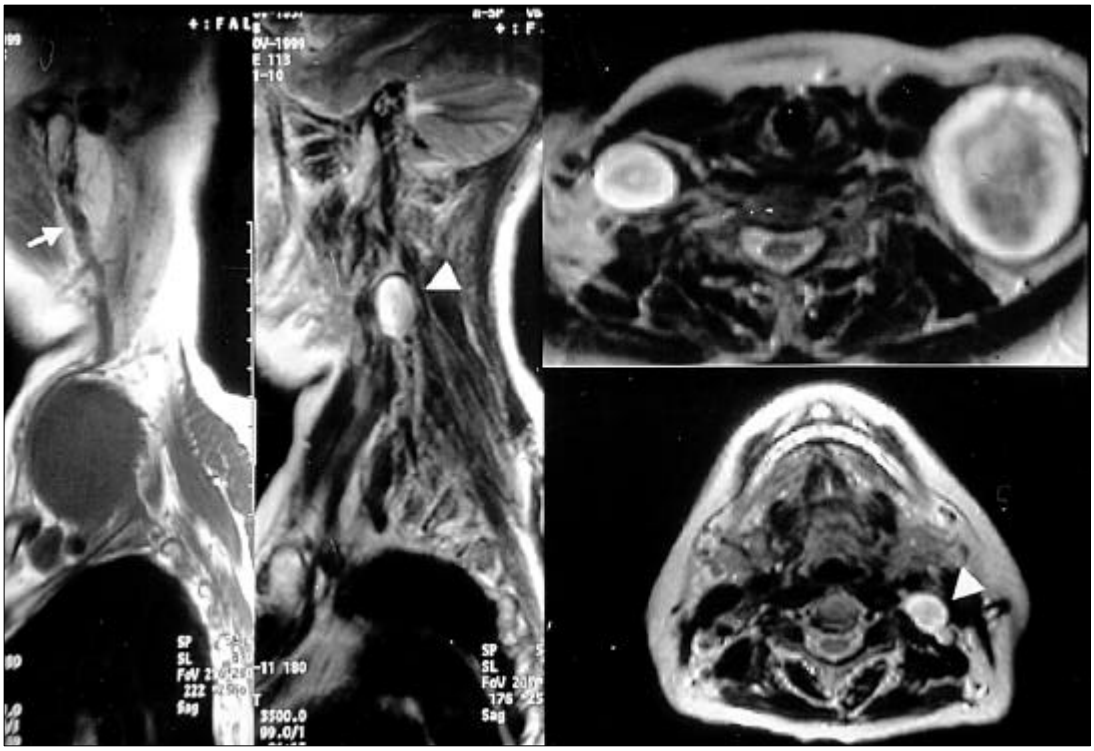

Fig. 2. Magnetic resonance imaging of the brachial plexus showing two enhancing masses at the bilateral brachial plexus and one small mass (arrowhead) located behind the jugular vein. The external jugular vein (arrow) is dilated due to compression of the tumor.

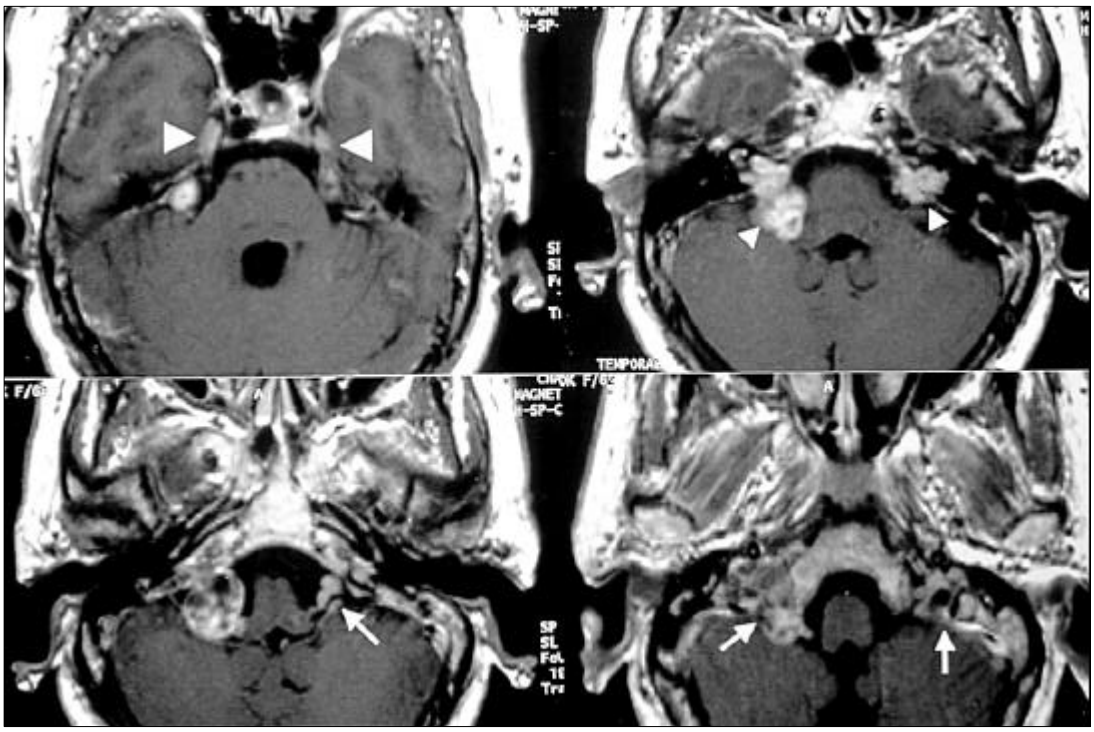

Fig. 3. Axial magnetic resonance imaging of the brain revealing multiple lesions in the bilateral cerebellopontine angles. The masses originated from the bilateral trigeminal (large arrowhead), acoustic (small arrowhead), and lower cranial nerves (arrow). The masses of the lower cranial nerve complex extend to the jugular fossa.

The patient's postoperative course was uneventful. Pathological examination revealed benign schwannomas. Microscopically all of the tumors consisted of spindle-shaped cells with eosinophilic cytoplasm. The nuclei were oval and round with fine chromatin granules and occasional prominent nucleoli. The microscopic examination revealed a parallel configuration of the tumor cells typical of a Verocay body. Immunohistochemical studies were positive for S-100 protein but nonreactive for epithelial membrane antigen, glial fibrillary acidic protein, vimentin, and myelin basic protein. We recommended that the patient undergo further surgery for the brain lesions, but she was reluctant to consent to this and did not undergo further treatment. She remains free of recurrence 12 months after surgery and her cranial nerve signs reveal no change.

DISCUSSION

Schwannomas, benign tumors of the nervous system originating in the neural sheath, most commonly manifest sporadically and only as a single neoplasm. However some 3 to 4% of patients presenting with a schwannoma do so in the form of multiple lesions.[6,7] Multiple schwannomas have been reported in association with neurofibromatosis.[1,2] The defining feature of over 95% of patients with NF2 is the eventual development of bilateral vestibular schwannomas.[8] Furthermore, at least two-thirds of these patients develop schwannomas in other locations as well, especially subcutaneously, and in NF2-affected children, this development of subcutaneous tumors may actually precede the development of vestibular schwannomas.[9] Meanwhile, the defining feature of neurofibromatosis 1 (NF1) is the presence/development of neurofibroma, histologically distinct from schwannoma. Although schwannoma is included in the criterion for NF1 diagnosis, its occurrence in NF1 is rare.[10]

Recent reports have suggested that some patients may develop multiple schwannomas without any associated NF1 or NF2 stigmata.[4,5] Such a presentation has been termed schwannomatosis[5,11,12] or neurilemmomatosis[4] and may be regarded as a distinct clinical entity. However, some of these patient case reports of multiple schwannomas presenting without clear anatomic localization were reported before the publication of the NIH consensus statement[10] and hence include patients who would now be classified as having NF2.[4,5]

Some differences have become apparent between schwannomatosis and neurofibromatosis with respect to their clinical manifestations. Firstly, the patient age at presentation differs. MacCollin et al.[11] presented a series of 14 schwannomatosis patients, eight female and six male, whose median age at onset was 26 years. Whereas, all patients in the study had been examined using cranial MR imaging, not all had undergone spinal MR imaging. The authors of this study considered schwannomatosis to be a clinical entity distinct from NF2. Seppälä et al.[13] reviewed a series of 9 patients with schwannomatosis, composed of three females and six males, all of whom presented at middle age. This age corresponds to that at which most patients with sporadic schwannomas present,[6,7] but contrasts with the earlier age of less than 20 at which NF2 patients tend to present. As for our patient, she became symptomatic after 50 years of age.

The second difference with neurofibromatosis is the absence of any family history in schwannomatosis. This was true of all 9 patients in Seppala's report,[13] and in MacCollin's study only one of the 14 patients with multiple schwannomas, who did not have vestibular schwannoma, had a family history.[11] Additionally, the genetic mechanism of schwannomatosis differs from that of NF2.[13] Seppala, et al.[13] found no evidence of germline mutations on direct sequencing of the NF2 gene among their 9 schwannomatosis patients. Furthermore, in a study on five families Evans et al.[12] described multiple non-vestibular schwannomas that were linked to the NF2 locus without any associated mutations in the NF2 gene. Somatic mosaicism of the NF2 germline mutation explains some cases of schwannomatosis,[14] and this makes the risk of inheritance more difficult to predict. Based on the data of these studies, schwannomatosis seems sporadic in most cases, but a number of affected individuals will have an inherited form of the entity.[13] Additionally, whereas a definite or presumptive diagnosis

of NF2 can be made with the objective diagnostic criteria,[3] schwannomatosis is not associated with any other abnormalities.

To summarize, this study has described a patient case report of multiple schwannomas presenting without any skin manifestations of neurofibromatosis. Schwannomatosis may be a rare disease of distinct clinical entity from neurofibromatosis. The occurrence of multiple peripheral schwannomas in the absence of any defining characteristics for neurofibromatosis may indicate the presence of central nervous system tumors or various neurologic deficits.

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