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Intradural Extramedullary Ganglioneuroma Associated With Multiple Hamartoma Syndrome

—Case Report—

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Abstract

A 51-year-old woman presented with a rare completely intradural and extramedullary spinal ganglioneuroma associated with multiple hamartoma syndrome and manifesting as complaints of neck pain and dizziness persisting for 8 months. Magnetic resonance imaging of the spinal cord revealed an intradural extramedullary lesion at the C1 level. She underwent right suboccipital craniectomy and C1–2 hemilaminectomy to remove the tumor. Histological examination confirmed ganglioneuroma. She also suffered from multiple facial trichilemmomas, thyroid goiter, multiple polyposis of the gastrointestinal tract, and pulmonary hamartoma indicating multiple hamartoma syndrome. These benign neoplasms were treated conservatively.

Key words: intradural ganglioneuroma, spinal neoplasm, surgical treatment, multiple hamartoma syndrome

Introduction

Ganglioneuroma arises from the ganglion cells of the sympathetic nervous system, and infrequently from the sympathetic nerves or other peripheral nerves.[1,2] Females are more affected than males.[11] These slow-growing benign neoplasms contain well-differentiated ganglion cell stroma resembling neurofibroma and are common in the posterior mediastinum but may occur in the cervical region, retroperitoneal region, adrenal glands, and sympathetic ganglion.[7,12,13] Ganglion cell tumors originate in a defect in developmental embryogenesis, with multipotent embryonal neurocytes deposited in abnormal positions.[17] Complete removal of a ganglioneuroma is usually curative.[6] Ganglioneuromas are rarely located in the spinal cord,[4,10,14] and are frequently dumbbell-shaped.[9,15] Spinal ganglioneuroma is usually benign in nature and remains asymptomatic until large enough to compress the spinal cord and nerves, resulting in localized pain, radiculopathy, and weakness of the extremities.[3]

We present a case of mature ganglion cell tumor within the intradural space of upper cervical spine and manifesting as neck pain and dizziness. The patient also suffered from multiple facial trichilemmomas, thyroid goiter, multiple polyposis of the gastrointestinal tract, and pulmonary hamartoma.

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Case Report

A 51-year-old woman presented with complaints of neck pain and progressive dizziness persisting for 8 months. Neurological examination revealed no motor weakness or sensory disturbance. Magnetic resonance imaging of the spinal cord showed an intradural extramedullary lesion at the C1 level appearing as isointense or slightly hypointense on T_1-weighted images and hyperintense to the spinal cord on T_2-weighted images, with enhancement by contrast medium (Fig. 1).

The patient underwent right suboccipital craniectomy and C1–2 hemilaminectomy. The dura was opened and the dentate ligament was resected to reveal a well-circumscribed, extramedullary, oval-shaped mass. The mass was attached to the C1 ventral root, and was totally excised. Histological examination revealed large ganglion cells with large vesicular nuclei and prominent eosinophilic nucleoli and spindle-shaped cells arranged in fascicles (Fig. 2A). Immunohistochemical staining with a panel of

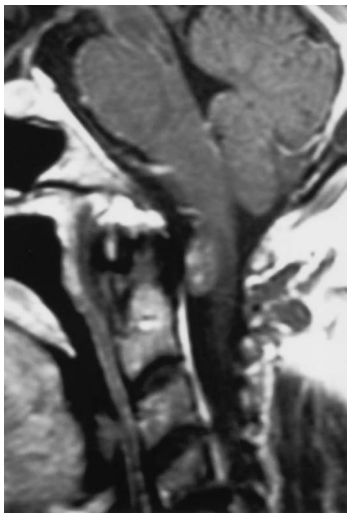

Fig. 1 Sagittal T_1-weighted magnetic resonance image of the spinal cord with contrast medium showing an enhanced intradural extramedullary lesion at the C1 level.

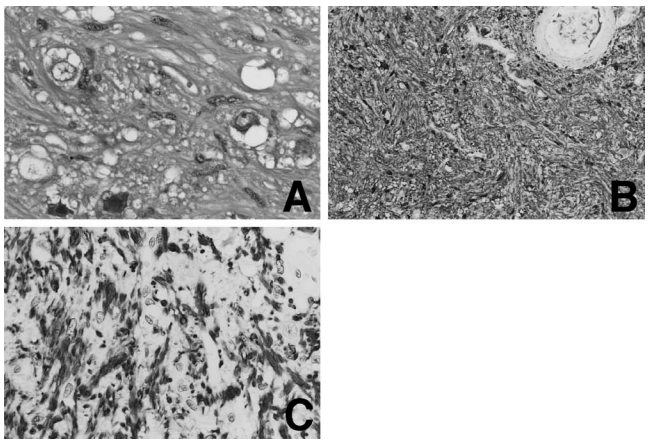

Fig. 2 A: Photomicrograph revealing large ganglion cells with large vesicular nuclei and prominent eosinophilic nucleoli and spindle-shaped cells arranged in fascicles. Hematoxylin and eosin stain, ×400. B: Photomicrograph showing positive immunoreaction for S-100 protein in the ganglion cells. ×100. C: Photomicrograph revealing positive immunoreaction for neurofilament in the ganglion cells. ×400.

monoclonal antibodies revealed positive reaction for S-100 protein (Fig. 2B), and neurofilament (Fig. 2C) in the ganglion cells. The final histological diagnosis was ganglioneuroma. In the pathological findings, MIB-1 labeling index was less than 1%.

Examination of the patient's skin revealed a large number of hyperkeratotic lichenoid papules, 1 to 3 mm in diameter, scattered over the forehead, cheeks, and chin. The patient had also suffered from multiple facial trichilemmomas, thyroid goiter, multiple polyposis of the gastrointestinal tract, and pulmonary hamartoma. Associated benign neoplasms were found incidentally, and were treated conservatively. The patient denied any similar skin lesions or significant medical problems in other family members, including her two children. She refused to allow examination of any family members.

Discussion

Only one case of pure intradural extramedullary ganglioneuroma has been reported.[6] The present case of mature ganglion cell tumor was located within the dura of the upper cervical spine and outside the spinal canal. We speculate that the ectopic tumor which underwent hamartomatous change originated in the intradural space but without the normal dumbbell-shaped growth pattern as a part of multiple hamartoma syndrome. Hamartomas also present as a part of multiple endocrine neoplasia (MEN) and could be associated with von Recklinghausen disease.[16] The tumors of MEN occur in the adrenal medulla, pancreas, and pituitary together with ganglioneuromas in the mediastinal and retroperitoneal regions.[5,18] The diagnosis of these tumors is usually based on the clinical presentation and neuroimaging findings.[2]

Histological examination revealed a neoplastic lesion consisting of spindle-shaped cells arranged in fascicles. The cells contained abundant faintly eosinophilic cytoplasm and indistinct boundaries. The nuclei were serpentine exhibiting minimal hyperchromasia and pleomorphism. Large ganglion cells with large vesicular nuclei and prominent eosinophilic nucleoli were interspersed between the spindle-shaped cells. No significant mitotic activity was found. The ganglion cells were positively stained for S-100 protein and neurofilaments.[2,6]

Cowden disease or multiple hamartoma syndrome is a rare autosomal dominant condition characterized by a complex mixture of endodermal, mesodermal, and ectodermal hamartomatous lesions. The pathognomonic hamartomatous features include multiple smooth facial papules, acral keratosis, and multiple oral papillomas. The facial papules are characterized by multiple trichilemmomas. Central nervous system manifestations were emphasized only recently and include megalencephaly, epilepsy, and dysplastic gangliocytomas of the cerebellum (Lhermitte-Duclos disease). Other lesions include benign and malignant diseases of the thyroid, intesti-

nal polyps, and genitourinary abnormalities.[8] Our patient also seemed to suffer from multiple hamartoma syndrome with ganglioneuroma, multiple facial trichilemmomas, thyroid goiter, multiple polyposis of the gastrointestinal tract, and pulmonary hamartoma, which were found incidentally and were asymptomatic. She was treated conservatively for these other lesions. We speculate that though the ganglioneuroma was incidentally found, it was inevitably associated with multiple hamartoma syndrome.

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