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Spinal Meningeal Melanocytoma

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A case of spinal meningeal melanocytoma is reported along with clinicopathologic, immunohistochemical and ultrastructural studies. This patient presented clinically with paraparesis, tingling sensation and numbness of both lower extremities of 4 months duration. No mucocutaneous pigmented nevi were found. On operation, scattered coal-black pigmented lesions were found in the meninges between T3 and T4-5 interspace level. Nearly total removal was carried out. The tumor was composed of spindle and epithelioid cells with heavy brown-black pigmentation. There was no pleomorphism, mitosis, hemorrhage, necrosis or invasion to the underlying cord tissue. In Korea, this case appears to be the first example of this disease. Neurologic deficit improved after surgical excision.

Key Words: *Meningeal melanocytoma, spinal canal, immunohistochemical study, ultrastructural study*

INTRODUCTION

Melanotic meningeal neoplasms have been reported under various names, such as melanotic or pigmented meningioma (Ray & Foot, 1940; Abbott et al., 1968; Scott et al., 1971; Keegan and Mullan, 1962; Turnbull and Tom, 1963), meningeal melanocytoma (Limas and Tio, 1972; Winston et al., 1987), melanotic schwannoma (Dastur et al., 1967; Mennemeyer et al., 1979) and cellular blue nevus of meninges (Graham et al., 1976). However, Winston et al. (1987) insted that melanotic meningioma had not been actually identified because none of the tumors examined by electron microscopy have had the features characteristic of meningioma and meningothelial cells do not produce melanosomes. Melanin producing cells of neural crest origin are exclusively of melanocyte with rare Schwann cell. "Melanotic schwannomas attached to meninges have been well documented, but they are extremely rare" (Lowman and Livolsi, 1980; Mennemeyer et al., 1979; Robertson and Ghadially, 1983).

Melanotic meningeal neoplasm can be either metastatic or primary, and it can also be benign or malignant. Metastatic lesions are by far the commonest since malignant melanomas comprise 12-16% of all tumors metastatic to the central nervous system (Bakody et al., 1950). However, primary ones are extremely rare. Among the reported primary meningeal melanocytic tumors, the majority are malignant form. Benign melanocytic tumors have been designated as "meningeal melanocytoma" which was first proposed by Limas and Tio (1972). Histochemical tests for melanin are not specific, and in such a controversial issue, a minimum requirement would be the electron microscopic demonstration of indubitable melanosomes or evidence of schwannian differentiation (Russell & Rubinstein, 1989). It would not be enough to show compound melanosomes or an occasional solitary melanosomes in the tumor cells because these would be endocytosed melanosomes. The key is the demonstration of indubitable melanosomes in various stages.

We present a case of meningeal melanocytoma along with clinicopathologic, immunohistochemical and electron microscopic studies and review of the literature.

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METHODS

Specimens received in formalin were routinely processed and embedded in paraffin. Sections were routinely processed an stained with hematoxylin and eosin, and Fontana Masson with bleach in hydrogen peroxide. For electron microscopy, a small part of the formalin fixed tissue was washed with phosphate buffer and refixed in 2.5% buffered glutaraldehyde, postfixed

in phosphate-buffered 1% osmium tetroxide, dehydrated through graded concentrations of ethanol and propylene oxide, and embedded in Epon. Thin sections were stained with uranyl acetate and lead citrate and examined with a Hitachi H600 electron microscope.

CASE REPORT

This 41 year old female presented with paraparesis, tingling sensation and numbness of both lower extremities, and low back pain which began 4 months before the admission to our hospital. She had been managed at a local clinic, but there was no improvement. She had been well except for weakness of the left lower extremity caused by poliomyelitis since youth. Physical examination revealed positive upper motor neuron sign in both lower extremities. There was no remarkable skin pigmentation.

Total myelogram revealed a right extradural mass at the level of T3-4. Computed tomography (CT) of thoracic spine revealed a soft tissue-density mass in the right spinal canal from T3 to T4-5 level with displacement and compression of the spinal cord and thecal sac (Fig. 1). Erosion of the medial portion of the right pedicle of T4 was found. A small paraspinal mass was also detected especially on the ventral side of the spinal canal.

On operation field, a coal-black mass was firmly attached to the external surface of dura and compressed the T4 nerve root (Fig. 2). The mass was 4.0×3.0cm in size. Multifocal dural, arachnoidal and pial pigmentations with mild leptomeningeal thickening were also seen. Total laminectomy of T1, T2, T3 with partial removal of pigmented meninges was done. On the next day, revision and nearly total removal of the mass with pigmented meninges were done.

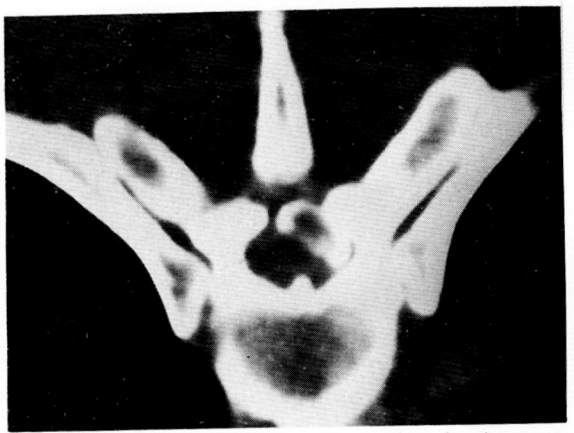

Fig. 1. CT of T3 thoracic spine shows a low density mass (arrow) in the right spinal canal with displaced and compressed spinal cord and thecal sac.

Fig. 3. The tumor is composed of spindle cells and epithelioid cells with heavy black pigmentation. (H&E, ×100)

PATHOLOGIC FINDING

The submitted specimen consisted of several frag-

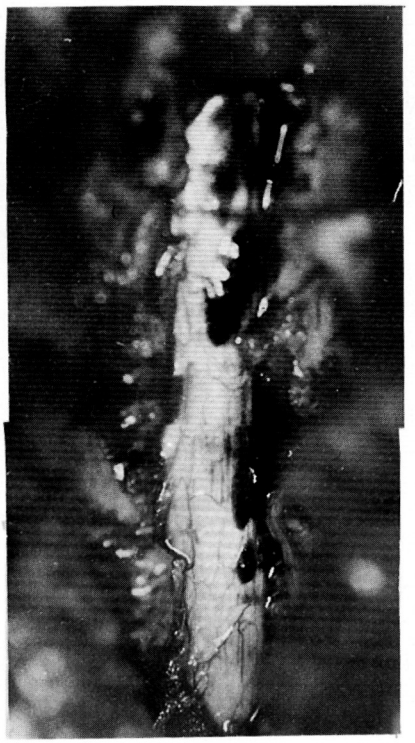

Fig. 2. On operation field, multiple coal-black pigmented lesion is noted, which is attached to the external surface of the dura.

ments of coal-black soft and friable tissue, measuring 2.0×1.0×1.0cm in total dimension.

Microscopically, the tumor was a heavily pigmented, cellular, biphasic lesion consisting of spindle cells and epithelioid cells (Fig. 3). The spindle cells were arranged in bundles and possessed a relatively large, elongated nucleus with a fine and vesicular chromatin pattern (Fig. 4). Small nucleoli were seen. The epithelioid cells were polygonal and had abundant cytoplasm packed with dense brown to black pigmentation on hematoxylin and eosin stain (Fig. 5). The nuclei were rounded and vesicular with small conspicuous nucleoli. The sheets of epithelioid cells and bundles of spindle neoplastic cells were around and within collagenous meninges. There were no marked nuclear pleomorphism, necrosis, hemorrhage, or mitoses. The Fontana Masson stain for melanin was positive whereas stain for iron was negative.

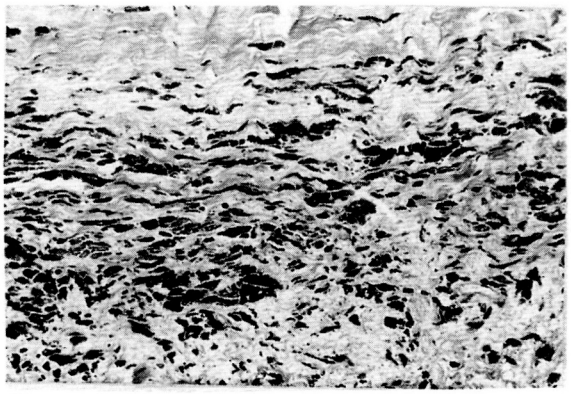

Fig. 4. The spindle-shape neoplastic cells are arranged in bundles and possessed heavy black pigmentation in wavy collagen background. (H&E. ×200)

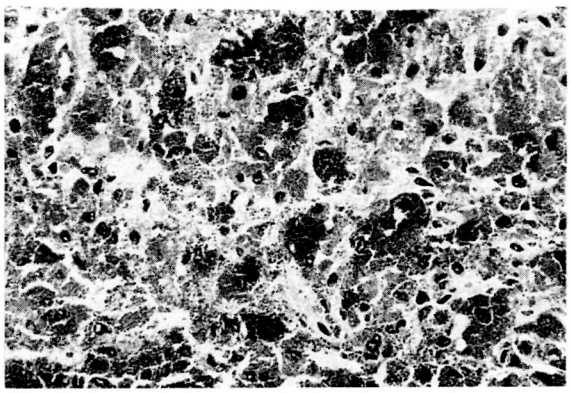

Fig. 5. The epithelioid neoplastic cells are polygonal and have abundant cytoplasm packed with brown to black particles. The nuclei are rounded or oval shape. There was neither mitosis nor necrosis. (H&E. ×400)

Immunoperoxidase stains for S-100 protein of the tumor cells revealed strong cytoplasmic and some nuclear positivity. Despite the fact that the tumor was heavily pigmented with melanin, when methy green counterstain was applied, the melanin granules stained dark green and contrasted with the dark brown staining of the diaminobezidine reaction. Epithelial membrane antigen was not expressed in the tumor cells.

Ultrastructural study showed sheets of tumor cells with irregulary contoured nuclei, prominent nucleoli, and abundant cytoplasm containing plentiful melanosomes in various stages (Fig. 6). Most were stage 3 (partially pigmented melanosomes) and stage 4 (densely pigmented mature melanin granules). Stage 2 melanosomes (premelanosomes) were quite rare. Compound melanosomes were also present. The cytoplasm also contained prominent Golgi apparatus, numerous mitochondria, free ribosomes, scanty intermediate filaments and a few rough endoplasmic reticula. There was no external lamina around the neoplastic cells. No pinocytotic vesicles were seen. Neither any junctional complex including desmosomes nor interlocking cytoplasmic membrane were found.

DISCUSSION

All melanin-producing cells are thought to be derived from the neural tube and neural crest. In normal humans, the melanin producing cells of neural tube origin are found in the pigmented epithelial cell of the eye. Those of neural crest origin are melanocyte and rarely Schwann cell. Melanin producing tumors of neural crest-derived cells found in meninges include (1) blue nevi (Graham et al., 1976), (2) meningeal melanocytoma (Limas and Tio, 1972), (3) malignant melanoma (Tolnai et al., 1966) and (4) melanotic schwannoma (Mennenmeyer et al., 1979). Normally presented meningeal melanin producing cells are melanocytes and in humans, these cells are more abundant over the ventral surface of the medulla and the upper spinal cord (Limas and Tio, 1972).

Menigeal melanocytic neoplasm can be classified as metastatic or primary and it can also be benign or malignant. The majority of the reported cases were metastatic malignant melanoma and the primary benign form is very rare (Becker, 1970; Gibson et al., 1957; Kiel et al., 1961; Pappenheim and Bhattercharzi, 1962; Tolnai et al., 1966). Benign one is designated as "meningeal melanocytoma" which was first proposed by Lima and Tio (1972). Bamborschke et al. (1985) listed a total of 220 reported examples of primary central nervous system and leptomenigeal melanomas, of which approximately two thirds were

either diffuse or multifocal and the remainder were solitary pigmented growth. An association with pigmented cutaneous nevi was documented in approximately 25 per cent of the entire series (Russell & Rubinstein, 1989).

Meningeal melanocytoma represents benign histopathology and a favorable clinical course although it involves diffuse or multifocal sites of the meninges. They usually have a long span of history at the time of diagnosis. On the contrary, malignant menigeal melanomas are usually diffuse or multifocal and may occur in any part of the central nervous system but predominantly involve the spinal cord and cerebral hemispheres. Histopathologically, the neoplastic cells show marked pleomorphism, numerous mitoses, necrosis, and hemorrhage. Spindle cells are consistently encountered. A short history of neurologic symptoms usually correlates with rapid tumor growth, a poor prognosis, and death within a year from the onset of symptoms (Russell & Rubinstein, 1989).

Diagnostic difficulties may occasionally arise in distinguishing between individual cases and these difficulties stem from the well-known protean cytological features of primary melanoma in general and the common derivation of these tumors from neural crest precursor cells. Whether benign or malignant, among meningeal melanotic tumors, melanoma, schwannoma and meningioma are the main diseases for differential diagnosis. The diagnosis is supported by immunohistochemical and ultrastructural studies. In contentious cases ultrastructural study may be essential in order to establish or exclude one of the alternative diagnoses because of the nonspecificity of the immunohistochemical marker for melanin. Meningeal melanomas and Schwannomas are typically S-100 protein-positive whereas the majority of meningiomas are not (Nakamura et al., 1983). Instead the majority of the menigiomas are positive for epithelial membrane antigen and vimentin. Ultrastructurally, the Schwann cells are surrounded by external lamina and Luse bodies are found in the stroma. The meningothelial cells characterized by interdigitating cytoplasmic membrane, cytoplasmic wavy intermediate filaments and well developed desmosomes. However, neither normal melanocytes nor neoplastic melanocytes of malignant melanoma bear external lamina or desmosomes

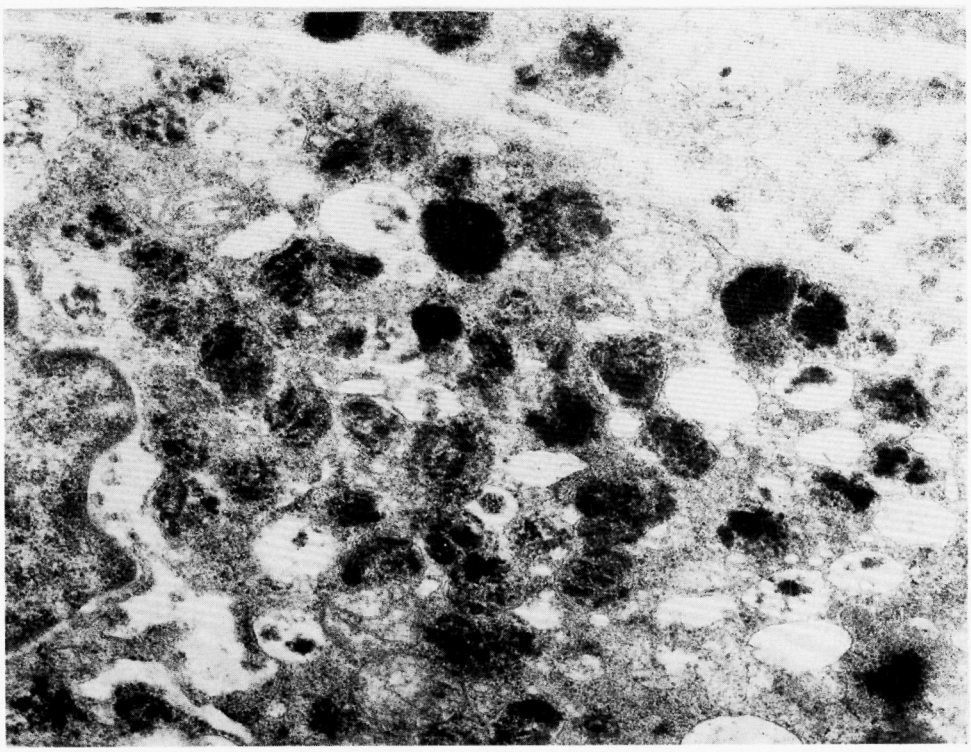

Fig. 6. Ultrastructurally, the neoplastic cell contains plentiful solitary melanosomes in various stages. Most are partially pigmented stage 3 melanosomes (arrows) and densely pigemented matured stage 4 melanosomes (arrow heads). (Uranyl acetate and lead citrate stain, ×34,500)

(Curran and McCann, 1976). The melanocytes contain melanosomes in various stages. It would not be sufficient to show compound melanososmes or occasional solitary melanosomes in the tumor cells because these would be endocytosed melanosomes, that is to say secondarily derived from a melanocyte and not producted by the tumor cell itself. Only melanin producing cells have the developing melanosomes of early stages. Winston et al. (1989) insisted that melanotic meningioma had not been actually identified because none of the tumors have shown evidence of meningioma by electron microscopic studies and the melanoblastic meningioma of Bailey and Bucy (1931) was probably a malignant melanoma as evidenced by the large number of pigmented lesions over the surface of the cerebral hemispheres and within the cerebellum, and by the presence of many mitotic figures. However, melanotic Schwannoma attached to leptomeninges have been well documented (Mennemeyer et al., 1979; Robertson and Ghadially, 1983; Lowman and Livolsi, 1980).

Our case confirmed immunohistochemically and ultrastructurally as meningeal melanocytoma. The tumor was mainly attached to the external surface of the dura and was accompanied by multifocal arachnoidal and pial pigmentations. However, no cutaneous melanotic lesion was associated. Histopathologically, the tumor was embedded in the meninges with exophytic growth. There was no evidence of malignancy such as, cellular pleomorphism, mitoses, hemorrahge, necrosis or spinal cord invasion. We committed the diagnostic error of reporting this case as malignant melanoma at frozen biopsy. Pathologists must be wary of wrong identification of this heavily melanotic lesion as malignant melanoma in frozen sections. This comment has already been described by Winston et al. (1987). In Korea, a case of recurrent intracranial primary meningeal melanoma has been described (Lee and Kim, 1991), however, a description of spinal meningeal melanotic lesions could not be found until now. The reported Korean intracranial primary melanoma case was associated with Ota's nevi of right periorbital area and mid-face and blue nevus of left upper extremity (Lee and Kim, 1991).

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