Coexistence of 3 Tumors of Neural Crest Origin

Neurofibroma, Meningioma, and Uveal Malignant Melanoma

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Objective: To describe the clinical findings in a patient who developed a neurofibroma, meningioma, and choroidal melanoma.

Methods: Clinical and histopathological findings of the case are reviewed and presented.

Results: The patient had a right superolateral periorbital neurofibroma, a right sphenoid wing meningioma, and a left choroidal juxtapapillary malignant melanoma. All 3 tumors are derived from neural crest cells.

Conclusions: To our knowledge, this is the first report of a patient with this combination of 3 neural crest–derived tumors. This case is most appropriately classified as a complex neurocristopathy, a disorder involving the aberrant and pathological proliferation of multiple tissues derived from neural crest cells.


Evidence of the simultaneous occurrence of neurofibromas and meningiomas in patients has been well established.1 This condition typically occurs when the patient has neurofibromatosis type 1 or type 2. Neurofibromas have also been associated with cutaneous and uveal malignant melanomas.2-4 In addition, patients with both meningiomas and cutaneous malignant melanomas have been described.5 To our knowledge, however, this is the first description of a patient who developed all 3 tumor types: a neurofibroma, a meningioma, and a uveal malignant melanoma.

REPORT OF A CASE

A 64-year-old woman was referred for evaluation of diabetic retinopathy. Her medical history included diabetes mellitus and systemic hypertension. She had no personal or family history of neurofibromatosis type 1 or type 2, nor did she have systemic, cutaneous, or iris lesions suggestive of either of these disorders. Visual acuities were 20/25 OD and 20/20 OS. External examination revealed a right superolateral periorbital mass (Figure 1). Funduscopic examination revealed mild bilateral background diabetic retinopathy and a flat, left juxtapapillary choroidal nevus of approximately 3 disc diameters. The patient subsequently underwent computed tomography and magnetic resonance imaging studies of her head and orbits. The computed tomographic scan demonstrated a poorly defined right superolateral periorbital soft tissue mass. The magnetic resonance imaging scan showed an intensely enhanced extra-axial 4-cm soft tissue mass in the right middle cranial fossa, consistent with a sphenoid wing meningioma (Figure 2). Excision of the right periorbital mass revealed a neurofibroma (Figure 3); results of an S100 immunohistochemistry test were strongly positive. Examination of the excised middle cranial fossa mass verified the radiographic diagnosis of a meningioma (Figure 4). Thirteen months after the initial examination, visual acuity had decreased to 20/400 OS. Funduscopic examination revealed an enlarged, elevated, pigmented superior juxtapapillary choroidal tumor (Figure 5). B-scan ultrasonography showed a choroidal mass with a maximum thickness of 3.5 mm; A-scan ultrasonography demonstrated medium internal reflectivity. A clinical diagnosis of a uveal malignant melanoma was made and an enucleation was performed. Pathological analysis revealed an epithelioid cell–rich, mixed cell–type juxtapapillary malignant melanoma of the choroid that was approximately 8 mm in diameter (Figure 6). On a microscopic level, the tumor extended past the sclera along several posterior emissarial canals of vessels and...
nerves to the epibulbar surface. The tumor had also invaded the subarachnoid space of the optic nerve. One year postoperatively, the patient is doing well and shows no evidence of tumor recurrence.

COMMENT

The peripheral nervous system, leptomeninges, and melanocytes all originate from neural crest cells. These specialized neuroectodermal cells form parallel ridges along the dorsolateral area of the embryonic neural tube and give rise to many structures in addition to the above tissues, including the entire autonomic nervous system, the...
chromaffin cell system (including the adrenal medulla), and the connective tissues of the face. Bolande has termed disorders resulting from aberrations in the growth and development of neural crest–derived structures “neurocristopathies.” Simple neurocristopathies are localized, unifocal pathological processes involving tissues derived from neural crest cells. Examples include pheochromocytomas, neuroblastomas, medullary carcinomas of the thyroid, and carcinoid tumors. Complex neurocristopathies are multifocal, variegated associations of simple neurocristopathies. The neurofibromatoses are the most common examples of complex neurocristopathies and are characterized by pathological hamartomatous proliferations of neural crest–derived tissues. Associated tumors include neurofibromas, schwannomas, pheochromocytomas, meningiomas, gliomas, and malignant melanomas. While our patient did not meet the criteria for either neurofibromatosis type 1 or type 2, the combination of 3 tumors of neural crest origin in this case classifies it as a complex neurocristopathy. This case serves to remind physicians encountering a patient with multiple tumors of neural crest origin to be suspicious of a complex neurocristopathy and to be aware of the potential existence of other benign and/or malignant tumors of neural crest origin.

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REFERENCES


100 Years Ago in the ARCHIVES

A look at the past . . .

Dr. NIEDEN of Bochum . . . read a paper on the use of cancer serum of Emmerich-Scholl and formol in inoperable tumors of the eye. Nieden cited two such cases from his practice upon which the serum had been used without benefit; in fact, it seemed as though the growth had been more rapid after its use. The first case was a melanotic sarcoma filling the entire orbit, recurring after enucleation of the eye a year previously. The injection of serum was begun with 1 decigr. and afterwards increased to 2 decigr. The tumor was, after several injections, seen to be growing more rapidly than before. The second case was a glioma retinae filling the orbit, which had recurred six weeks after removal of the eye and infiltration of nerve. Fourteen injections, the first in the periphery and then in the growth proper, had been made in four weeks. After the tenth injection a more rapid growth of the tumor was noticeable. On the surface necrosis of the pseudoplasma had taken place. To overcome the odor in this condition and prevent new tissue involvement a 2% solution of formol was found to be of service.