Neurocutaneous melanosis with extensive intracerebral and spinal cord involvement

Report of two cases

WALTER J. FAILLACE, M.D., SHIGE-HISA OKAWARA, M.D., PH.D., AND JOSEPH V. MCDONALD, M.D.

Division of Neurological Surgery, University of Rochester Medical Center, Rochester, New York

Two unusual cases of neurocutaneous melanosis are presented. Both patients had congenital giant hairy nevi and both developed hydrocephalus, seizures, and myelopathy. The first patient displayed multicentric cerebral and spinal cord melanosis, as opposed to the more commonly described basilar leptomeningeal involvement. The second patient had total spinal leptomeningeal involvement, and ventriculoperitoneal shunting for hydrocephalus produced peritoneal metastasis of melanoma. An individual born with a congenital giant hairy nevus or marked generalized cutaneous pigmentation should be closely observed for the development of malignant melanoma of the nervous system.

KEY WORDS • hydrocephalus • melanoma • melanosis • hairy nevus • nevus • skin pigmentation • spinal cord

The first description of an individual with the stigmata of neurocutaneous melanosis was made by Rokitansky in 1861. Almost a century later, in 1948, Van Bogaert recognized an association between congenital giant pigmented nevi of the skin and marked melanin pigmentation of the leptomeninges, along with the propensity for development of malignant melanoma of the nervous system. Van Bogaert named this uncommon condition "neurocutaneous melanosis," a phacomatosis characterized by a diffuse thickening and brownish-black melanin pigmentation of the central nervous system pia mater, associated with the presence of one or more congenital giant hairy nevi, multiple large pigmented nevi, or marked generalized brown cutaneous pigmentation. All the cutaneous nevi were histologically benign, but the pial melanin-bearing cells have a potential for malignant transformation. In a review by Fox covering 40 cases of this syndrome, melanin infiltration of the cerebral cortex was uncommonly noted, but pigmentation of the cerebellum was observed in 25% of the cases, and 20% of all cases had diffuse spinal cord pigmentation.

We report two unusual cases of neurocutaneous melanosis. The first patient showed extensive multifocal cerebral and spinal cord melanosis, whereas the second demonstrated complete infiltration of the spinal cord leptomeninges.

Case Reports

Case 1

This white male first came to medical attention during infancy for treatment in the Dermatology Clinic of a congenital garment-type blackish-brown pigmented hairy nevus, which covered the shoulders and back. At 26 years of age, the patient began to experience excessive sweating of the palms and soles. Two years later numbness of the second and fifth fingers of the right hand developed and spread to the thumb. This was followed by throbbing headache, speech difficulty, and weakness of the right upper extremity. He developed a Jacksonian seizure of the right arm, which progressed to a generalized convulsion. This prompted hospital admission.

Examination. Neurological examination revealed diplopia, vertical nystagmus, an unsteady gait, and a positive Romberg sign. The opening pressure at lumbar puncture was 290 mm H2O; the cerebrospinal fluid (CSF) had normal chemistry values and a normal cell count. An electroencephalogram (EEG), brain scan,
Neurocutaneous melanosis

FIG. 1. Case 1. Coronal section of the brain at the level of the mamillary bodies. A 3-cm nodule of malignant melanoma is visible in the left parietal cortex, along with extensive bilateral multicentric primary malignant melanoma of the cerebral hemispheres.

cervical myelogram, and pneumoencephalogram were normal. A carotid arteriogram suggested a focal lesion in the left parietal region.

Clinical Course. The patient was discharged from the hospital and during the ensuing 5 months he ran a progressive downhill course. He had two more Jacksonian seizures and began to experience blurred vision and the "odor of cigarette lighter fluid." Pain developed in his right thigh and radiated to the calf and foot. He developed diabetes mellitus and was treated with tolbutamide.

During his second hospital admission he had disturbed language function, bilateral papilledema, right hand weakness, a positive straight-leg raising test on the right side, a wide-based gait, and adiodychokinesia of all four limbs. An EEG showed a slow-wave focus in the left temporal region. Noncommunicating hydrocephalus was demonstrated by ventriculography.

Operation. An occipital craniectomy for posterior fossa exploration was performed and no lesion was found. A Torkildsen shunt was inserted. In the postanesthesia room, the patient became apneic and an emergency ventriculostomy produced bloody CSF under increased pressure. The patient regained spontaneous respirations but remained comatose and died the following day.

Postmortem Examination. There was marked flattening of all surfaces of the brain. A 3-cm spherical black superficial mass was present in the left parietal cortex. Coronal sections revealed multicentric 3- to 8-mm dark gray nodules throughout the cerebral hemispheres (Fig. 1). There were well defined areas of black discoloration in the midline of the midbrain and pons. The optic chiasm was enveloped and infiltrated by thick layers of pigment. The spinal cord, primarily along its ventral surface, was studded with multiple dark grayish-black pigmented plaques; this pigment did not extend into the cord parenchyma. Over large portions of the cauda equina, there was abundant grayish-black pigment accumulation extending into the nerve roots.

Microscopic examination of the cerebral cortex showed malignant melanoma of the leptomeninges with many foci of tumor cells infiltrating the gray matter along the course of penetrating vessels in the Virchow-Robin spaces. The cerebellum had extensive hemorrhage and necrosis but no infiltration by tumor. The pons contained scattered foci of melanoma. There were foci of melanoma infiltration along the leptomeninges of the spinal cord, most marked around the nerve roots of the cauda equina, and there was infiltration of nerve roots. Microscopic sections of the skin from three separate biopsy sites showed benign intradermal nevi with no junctional nests, minimal pleomorphism, no mitotic figures, and no inflammatory reaction.

Case 2

This white female was born with a large brown garment-type nevus extending from the neck to the buttocks. The nevus became progressively more verrucous and hairy as she grew older, and numerous satellite lesions appeared on her legs (Fig. 2). Multiple biopsies of the nevus showed no evidence of malignancy.

Clinical Course. At 2 years of age, she had a generalized seizure after an injection of meperidine in preparation for skin grafting. An emergency computerized tomography (CT) scan of the head showed hydrocephalus with no mass lesion identified. A ventriculoperitoneal (VP) shunt was inserted and she subsequently fared well except for occasional episodes of irritability and headache. Later she developed amblyopia with intermittent left exotropia, and this was treated with an eye patching regimen. After a fall she abruptly lost consciousness, briefly had generalized muscle twitching, and had residual right upper extremity weakness. Over the following 3 weeks, her gait became unsteady and she was unable to walk without assistance. She did not experience back pain.

She was admitted to the hospital. A complete spine x-ray series showed increased interpedicular distances...
and scalloping of the vertebral bodies, most prominently in the region of T-6. A myelogram was unsuccessful because the arachnoid space could not be entered at any level of puncture and no CSF was obtained. A CT scan of the spine revealed an intraspinal mass completely filling the spinal canal from the cervical to the lumbar level. Cerebrospinal fluid obtained from the VP shunt reservoir had normal chemistry values, but five malignant-appearing cells were identified.

Operation. A bilateral thoracic laminectomy was performed at the T-6 level. At surgery there was no tumor involvement of the vertebral bones and extradural space. When the dura was opened, CSF was absent and a dense gray tissue filled the leptomeningeal space. This tissue was biopsied, and tissue from the epidural space and skin was also obtained for histological evaluation.

Pathological Findings. Microscopic examination of the intradural tissue revealed a melanoma involving leptomeninges and spinal cord (Fig. 3). The tumor consisted of sheets of oval, polygonal, or spindle-shaped cells, disposed within a dense collagenous matrix. The cells had a high nuclear to cytoplasmic ratio, with oval, euchromatic or hyperchromatic nuclei, and rare nucleoli. There was no cellular atypia and mitotic figures were not identified. Melanin granules were identified within the tumor cells. The epidural tissue contained adipose cells without any tumor. The skin biopsy specimen contained a benign melanocytic junctional nevus.

Postoperative Course. After laminectomy, the patient was given dexamethasone and 2500 rads of craniospinal irradiation. Her unsteadiness, gait, and lower extremity weakness improved following the radiotherapy. Repeat CT scanning of the spine showed areas of decreased density consistent with tumor necrosis. In the following months, she slowly developed abdominal distension and became dyspneic. An abdominal CT scan showed loculated ascitic fluid and a right pleural effusion. It was suspected that melanoma cells were lining the peritoneum, interfering with peritoneal absorption of CSF from the VP shunt. A peritoneal needle biopsy confirmed the presence of melanoma and thoracentesis yielded copious reactive fluid with atypical cells.

The patient was given a double course of chemotherapy with vincristine, cyclophosphamide, and actinomycin D, followed by cyclophosphamide, vincristine, and actinomycin D. Four months later, her abdominal girth again increased. During an exploratory laparotomy for tumor debulking with a laser, the omentum was found to be infiltrated with malignant melanoma. An attempt at surgical excision of the tumor failed and the patient died immediately postoperatively. An autopsy was not permitted.

Discussion

Neurocutaneous melanosis is a disorder in which individuals with a large congenital nevus develop malignant melanoma of the central nervous system (CNS). The criteria for this diagnosis require: 1) that an individual have from birth a nevus or diffuse melanotic skin pigmentation that is unduly large (more than 20 cm in diameter); 2) that there is no malignant transformation of the involved skin area; and 3) that there is no evidence of primary malignant melanoma in any organ other than the nervous system. For correct diagnosis an autopsy or extensive surgical biopsies are essential.3 Neurocutaneous melanosis is considered a phacomatosis because it is thought to result from a congenital dysplasia of the neuroectodermal melanocyte precursor. There is evidence supporting the common embryological derivation of the nevocytes of a hairy nevus and cerebral melanoblasts.

Congenital melanocytic nevi have three histological features that distinguish them from the more common acquired melanocytic nevi:11 1) nevus cells are present in the lower two-thirds of the reticular dermis; 2) nevus cells are disposed between collagen bundles singly or in Indian file; and 3) nevus cells commonly involve skin appendages and nerves and vessels in the lower two-thirds of the reticular dermis. There is an association between large congenital melanocytic nevi, or multiple pigmented nevi of the scalp and nuchal regions, and the development of leptomeningeal melanoma.15 Malignant transformation within giant congenital melanocytic nevi of the skin has been reported to occur, particularly prior to puberty, with an incidence that varies from 2% to 31%, and an average of 12%.9

In the cases of neurocutaneous melanosis analyzed by Fox, et al.,3,4 over 85% showed marked pigmentation of the leptomeninges at the base of the brain and over the brain stem. The areas most frequently affected were the pons, medulla, cerebellum, cerebral peduncles, interpeduncular fossa, and inferior surfaces of the frontal, temporal, and occipital lobes. The cerebral hemispheres had patchy or diffuse meningeal thickening, but melanoma pigmentation over the cerebral hemispheres was found in only one case and over the cerebellum in seven cases. Our first patient had a 3-cm nodule of melanoma in the parietal cortex, as well as numerous 3- to 8-mm

FIG. 3. Case 2. Spinal biopsy specimen showing melanoma cells arranged in sheets and nests extending from the subarachnoid space into the spinal cord. Modified Warthin-Starry stain for melanin, × 50.
Neurocutaneous melanosis

multicentric pigmented nodules throughout the cerebral hemispheres. This pattern differed from the basilar meningeal infiltration which has been more commonly reported. Fox, et al., noted that 20% of cases displayed widespread pigmentation and thickening of the full length of the spinal cord meninges. In both of our cases, there was an extensive melanoma infiltration of the spinal meninges. Case 1 had widespread melanoma infiltration of the leptomeninges of the cauda equina with extension into the nerve roots causing sciatric pain. Case 2 had total spinal cord leptomeningeal infiltration resulting in a myelopathy and mass effect on x-ray examination.

A variety of neurological features may be present in neurocutaneous melanosis. Hydrocephalus occurs in almost all cases. Our Case 2 had a noncommunicating hydrocephalus that we were able to treat with a VP shunt, but the shunting led to dissemination of melanoma throughout the peritoneal cavity. Hoffman and Freeman experienced the same complication in their two fatal cases of neurocutaneous melanosis. We propose that placing a filter in the shunt would prevent this complication. Symptoms and signs of mass effect often accompanied by seizure activity are present in older patients. In our Case 1, the focal seizures and localized EEG slowing suggested a left temporoparietal lobe mass, which was confirmed at autopsy. Chronic basal meningitis with multiple cranial nerve palsies or chronic spinal arachnoiditis are found less commonly.3,4 Our Case 2 had amblyopia and intermittent exotropia of the left eye. Both of our patients had hydrocephalus, seizure activity, and spinal arachnoiditis.

Neurocutaneous melanosis must be distinguished from the melanotic neuroectodermal tumor of the cranium of infancy, and from the melanotic nerve sheath tumor. Melanotic neuroectodermal tumor is a benign pigmented tumor arising from neural crest cells, and, from the melanotic nerve sheath tumor. Melanotic neuroectodermal tumor of the cranial meninges is a benign pigmented tumor arising from neural crest cells, and, when present in the cranium, most frequently involves the region of the anterior fontanel. Gilmor and Mealey described eight cases involving the cranial meninges and found the tumor mass usually adherent to the underlying dural sinuses and invading adjacent bone. There is an excellent prognosis with early, complete excision of the cranial neuroectodermal tumor, and radiotherapy is effective in incompletely resected lesions. The melanotic nerve sheath tumor is an unusual, solitary, melanin-bearing plexiform neurofibroma. It is a slow-growing benign tumor of young adults, does not metastasize, and in almost all reported cases is subcutaneous in location.10 The melanotic nerve sheath tumor has been found in the presence of meningeal melanomatosis; Mandybur described one case with the additional findings of spinal cord compression at T-7, vertebral body erosion, and incomplete block at myelography.

Neurocutaneous melanosis is a phacomatoses with a potential for serious neurological complications. Individuals with congenital giant melanocytic nevi or marked generalized cutaneous pigmentation should be carefully observed for the development of CNS disease. If hydrocephalus should develop, it can be treated with a VP shunt, but a filter should be placed in the shunt to prevent dissemination of melanoma from the leptomeningeal space to the peritoneum.

Acknowledgments

The authors would like to express gratitude to Drs. Lowell Lapham, Thomas Eskin, and Roger Brumback of the Division of Neuropathology for analyzing the pathological material, and to Dr. Robert Emmens of the Department of Surgery for his surgical collaboration.

References


Manuscript received July 14, 1983.
Accepted in final form May 23, 1984.

Address reprint requests to: Walter J. Faillace, M.D., University of Rochester Medical Center, Division of Neurological Surgery, 601 Elmwood Avenue, Box 661, Rochester, New York 14642.