Sensorineural Hearing Loss and Metastatic Leptomeningeal Malignancy

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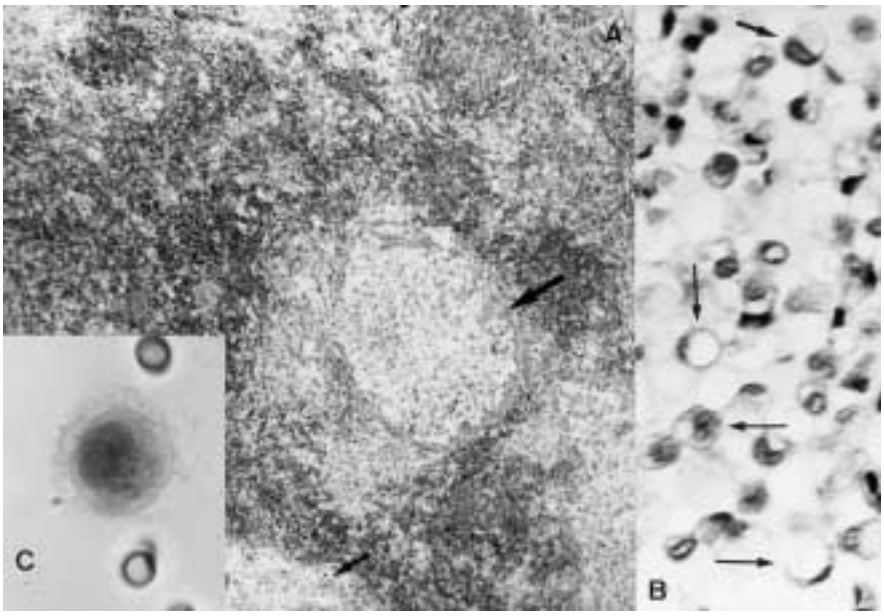
The most prevalent primary tumors associated with leptomeningeal metastatic spread are bronchogenic carcinoma, breast carcinoma and malignant melanoma [1,2], although other primary sites, such as gastrointestinal tract, gall bladder and urinary tract, have been reported. Patients with LMM may exhibit diverse neurologic symptoms and clinical signs resulting from multifocal seeding of the meninges and brain parenchyma, with consequent mimicry of various other intracranial processes, thereby hampering the establishment of an accurate diagnosis [3]. We report on a patient who presented with a solitary right cervical mass proceeded by sudden unilateral sensorineural hearing loss, rapidly progressing to profound bilateral SNHL, arising from LMM.

Patient Description

A 62 year old man with a right cervical mass of 4 weeks duration and mild disequilibrium, without true vertigo, was seen at the outpatient clinic. In his medical history, an excision of a malignant melanoma of the left auricle was performed 10 years earlier, required no supplementary treatment and did not recur.

Physical examination revealed a right submandibular mass of 2 x 2 cm. Fine-needle aspiration was inconclusive. A hearing test disclosed a bilateral symmetric sloping high tone SNHL of up to 50 dB. Word discrimination was 92% in the right ear and 88% in the left. The patient was referred for computerized tomography of the neck and chest, but arrived at the emergency room after only 2 weeks with a sudden worsening of the left hearing loss accompanied by bilateral tinnitus and severe disequilibrium, without true vertigo. On physical examination, no nystagmus was found, and he fell to the left (lateral displacement) in Romberg's test. The audiogram demonstrated a profound left SNHL as well as worsening of the right SNHL. CT scan showed lymphadenopathy of the right deep cervical chain and mediastinum. CT scan of the brain and high resolution CT of the posterior fossa and internal auditory canals were normal. The patient was treated for sudden hearing loss with oral prednisone, 80 mg per day for 5 days in tapering doses of 20 mg every 4 days. Excisional biopsy of the right submandibular mass revealed a lymph node invaded by metastatic signet-ring cell adenocarcinoma positive to colloidal iron stain [Figure 1A and B]. Immunohistochemistry revealed positive staining for epithelial membrane and cytokeratin, and



[A] Metastatic signet-ring cell adenocarcinoma in a cervical lymph node. The lymphatic tissue is partially replaced by lightly stained foci (arrows) of signet-ring cell carcinoma (Hematoxylin and eosin x 30). **[B]** Higher magnification showing signet-ring cell (arrows) characterized by large intracytoplasmic vacuoles pressing crescent-shaped nuclei to one pole of the cell body (Hematoxylin and eosin x 320). **[C]** Cerebrospinal fluid cytology demonstrating colloidal iron-positive adenocarcinoma cell consistent with the histology of the cervical lymph node presented in A and B (Papanicolaou stain x 500).

LMM = leptomeningeal metastasis
SNHL = sensorineural hearing loss

negative staining for common leukocytic antigen, prostatic-specific antigen, prostatic acid phosphatase, and the melanoma markers S100 and MB45. Serum prostatic specific antigen was within the normal range. Abdominal CT and ultrasound were normal except for the presence of cholelithiasis. Gastroscopy and colon barium enema were normal.

The patient continued to suffer from severe bilateral tinnitus and no hearing improvement was observed. One week after admission the patient developed sudden profound right hearing loss, becoming totally deaf in both ears despite steroid therapy. Magnetic resonance imaging of the brain and internal auditory canals revealed bilateral confined internal auditory canal lesions. No additional lesions of the cervical spine, meninges or brain were detected. However, cerebrospinal fluid cytology following cytocentrifugation showed adenocarcinoma cells that were positive to colloidal iron stain, consistent with the histopathology of the neck biopsy [Figure 1C]. The patient was therefore referred for intrathecal chemotherapy with methotrexate and for whole-brain radiotherapy. However, 2 weeks later the patient died, about 8 weeks after he was first seen by us. A postmortem examination was not performed lacking familial consent.

Comment

Leptomeningeal metastasis is an important neurologic complication of systemic cancer [2]. The occurrence of meningeal spread as a presenting symptom of cancer poses a formidable challenge to the clinician, demanding a high index of suspicion since it may be manifested in confusing symptomatology and clinical signs arising from multifocal seeding [3]. The most common primary tumors associated with LMM are small-cell lung cancer, breast cancer and melanoma [1]. Our patient's reported histologic findings of metastatic signet-ring cell adenocarcinoma in the cervical lymph nodes pointed to the possibility of a rare primary origin, the gastrointestinal tract, gall bladder or urinary tract. Thorough investigation failed to locate the primary tumor.

Eighth nerve involvement was reported to occur in 10% of patients with LMM [4] and in 30% of patients with neurologic deficits at the time of LMM diagnosis [3]. Such involvement may be manifested as unilateral SNHL associated with tinnitus, or unilateral SNHL rapidly progressing to severe bilateral involvement (as in our patient), and may be accompanied by facial nerve palsy. Damage to the eighth nerve was attributed to one of two mechanisms: compression of the nerve, or direct metastatic invasion of the nerve with segmental demyelination or axonal loss [3]. Neuroimaging of LMM is most effectively achieved by contrast-enhanced CT and gadolinium-enhanced MRI, particularly the latter. Differential diagnosis of bilateral internal auditory canal lesions on MRI includes: a) bilateral acoustic neuromas, as part of a neurofibromatosis type II; and b) a rare and unusual presentation of LMM that is restricted to the internal auditory canals with no additional signs of seeding in other loci of the meninges or brain, or of diffuse dural enhancement, as in our patient. The reason for internal auditory canal preference in LMM remains obscure. Cerebrospinal fluid examination is usually diagnostic for LMM, but several lumbar punctures may be required in order to establish the presence of tumor cells [1]. Immunocytochemistry and biochemical testing for tumor markers should be employed in order to avoid false negative results. They may also serve as a reliable means of therapy control.

Treatment of LMM consists of intrathecal chemotherapy and/or neuro-axis irradiation, together with steroids to relieve cerebral edema [3,5]. It is more difficult, however, to decide on the line of treatment when dealing with tumors of unknown origin. The toxicity of this combined modality therapy is significant, and patient survival is poor despite aggressive treatment [5]. Decisions regarding treatment modalities in such patients require a comprehensive approach, which considers prognosis of the disease, expected benefits and side effects of alternative possible treatment options and their risks. It is therefore debatable whether aggressive regimens should be advocated for patients with LMM secondary to solid tumors not respondant to induction chemotherapy.

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The Family! Home of all social evils, a charitable institution for indolent women, a prison workshop for the slaving breadwinner, and a hell for children.

August Strindberg (1849–1912), Swedish playwright and novelist who influenced the development of dramatic technique