The IVIg contained normal polyvalent immunoglobulin-G derived from a large number of blood donors. Originally, it was developed as replacement therapy for hypogammaglobulinemia to prevent infections.[8] After observing improvement of immune-mediated thrombocytopenia in patients with hypogammaglobulinemia, further studies have been undertaken in a variety of immune-mediated disorders.[9] Immune mechanisms have been implicated in the pathogenesis of a variety of neurological syndromes or diseases involving every aspect of the neuroaxis. Therapy with IVIg has been used in most of these conditions, with varying degrees of success. The first positive results in neurological diseases were obtained in patients with chronic inflammatory demyelinating polyneuropathy.[10] Ever since, a large number of studies have followed. IVIg has proven efficacious and is a standard therapy in several of these diseases, including inflammatory myopathies such as dermatomyositis, immune disorders of the neuromuscular junction such as Lambert–Eaton myasthenic syndrome and myasthenia gravis, and immune disorders of the peripheral nerves such as Guillain–Barre syndrome and multifocal motor neuropathy.[11] Verma and Bradley[4] first described the treatment of two patients with chronic progressive LSP using IVIg. Triggs *et al.*[3] also reported the dramatic effect of IVIg therapy on five patients with idiopathic LSP. In both reports, patients had chronic progression or drawn-out clinical features (one month to three years) before the treatment with IVIg. Moreover, those cases were all idiopathic. Although some relapses developed, the responses were dramatic and rapid, even on recurrence. The treatment was a five-day course of IVIg at 0.4 g/kg/day. It was increased to 0.8 g/kg/day in those patients who relapsed or were refractory to the initial therapy. Oral prednisone or intravenous methylprednisolone was added in some cases. Our case was similar to those cases with respect to clinical features, dosage and the response to IVIg, despite the rapid clinical deterioration prior to treatment. Our patient has remained in remission for six months after a single cycle of IVIg therapy.

Improvement associated with immunotherapy in idiopathic LSP suggests an inflammatory etiology. In some cases, there is evidence consistent with this interpretation. Idiopathic LSP may be the lower extremity counterpart to idiopathic brachial neuritis.[7] Patients with this syndrome may show complement-fixing anti-myelin antibodies[12] and mononuclear inflammatory cell infiltrates of the affected plexus.[13] Nerve biopsies have shown evidence of an inflammatory microvasculopathy in diabetic[14] and non-diabetic patients with LSP.[6,15] However, these pathological findings are not prerequisites for a clinical response to the immunotherapy. In the seven reported cases of patients with LSP treated with IVIg, sural nerve biopsies in four patients showed no evidence of vasculitis or inflammation except for axonal loss.[3,4] We are uncertain whether our case was truly idiopathic, although this seems the most likely explanation. It has not been reported that recent spinal surgery and associated peri- and/or postoperative conditions should predispose towards immune mediated neuromuscular diseases.

It is interesting that LSP developed soon after spinal surgery in this patient, whether or not it was idiopathic. No reports of LSP associated with previous spinal surgery have been published. Spine surgeons often conclude that the various neurological problems that develop after spinal surgery must be related to it and residual deficits are a complication. However, this under-recognized syndrome should not be overlooked in the differential diagnosis. It is important to distinguish this unusual disease from cases of compressive lumbosacral radiculopathy with weakness preoperatively. Although IVIg treatment is expensive and may not guarantee a response in all immune-mediated neuromuscular diseases, including LSP, it should be considered as it can have dramatic effects on severe, rapidly progressive, or refractory cases.

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Bilateral profound hearing loss due to meningeal carcinomatosis

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Summary Meningeal carcinomatosis (MC) is an uncommon form of metastasis of solid tumors. Hearing loss as the presenting symptom of MC is very uncommon. A patient with an esophageal signet ring cell carcinoma 3 years previously presented with sudden onset of profound hearing loss affecting both ears. He had no evidence of local tumor recurrence. Brain magnetic resonance imaging (MRI) showed swelling and increased signal intensity on T2 weighted images of both acoustic nerves and the right trigeminal nerve. After gadolinium administration, enhancement of both acoustic and trigeminal nerves was seen. He later developed unsteadiness and head-movement-dependent oscillopsia due to vestibular areflexia and diplopia. At that time MRI showed leptomeningeal enhancement. MC was diagnosed, although cerebrospinal fluid cytology could not confirm that diagnosis. The patient died 16 weeks after the onset of deafness. In patients with progressive unilateral and bilateral hearing

loss, meningeal carcinomatosis should be considered, especially if there is a history of previous malignancy.

Journal of Clinical Neuroscience (2005) **12**(3), 315–318
0967-5868/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jocn.2004.07.012

Keywords: meningeal carcinomatosis, hearing loss, magnetic resonance imaging, signet ring cell carcinoma, cerebrospinal fluid cytology

Received 27 October 2003
Accepted 30 July 2004

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INTRODUCTION

Meningeal carcinomatosis (MC) is an uncommon form of metastasis of solid tumors. Although MC presenting as multiple cranial neuropathies is well recognised, hearing loss as the presenting symptom is uncommon. We present a patient with sudden onset of profound hearing loss affecting both ears over one week.

CASE REPORT

A 52-year-old man presented with an acute progressive bilateral hearing loss. Three weeks prior to admission, right-sided deafness developed over a few days and within one week this was followed by hearing impairment in the left ear, as well as bilateral tinnitus. He had a history of Menière's disease affecting the right ear starting at the age of 43 years (Table 1). A stage IIA high grade esophageal carcinoma (signet ring cell adenocarcinoma) was resected 3 years earlier. He had no evidence of local tumor recurrence. In view of his Menière's disease, episodes of hearing impairment and dizziness were well known to him. He visited the Ear–Nose–Throat Department only when he noticed hearing loss on the left side also. The audiogram (Table 1) confirmed bilateral sensorineural hearing loss (SNHL), more pronounced on the right side. SNHL increased over three weeks to complete deafness. He also experienced dysequilibrium, dryness of his mouth and alteration of taste. Vertigo was absent. He complained of head-movement-dependent oscillopsia. The head-thrust test showed corrective saccades during head rotation in either direction. Vestibular tests, including bithermal caloric testing, revealed bilateral vestibular areflexia, but no ocular motor abnormalities. Brain magnetic resonance imaging (MRI) showed swelling and increased signal intensity of both acoustic nerves and the right trigeminal nerve in T2 weighted images (Fig. 1a). After gadolinium administration, enhancement of both acoustic and trigeminal nerves was seen (Fig. 1b). One week later, his gait became more unsteady and he had vertical diplopia during reading. He complained of feeling nauseated and had headache. There were tingling sensations in his hands and feet. On neurological examination, he was completely deaf. He had bilateral trochlear nerve palsies. There was no nystagmus. He had head-movement-dependent oscillopsia. The head-thrust test was abnormal in both directions. His taste and salivation were diminished. Muscle strength was normal. Tactile sensation and proprio-

Table 1

Age (y)	Air conduction threshold (dB)											
	Right Ear						Left Ear					
	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	8000 Hz	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	8000 Hz
46	15	5	5	10	25	55						
47	45	50	35	20	30	60						
48	30	25	15	5	25	65	10	10	10	5	10	15
52[a]	100	105	100	>120	>120	110	50	50	50	50	70	50
52[b]	105	110	>120	>120	>120	110	90	85	80	70	75	60
52[c]	>120	>120	>120	>120	>120	110	90	95	>120	75	>120	110

[a] First audiogram this episode, age 52.
[b] 12 days later.
[c] Again 8 days later at the age of 52.

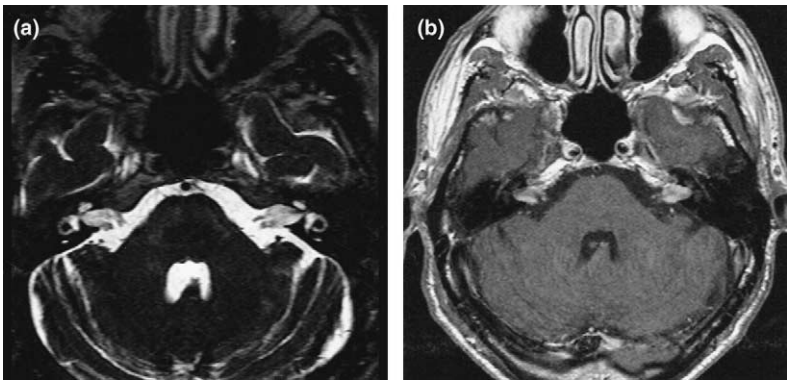

Fig. 1 Brain axial MRI T2-weighted TSE (5000/250, 1.4 mm slice thickness) reveals the swelling and a high signal intensity of the acoustic nerves due to edema (a). T1-weighted SE sequence (500/20, 3 mm) after intravenous gadolinium administration shows enhancement of the acoustic nerves.

ception were disturbed. Vibration and position sense was diminished in arms and legs. Finger-to-nose testing on the left side showed slight ataxia. The Romberg test was positive and he was unable to perform tandem gait. Tendon reflexes within the upper limbs were diminished symmetrically and they were absent in the lower limbs. There were bilateral extensor plantar responses. The clinical diagnosis was meningeal carcinomatosis and paraneoplastic polyneuropathy.

Hematological and biochemical investigations including liver function tests, ESR and carcinoembryo antigen levels were normal. Cerebrospinal fluid (CSF) protein level was 1.63 g/l (N: 0.2–0.5 g/l) and the CSF glucose concentration of 3.5 mmol/l (N: 2.6–3.7 mmol/l; serum level 5.0 mmol/l, N: 4.0–8.0 mmol/l). In the CSF (3 punctures), small numbers of macrophages were found, as well as numerous undifferentiated cells (Fig. 2). Additional serological and CSF analysis for neurotropic infections (including herpes simplex, borrelia, varicella zoster, mycoplasma pneumoniae, tuberculosis) were negative. Gadolinium-enhanced spinal MRI showed numerous nodules surrounding the spinal cord and spinal roots (Fig. 3).

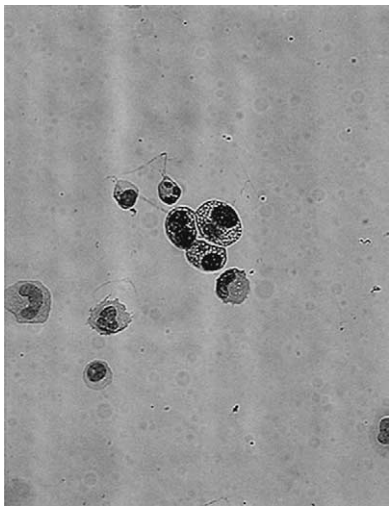

Fig. 2 Cytology of the cerebrospinal fluid showed atypical cells. Papanicolaou stain 1000×.

Fig. 3 MRI Sagittal T1-weighted TSE (772/13, 4 mm) of the lumbar spine after intravenous gadolinium administration with nodular enhancement of the nerve roots and meningeal structures.

Despite the absence of cytological confirmation in the CSF, the diagnosis of meningeal carcinomatosis was made. As the patient had no malignant disease other than the esophageal carcinoma in the past, this tumor was considered to be the primary lesion. Radiotherapy of the skull base was initiated. Despite radiotherapy, signs and symptoms progressed and paresis of arms and legs, a neurogenic bladder and finally nausea and impaired consciousness supervened. The patient died at home 16 weeks after the onset of hearing loss. Permission for autopsy was denied.

DISCUSSION

Sudden bilateral profound loss of hearing is a rare clinical presentation. When it is present, MC must be considered in the differential diagnosis. Saenger[1] in 1900 was the first to describe hearing loss due to MC. He reported a 74-year-old man with progressive bilateral hearing loss and unsteady gait one year after surgery for gastric cancer. Since then some 40 cases have been reported in the literature.[2–6] Bilateral hearing loss as the presenting symptom of MC is rare and even less common is hearing loss due to MC as the first manifestation of a malignancy.[6,7] Several reports described unilateral hearing loss progressing to bilateral deafness within weeks. The hearing loss is often accompanied by a facial nerve palsy and periaural headache. Although patients rarely complain of hearing loss in MC, 8th nerve involvement is not uncommon. Signs of 8th nerve involvement can be found in 15–25% at the initial examination, even in the absence of symptoms.[8,9]

Hearing loss is also a common (about 10%) complication of bacterial meningitis, especially in children.[10] The pathological process is still uncertain. All parts of the auditory system may be involved, but cochlear involvement seems most important, confirmed in animal studies. Deafness develops early in meningitis and seems to progress if the meningitis is not treated early.[11]. Increased intracranial pressure and low CSF glucose levels predict hearing loss.[12] Both factors might be involved in MC too.

Meningeal carcinomatosis can be difficult to diagnose. Patients often develop multifocal neurological signs and symptoms referable to various sites in the neuraxis including the brain, the cranial nerves, the spinal cord or the spinal roots. Most patients have a history of pre-existing malignancy. In most cases, MC is caused by breast and lung adenocarcinoma or malignant melanoma.[7]

Our patient is illustrative of the difficulty of making the diagnosis at first presentation. In light of his history of Menière's disease, our patient was not alarmed by the unilateral hearing loss and tinnitus, even when it became bilateral over one week. Only when he developed multifocal neurological symptoms did he seek medical help and appropriate investigations were performed. CSF cytology did not definitively confirm the diagnosis.

Vestibular impairment is often not clinically manifest due to vestibular compensation, but it can be demonstrated in almost all cases.[3,13] Auditory and vestibular impairment seem to be caused by direct neural infiltration by tumor cells in combination with ischemia through compression of the vasa nervorum by the cuff of tumor cells.[3,14,15] Saenger[1] described tight accumulation of tumor cells at the entry zone of the acoustic nerves. Hearing loss precedes facial paralysis in most cases.[15] Sensory nerve fibers seem to be more vulnerable than are motor nerve fibers.[14] In determining their vulnerability, the relative position of the nerves

in the internal auditory canal might also be important. This is in line with our finding of decreased taste and dryness of the mouth without facial palsy. It is important to note that in rare cases hematogenous metastases in the petrous temporal bone can cause similar otologic symptoms.[15]

The multifocal involvement of the meninges in MC allows for a large variety of presentations, making early diagnosis a challenge. Cerebrospinal fluid cytology may not show malignant cells at first, although an elevated protein level and lowered glucose concentration are often present in these patients. Although, CSF cytology is useful, malignant cells are absent in 20–30% of patients who have compelling clinical and radiological evidence of MC, as in our patient.[16] In most cases, cytology will be eventually positive after repeated lumbar punctures.[9] Similarly, CT and MRI may be normal in the early phase of the disease.

The prognosis of MC is poor. Median survival in untreated patients is 4–6 weeks, which may extend from 4 to 6 months with aggressive treatment in some cases.[16,17] The poor prognosis and usually fast progression of MC make early diagnosis important. When symptoms of MC appear, treatment is rarely curative and is mostly palliative through the use of chemotherapy and radiotherapy.[16]

In summary, for early diagnosis of MC a high level of suspicion is warranted. In patients with progressive unilateral and bilateral hearing loss, meningeal carcinomatosis should be considered, especially if there is a history of malignancy.

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Silent pituitary macroadenoma co-secreting growth hormone and thyroid stimulating hormone

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Summary Silent pituitary adenomas are a group of tumors showing heterogenous morphological features with no hormonal function observed clinically. To date no explanation has been provided as to why these tumors remain "silent". We report a case of a silent macroadenoma with both growth hormone (GH) and thyroid stimulating hormone (TSH) staining and secretion but with no clinical manifestations, in particular, the absence of features of acromegaly or hyperthyroidism. The relevant literature is reviewed.

Journal of Clinical Neuroscience (2005) **12**(3), 318–320
0967-5868/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jocn.2004.05.011

Keywords: pituitary adenoma, plurihormonal, silent

Received 22 July 2003
Accepted 28 May 2004

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INTRODUCTION

Silent pituitary adenomas are a group of tumors with heterogenous morphological features but with no clinical hormonal function. Based on their immunohistochemical and electron microscopic appearances, they can be separated into two categories. The first group includes null cell adenomas and oncocytomas with no characteristics of normal adenohypophyseal cells. Neither their morphological features nor immunohistochemical markers indicate their cytogenesis or of differentiation. The second group includes adenomas exhibiting immunohistochemical and ultrastructural features of adenohypophyseal cells with no clinical signs of hormone excess. These tumors are called silent somatotroph, corticotroph, thyrotroph, and gonadotroph adenomas.[1,2] We report a patient with a silent pituitary macroadenoma, co-secreting growth hormone (GH) and thyroid stimulating hormone (TSH), but with no signs of acromegaly or hyperthyroidism.

CASE REPORT

A 57-year-old female patient was admitted to our clinic complaining of persistent headache. She was married and nulliparous and had experienced no regular menses for the past seven years. The medical history was unremarkable except for a 10 year history of hypertension, well regulated by antihypertensives, and a strong

