ease and distributed in a pattern typical for HSE. However, the degree of white matter edema and cortico-meningeal contrast enhancement was rather unusual for HSE. CSF analysis confirmed a severe BBB disruption, was HSV PCR negative and showed a normal cell count but a persistent intrathecal oligoclonal immune stimulation. There was improvement when steroids were started, contrary to the initial antiviral treatment.

There have been reports suggesting an immuno-allergic pathomechanism responsible for relapses [1, 3–5]. Similar to our case, others [3, 5] have reported steroid treatment response. Histological investigations by König et al. [5] revealed severe inflammation and demyelination in 'striking resemblance to that occurring in experimental allergic encephalomyelitis', and Barthez-Carpentier et al. [1] described severe inflammation with diffuse edema and neuronal necrosis, but no focal demyelination. Edema was a striking feature on the MRI in our case as well. Contextually, we noticed a normal or decreased CSF cell count in our and other cases [1, 5]. In contrast to these reports, there is evidence that relapses can be caused by viral reactivation: most of the patients reported by Ito et al. [2] responded to a second course of antiviral treatment, some showed reappearance of HSV DNA, and CSF cell counts were persistently elevated. In addition to these reports, there is evidence of persistent inflammation and progressive changes after HSE without clinical signs of relapses [6, 7].

We suggest a postinfectious autoimmune process in our patient for the following reasons: there was no evidence of any specific infection, no antiviral treatment response (opposed to steroid treatment response), no pleocytosis and a negative HSV PCR. Additional features were prominent white matter edema, disturbance of the BBB and a persistent intrathecal oligoclonal immune response. The time delay was very unusual. Only a few late recurrences in infants (HSV type 2) have been reported [8]. However, we cannot completely rule out that an infection not covered by our investigations or an autoimmune process not related to HSE was the cause. A brain biopsy was not done.

Persistent intrathecal immune activation (elevated IgG index, oligoclonal bands, intrathecal antibodies against epitopes of various viruses, the latter possibly resembling the polyspecific MRZ-reaction [9]) may predispose a patient to an autoimmune-mediated encephalitis, but this is entirely speculative. A persistently elevated IgG index as well as other inflammatory markers are known sequelae of HSE [10]. An interesting argument has been raised [6, 10]: viral persistence in the brain tissue, if only focal, might give rise to a persistent immune response, eventually leading to persistent or progressive damage and relapses. The presented case demonstrates that relapses have to be considered long after the immediate postinfectious period of HSE and that steroid treatment should be considered, provided there is no antiviral treatment response and no evidence of any specific infection.

Acknowledgment

We thank Ms. Laura Rigby for her assistance in translating the manuscript.

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Eur Neurol 2003;50:56–57
DOI: 10.1159/000070861

Unilateral Facial Pain Associated with Recurrence of Malignant Thymoma: A Case Report

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Referred facial pain associated with nonmetastatic lung carcinoma is a rare but well-recognized clinical entity that should be considered in the differential diagnosis of atypical facial pain [1–3]. We describe a woman who presented with severe unilateral facial pain as the first symptom of thoracic recurrence of a malignant thymoma.

Case Report

A 60-year-old woman was admitted to our Headache Clinic in November 2001 because of a 7-month history of persistent facial pain.

In 1995, she had been diagnosed as having myasthenia gravis and malignant thymoma (Masuoka stage III). The thymoma had subsequently been surgically removed, and the muscular symptoms had improved and were successfully controlled with anticholinesterase drugs and intermittent oral prednisone administration. The patient

had undergone regular clinical, radiological and serological follow-up control examinations. A total-body CT scan performed in March 2001 had been normal.

In April 2001, the patient had developed a deep, aching pain localized around the zygoma, ear and temporal region on the left side of her face. One month later, it had spread to most of the left side of her face and part of the neck. It was of a constant, severe aching nature with superimposed paroxysmal worsening. No aggravating or precipitating factors were identified.

The patient was initially referred for a dental evaluation but, despite the extraction of several teeth, the pain persisted and was not relieved by analgesics. A diagnosis of trigeminal neuralgia was made by a neurologist, but sequential trials of carbamazepine, amitriptyline and gabapentin did not lead to any improvement.

On admission, the physical examination showed digital clubbing and a tender point in the region of the left temporal superficial artery. The neurological examination was normal except for mild, diffuse muscle weakness due to the MG. A laboratory examination was normal. Skull X-rays, sinus X-rays, temporomandibular joint radiograms and cranial and facial CT scans did not reveal any abnormalities. After a biopsy of the left temporal artery had excluded a diagnosis of giant cell arteritis, the patient was diagnosed as having atypical facial pain.

In order to exclude a secondary headache, the patient underwent a chest X-ray (December 2001), which revealed an enlargement of the left mediastinum and small bilateral nodular infiltrates. A total-body CT scan showed multiple pulmonary nodules (around 1 cm), a single 1.5-cm nodule in the left cardiophrenic sinus and the presence of enlarged pretracheal lymph nodes. An MRI scan of the head with gadolinium was normal.

The diagnosis of recurrence of malignant thymoma was made by a bioptic examination.

The patient underwent a first trial of radiotherapy (March 2002), which had no effect on the thoracic lesions and facial pain, whereas prednisone 60 mg/day successfully relieved the pain. A second trial of radiotherapy resulted in a significant reduction in the thoracic lesions and relief of the pain and local facial symptoms (May 2002).

Discussion

Since the first case described by Des Prez and Freemon in 1983 [4], there have been several reports of facial pain as a complication of nonmetastatic lung carcinoma [1, 2, 4–12]. The reported cases share many characteristics, which has led to a good definition of the clinical, diagnostic and pathogenetic features of this rare syndrome [2].

The pain is described as aching and severe, and is typically located in or around the ear, temporal region and the jaws [2, 9].

Digital clubbing and hypertrophic osteoarthropathy are often present and represent an important clue to an early diagnosis [1, 2, 9].

The current pathogenetic mechanism for this kind of nonmetastatic facial pain is a referred pain from the vagus nerve [1, 2, 4]. It has been hypothesized that infiltration or compression of the vagus nerve by mediastinal lymph nodes may irritate its visceral afferents [1, 2, 4, 6]. The convergence of visceral afferents with vagal and other somatic cranial afferents (V, VII and IX), at different levels of the central sensory pathways, may explain the topographical characteristics of pain [2, 4, 6].

Our case matches all the characteristics of this clinical entity, including the response to local irradiation.

Interestingly, the primary tumor associated with facial pain was not lung cancer. The association of facial pain with an invasive thymoma or other malignancies has not been reported previously [12, 13]. However, if we accept the local infiltrative/compressive mechanism as a plausible explanation for this syndrome, it is not surprising that mediastinal tumors other than lung cancer give rise to this clinical picture. A thorough review of the radiological locations of the lung cancers that have been reported in association with this syndrome [2, 9, 11] did not reveal any specific site. Therefore, the association of nonmetastatic facial pain with lung cancer should not be considered exclusive as it probably merely reflects the higher prevalence of this kind of malignancy in the mediastinum [14].

It is noteworthy, that the facial pain in our patient was relieved by corticosteroids. The therapeutic efficacy of oral steroids in this syndrome has never been reported. We speculate that the disappearance of headache after steroid therapy may be secondary to the peripheral anti-inflammatory effect of this drug in relieving vagal compression, though central analgesic mechanisms cannot be excluded.

In conclusion, we suggest that unilateral facial pain may be associated with thoracic malignancies other than lung cancer, such as malignant thymoma. As reported elsewhere, patients with chronic facial pain 'need as priority a correct diagnosis' [3].

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