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Neurogenic pulmonary oedema in a patient with leptomeningeal carcinomatosis

We present the case of a patient with leptomeningeal carcinomatosis from a primary breast adenocarcinoma. On admission to hospital, she developed neurogenic pulmonary oedema due to increased intracranial pressure (ICP), as confirmed by lumbar puncture. Tapping of the CSF resulted in abrupt relief of the clinical sequelae.

A woman in her late 40s, with a medical history of breast adenocarcinoma, for which she underwent a modified radical mastectomy with axillar lymph node resection, was admitted to our hospital for intrathecal chemotherapy. Just 1 month earlier, she underwent craniotomy for a solitary metastatic intracerebral lesion in the left frontal lobe. After this uneventful procedure, she continuously complained of drowsiness, nausea and vomiting. A CT scan showed enhancement of cerebral and cerebellar sulci, typical of leptomeningeal metastasis.

This diagnosis prompted admittance to our hospital, a tertiary care oncology centre, for further treatment. On admittance, the patient had increasing dyspnoea. Pulmonary and cardiac examination showed basilar crepitations on both lungs, tachypnoea (>24/min), tachycardia (145 beats/min) and a blood pressure of 80/40 mm Hg. No cardiac murmurs were heard and the electrocardiograph showed no signs of myocardial infarction. The peripheral oxygen saturation at that time was 80% with no oxygen support. Blood gas analysis showed hypoxia: pH 7.46, partial pressure of carbon dioxide (pCO_2) 4.7, partial pressure of oxygen (pO_2) 5.4, HCO_3^- 24.7, (BE) 1.3 and arterial oxygen saturation (SaO_2) 0.79. A chest radiograph showed a normal heart with evidence of bilateral alveolar filling (fig 1B; fig 1A shows the chest radiograph taken 1 day earlier, which was without abnormalities).

The patient was admitted to the intensive care unit and respiration was supported by mechanical ventilation through a facemask and administration of oxygen. Nevertheless, her neurological condition deteriorated to a Glasgow Coma Scale (GCS) score of 6. On reconsidering the CT scan and the diagnosis of leptomeningeal carcinomatosis, we hypothesised that increased ICP, due to a CSF resorption disturbance, caused neurogenic pulmonary oedema. Therefore, we carried out a lumbar puncture, showing an increased CSF pressure of 60 cm H_2O. We drained 30 ml of the CSF, during which the patient regained consciousness acutely (GCS 13). Cytology showed the presence of malignant cells. The tachypnoea and tachycardia resolved, although the basilar crepitations could still be recognised on pulmonary auscultation. Blood gas analysis showed recovery: pH 7.42, pCO_2 5.2, pO_2 8.0, HCO_3^- 24.8, BE 1.0 and SaO_2 0.93.

The patient was readmitted to the neurosurgical department for a CSF shunt procedure. She was, however, not fit for surgery, and attempts to alleviate the increased ICP with an external lumbar drain failed. Treatment was discontinued when her condition deteriorated again 5 days later, after which she died.

As far as we know, leptomeningeal metastasis has not been described as the cause of neurogenic pulmonary oedema. Although the association of an increased ICP and neurogenic pulmonary oedema has been described previously, the pathophysiological mechanisms remain obscured.[1–3] The medulla oblongata is believed to be the critical anatomical structure responsible for the pathogenesis of neurogenic pulmonary oedema, probably acting through the sympathetic component of the autonomic nervous system.[1 2]

The rapid improvement after the normalisation of the increased CSF pressure is more consistent with neurogenic lung oedema than with other causes of respiratory distress. As reviewed by Fontes *et al*,[4] the clinical features as described in our patient—that is, tachypnoea, dyspnoea, tachycardia and hypotension—often occur in acute neurogenic pulmonary oedema. As Fontes *et al* conclude, we believe that doctors should always be aware of this clinical condition after neurological events, especially when no other causes of pulmonary oedema can be established. Supportive measures are the treatment of choice. In our patient, relieving the increased ICP corrected the respiratory failure.

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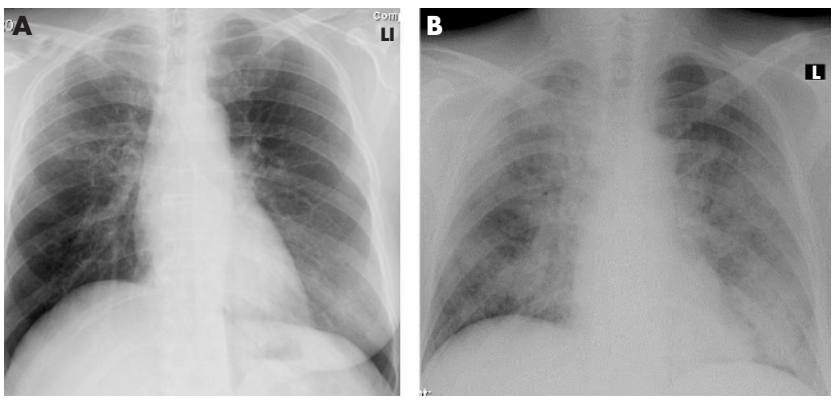

Figure 1 Chest radiograph: (A) taken 1 day earlier; (B) with evidence of bilateral alveolar filling.

Onset of cluster headache triggered by emotional effect: a case report

Cluster headache is a strictly unilateral headache that occurs in association with autonomic symptoms. Stress is a recognised precipitant of migraines, but not of cluster attacks. We describe the case of a patient having migraine for years, in whom extreme emotional stress triggered cluster headache attacks.

Background

Neuroimaging has contributed considerably to the knowledge about the neurobiology of cluster headache. Activation in the region of the posterior hypothalamus is observed,[1] coinciding with subtle structural abnormalities in the same region.[2]

Genetic studies indicate an autosomal dominant inheritance with low penetrance and an increase in risk of 4–18 times for

cluster headache in first-degree relatives when compared with the general population.[3]

Although the triggers for individual episodes are well recognised, the most important ones being nitroglycerin,[4] alcohol,[5] increased body heat and exertion,[6] this is not the case for the triggers for bouts.

Case report

A man, about 50 years old, had been treated by us for a decade. He had experienced migraine without aura from his early teens. He had a positive family history of headache, with both his parents and two siblings having migraine. A typical migraine episode consists of pain that is mostly unilateral but with the side changing, periorbital or temporal, and sometimes bifrontal, accompanied by nausea, phonophobia, photophobia and often osmophobia. Our patient never had any autonomic signs accompanying his migraine episodes. The headache would typically be severe, with a throbbing character and exacerbated by movement. The episode lasted from 1 hour, when treated, to several days and prevented him from carrying out his daily activities.

The episodes responded best to subcutaneous sumatriptan 6 mg and only partially to combined over-the-counter painkillers or non-steroidal anti-inflammatory drugs. The frequency of episodes varied between twice a month and twice weekly over the 10 years of review. Overuse of drugs for acute migraine had been a recurring problem and attempts to reduce the number of days of taking drugs for acute headache on an outpatient basis proved successful and were followed by periods of prophylactic treatment. During phases of increased frequency of episodes and owing to overuse of drugs for acute headache, the headache had less features and was less severe, but returned to its original characteristics and frequency after withdrawal of treatment. In the past, the patient had used several β-adrenoreceptor blockers and tricyclic antidepressants, as well as valproate and gabapentin, to prevent migraine.

The patient is a non-smoker and does not drink alcohol. A few years ago, he had severe mouth ulcers and was examined to exclude possible Behçet disease. He has hypercholesterolaemia and arterial hypertension, which is treated with pravastatin (20 mg/day) and ramipril (10 mg/day). He is an academic and has held several responsible positions. After 10 years of marriage, he had gone through a difficult divorce and subsequently struggled to maintain contact with his three children. His private life has become quieter only in the past few years. He had remarried and his 21-year-old son had been living in his house for a few years.

He came to see us via an emergency appointment in autumn 2004, because of a new, previously unknown type of headache that had started 2 weeks before the appointment. At this time, he was not taking any migraine prophylactics, had not changed his regular drugs and did not use any psychotropic substance, including illicit drugs.

''Totally unexpectedly'', his son had announced that he was moving back in with his mother, the patient's ex-wife. The patient described this as the worst moment of the past years, of having had the feeling that ''everything is taken away''; he was tearful while describing it. He said, ''... during the afternoon I tried to rationalize this ... but it did not work and I had to cry several times''. In the early evening of the same day, after an afternoon of intense worrying, he started to have a type of headache, which he had not had previously. The new headache occurred regularly thereafter, with a frequency of one to two attacks every 24 h, mostly occurring during the night and waking him up. This pain, starting abruptly, peaked in minutes, was strictly left temporoparietal and was accompanied by lacrimation and conjunctival injection. Whereas the previous headaches were worsened by movement and he preferred to lie down and rest, the new headaches were not exacerbated by movement, and he was restless and paced around. The intensity of the new episodes was higher than those previously experienced, with 10 out of 10 on a verbal rating scale. The pain was stabbing, not pulsating. As the pain was so unbearably severe, he always treated it with subcutaneous sumatriptan 6 mg, with resolution in 15–30 min. A magnetic resonance image with gadolinium showed no abnormality and particularly no hypothalamic or cavernous sinus or pituitary lesions.

Cluster headache was diagnosed, and we started him on a course of steroids with prednisolone 60 mg over 5 days, tapering it down over 5 days. We introduced methysergide, which was increased to 5 mg/day, when no further headaches occurred. Eventually the dose was titrated down to 2 mg/day, with control of the headache and bearable, mild side effects. When the dose of methysergide was reduced to below 2 mg after 1 and 4 months, the new type of headache recurred twice daily, and was controlled when the patient increased the methysergide back to 2 mg daily. During the 2 weeks between the onset of the new headache and the appointment, and while he was on methysergide, no episodes of migraine occurred.

Discussion

This patient presented with a new type of headache fulfilling the International Headache Society criteria[7] for cluster headache after having been treated in our specialised headache clinic for migraine without aura for 10 years and headache caused by the overuse of drugs. A careful study of the clinical notes and correspondence over the past 10 years did not suggest any previous occurrence of cluster headache.

Several cases of cluster headache triggered by, or secondary to, lesions localised in the trigeminal territory, such as those caused by head injury,[8] dental extraction,[9] impacted superior wisdom tooth[10] and ocular enucleation,[11] have been published.

Emotional triggers are well recognised for cardiac death,[12] stroke[13] and also for migraine.[14] For cluster headache, the only reported emotional trigger for a first-time cluster headache is orgasm.[15] The emotional stress temporally associated with the onset of cluster headaches was extreme in our patient and he became tearful, even when talking about it 4 months later.

Cluster headache is very rare, with a prevalence of about 0.2%,[3] and an incidence of 1.6 per million people per person-year.[16] Against this background, we propose a causal relationship between the extreme emotional stress in our patient and the onset of his cluster headaches. Clinical or imaging hints for a secondary origin of the new type of headache were absent.

In conclusion, we describe a patient who had migraine for years and in whom extreme emotional stress triggered a new type of headache. Placebo effects in the treatment of cluster headache are mediated by information and induce neurobiological changes. In a recent review, it was described as comparable in magnitude to migraine.[17] Emotional stress as a trigger, also mediated by information, may be another example that the heritage in research from Descartes, of trying to conceptually separate the brain from the results of its function, is outdated.

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Misoplegia: a review of the literature and a case without hemiplegia

Brain damage may cause profound changes in people's attitudes towards their own bodies. Relatively common after unilateral lesions are anosognosia and anosodiaphoria—that is, the denial of, or unconcern about, a sensorimotor hemisyndrome. Less familiar forms of altered limb perception include asomatognosia (lack of awareness of a part of the body), somatoparaphrenia (lack of ownership of a paralysed limb), the experience of supernumerary phantom limbs (reduplication of limbs on the affected side of the body), personification (nicknaming a limb and giving it an identity of its own) and misoplegia. The term misoplegia was coined by Critchley[1 2] and refers to the morbid dislike or hatred of paralysed limbs in patients with hemiplegia. Minor manifestations of this condition may be restricted to verbal aggression towards a limb, but commonly misoplegia includes physical acts such as striking and beating the hemiplegic extremity.[1–3] Although these verbal or physical acts of self-directed aggression are impressive, detailed case reports are rare. Apart from the anecdotal communications by Critchley[1 2] and some passing notes by others, we are aware of only six published accounts. These cases and our new observation are summarised in the supplementary data available online at http://jnnp.bmjjournals.com/supplemental.

Case history

A 79-year-old ambidextrous woman had poliomyelitis with atrophia and shortening of the left leg (about 6 cm) in her early childhood. Wearing an orthopaedic shoe, she was fully mobile, enjoyed sports and led a normal life with a career as a bank assistant. Her medical history was otherwise uneventful.

She was admitted to hospital because of sudden mood changes, abdominal pain, dizziness, cognitive decline, uncomfortable feelings of coldness in her left toes and complaints about gait problems. On admission, neurological examination was normal except for gait difficulties because of the shortened left leg and the behaviour syndrome described later in the article. Brain imaging (fig 1) showed a tumorous lesion located in the right hippocampus and extending to the medial regions of the right temporal gyrus and to the right temporal horn and parietal region.

The patient was fully oriented. Her language was characterised by a heightened flow and a theatrical way of intonation. Her remote memory was intact, but her verbal and figural learning and recall were poor. No apraxia, personal or extrapersonal neglect or visual agnosia was noted, except for a mild topographagnosia. Executive functions were impaired, and she displayed a maniforme behaviour syndrome with frequent mood switches, moria and hyperverbality. Most impressive was her talking to her left leg as to another person; she was calling it names, cursing it and sometimes even beating it (fig 1; video clip is available online at http://jnnp.bmjjournals.com/supplemental). She addressed her right leg as her friend and the left as her enemy and repeatedly expressed her wish to get rid of this ''bugger''—that is, her left leg. According to relatives, all symptoms became evident only a few weeks before admission.

The tumour was resected, and histological examination showed a gliosarcoma that was a World Health Organization grade IV type. An initial left motor hemisyndrome, more dominant in the upper extremity, was rapidly improving. An examination 3 days after the operation showed a left-sided homonymous hemianopia and severe visual neglect. The patient was repeatedly found crying and having fights with her left leg, which showed bruises. She said she would feel happier if her left leg ''were just dead''. Five days later, her cognitive deficits were unchanged. A change was seen, however, in the verbalisations directed to her left leg—that is, she would at times embrace and caress it and talk to it in an overly friendly way. She said that her left leg and herself ''belonged together'' and, on being questioned, denied any previous disputes or self-injurious behaviour. But only minutes after having called her left leg her ''best companion'', she would curse it as her enemy again. In fact, an ongoing switching between caressing and physically expressed hatred towards her left leg was observed. Signs of anosognosia were observed. For instance, despite the fact that she was confined to a wheelchair, she claimed that she could run.

The patient was discharged 9 days after the operation. She refused radiotherapy. Her state deteriorated rapidly and she died 6 weeks after surgery. No autopsy examination was carried out.

Discussion

Although this case shares major features in common with previously published cases, it is in striking contrast with respect to one accompanying symptom, at least tacitly considered to be an almost defining feature of misoplegia: the absence, in our patient, of hemiplegia, or even of any marked sensory or motor impairments due to the central lesion. Aetiological differences (space-occupying lesion in our patient *v* acute vascular incidence in all previous cases) would probably not account for the occurrence of misoplegia without hemiplegia. We suggest that the premorbid history of our patient should be taken into consideration. Critchley[2] had argued that certain premorbid personality traits may predetermine a person's failure to cope with a sudden change in bodily functioning. Specifically, he contended that ''such an individual has perhaps always been an obsessional and a candidate for hypochondriacal trends by reason of an innate preoccupation with bodily efficiency and physical fitness'' (p 86). In contrast with Critchley, we do not consider premorbid personality to be a key element in our patient. It would rather seem that the physical and minor functional impairments of our patient's left leg from early childhood on may have produced an imbalance in the body image of the left leg as compared with the right leg. Even if entirely compensated during most of her life, this imbalance may have made her left leg the target of negative emotions, which were released only by a brain tumour. Obviously, this lesion markedly affected the patient's inhibitory control of affective impulses. The case presented here may thus redirect Critchley's idea of a premorbid personality influence to more recent accounts of misoplegia[4 5] in terms of a dysfunctional system of emotion regulation—that is, a release of repressed negative feelings about a premorbidly affected body part. Why some patients are inclined to deny or play down paralysis or to reject the presence or ownership of a dysfunctional limb, whereas others develop an overly hostile or, conversely, an overly caring[6] attitude towards the affected limbs, remains an unresolved issue.

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Figure 1 Preoperative MRI of the patient (leftmost); the patient calling her left leg names and striking it hard (video is available online at http://jnnp.bmjjournals.com/supplemental). Informed consent was obtained for publication of this figure.