

Case Report

Clusterlike Headache as a First Sign of Brain Metastases of Lung Cancer

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We report on a patient with clusterlike headache and multiple brain metastases of lung cancer. Initially, cluster headache was suggested clinically by characteristic symptoms without any focal central nervous system signs. However, magnetic resonance imaging demonstrated multiple brain metastases. It is possible that tumor necrosis factor may have played a role in initiating the clusterlike headache.

Key words: clusterlike headache, multiple brain metastases of lung cancer

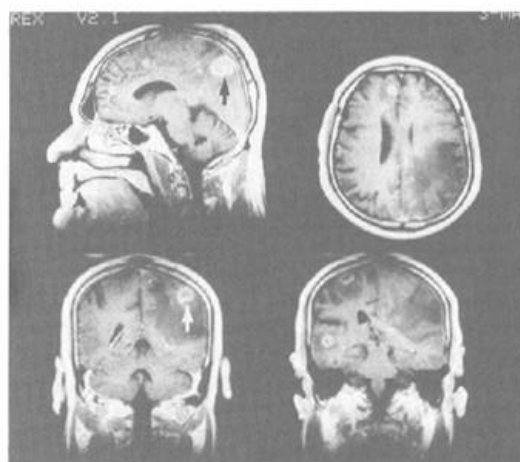
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Among the diagnostic criteria of cluster headache put forward by the International Headache Society, neuroradiological investigations should not demonstrate any pathological or morphological lesion in the central nervous system. Recent reviews described the association of clusterlike headache with anatomical disturbances of the central and peripheral nervous systems.^{1–9} We report here the occurrence of clusterlike headache in a patient with multiple brain metastases. The results of early neurological examinations were normal with the exception of the tactile hypesthesia of the region of the left ophthalmic branch of the trigeminal nerve. Neuroradiological investigations revealed multiple brain metastases.

CASE HISTORY

For 5 weeks prior to investigation, a 55-year-old taxi driver had severe sharp pains in the left eye and temporal region. The pains were excruciating and usually lasted 30 to 60 minutes. The attacks were associated with conjunctival injection, lacrimation, and nasal congestion. At the beginning of the symptoms, the pain occurred once daily, but increased in frequency over time. Common analgesics had no benefit. Prior to the onset of the symptoms, he had never been admitted to hospital. Since adolescence, he had been a heavy smoker.

On the initial neurological examination, the only noteworthy finding was hypesthesia in the distribution of the first division of the left trigeminal nerve. Since he had never previously experienced headache, a head CT scan was performed; the result was the possibility of several cerebral metastases of a systemic tumor. The MRI findings were also positive (Figure). In a search for the primary tumor, the following examinations were performed: chest x-ray and CT scan, radionuclide bone scan, ultrasound and radionuclide scans of the thyroid gland, abdominal and pelvic ultrasound scans, prostate ultrasound scan and proctoscopy. None of these examinations demonstrated the presence of a primary tumor. To obtain a histological diagnosis of the brain metastases, CT-guided brain biopsy was performed from different levels of the



Sagittal, axial, and coronal T1-weighted MRI images of the brain, enhanced by contrast material, demonstrating multiple cerebral metastases (arrows) surrounded by edema.

left parietal lobe. The cytological examination revealed malignant epithelial tumor (suspected to be of pulmonary origin).

The following tumor marker levels were measured: carcinoembryonic antigen 15.68 ng/mL (normal: < 4 ng/mL), tissue polypeptide antigen 7.88 U/mL (normal: < 4 U/mL), and prostate specific antigen 0.12 ng/mL (normal: < 3 ng/mL). Six weeks following the onset of the pain, a severe right hemiparesis developed with signs that the corticospinal tract was affected. The patient became diabetic. In time, brain irradiation was administered.

At this point, he developed bilateral femoro-popliteal thrombosis, followed by pulmonary embolism. At a later stage, he exhibited severe cardiorespiratory insufficiency, and was admitted to the Department of Pulmonology where he died. (The first neurological examination took place in March 1994 and he died in July 1994.)

Autopsy showed that the primary cause of death was pulmonary embolism. The basic illness was bronchogenic carcinoma in the left superior lobe. Other autopsy findings were bilateral thrombosis in the femoral vein, cerebral edema, and herniation of the cerebellar tonsils.

COMMENTS

The pathogenesis of cluster headache is unknown.¹⁰ However, several lines of evidence suggest that the final common pathway to pain and the periodicity of cluster headache involves the trigeminovascular system as in migraine,^{11–14} or a lesion in and around the cavernous portion of the carotid artery¹⁵ and the hypothalamic–pituitary axis.¹⁶

Recent studies of the neuroimmuno-modulatory system have suggested important roles of inter-leukin-1 (IL-1) and tumor necrosis factor (TNF) in the pathogenesis of cluster headache.¹⁷ The development of TNF in patients with malignant tumors is more frequent than that in healthy individuals.¹⁸

Tumor necrosis factor, IL-1, and interferons control the local and systemic events of the immune response, inflammation, and the hypothalamic-pituitary-adrenal axis.¹⁷

Interleukin-1 increases the synthesis of substance P in the painful area of cluster headache patients, and this may be the first step of the cluster attack.¹⁷ We suspect that TNF and IL-1 may have played basic roles in initiating cluster headache in our patient with multiple brain metastases of lung cancer.

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REFERENCES

1. Noronha A, Applebaum J. Symptomatic cluster. *Neurology*. 1993;43:1270.
2. Mathew NT. Cluster headache. *Neurology*. 1992;42(suppl 2):22–31.
3. Kuritzky A. Cluster headache-like pain caused by an upper cervical meningioma. *Cephalalgia*. 1984;4:185–186.
4. Mani S, Deeter J. Arteriovenous malformation of the brain presenting as a cluster headache - a case report. *Headache*. 1982;22:184–185.
5. Reik L Jr. Cluster headache after head injury. *Headache*. 1987;27:509–510.
6. Testa D, Frediani F, Bussone G. Cluster headache-like syndrome due to arteriovenous malformation. *Headache*. 1988;28:36–38.
7. Tfelt-Hansen P, Paulson OB, Krabbe AA. Invasive adenoma of the pituitary gland and chronic migrainous neuralgia. A rare coincidence or a causal relationship? *Cephalalgia*. 1982;2:25–28.
8. Herzeberg L, Lenman JA, Victoratos G, Fletcher F. Cluster headaches associated with vascular malformations. *J Neurol Neurosurg Psychiatry*. 1975;38:648–649.
9. Masson C, Lehericy S, Guillaume B, Masson M. Cluster-like headache in a patient with a trigeminal neurinoma. *Headache*. 1995;35:48–49.
10. Clifford R. New Advances in Headache Research: 3. London: Smith-Gordon, Nishimura; 1994:193–250.
11. Moskowitz MA. The neurobiology of vascular head pain. *Ann Neurol*. 1984;16:157–168.
12. Knyihar-Csillik E, Tajti J, Mohtasham S, Sari G, Vecsei L. Electrical stimulation of the Gasserian ganglion induces structural alterations of calcitonin gene-related peptide-immunoreactive perivascular sensory nerve terminals in the rat cerebral dura mater: a possible model of migraine headache. *Neurosci Lett*. 1995;184:189–192.
13. Kovacs K, Kapocs G, Widerlov E, et al. Suboccipital cerebrospinal fluid and plasma concentrations of calcitonin gene-related peptide and corticotropin releasing hormone in patients with common migraine. *Nord J Psychiatry*. 1991;45:11–16.
14. Vecsei L, Widerlov E, Ekman R, et al. Suboccipital cerebrospinal fluid and plasma concentrations of somatostatin, neuropeptide Y and beta-endorphin in patients with common migraine. *Neuropeptides*. 1992;22:111–116.
15. Moskowitz MA. Cluster headache: evidence for a pathophysiologic focus in the superior pericarotid cavernous sinus plexus. *Headache*. 1988;28:584–586.
16. Chazot C, Claustrat B, Brun J, Jordan D, Sassolas G, Schott B. A chronological study of melatonin, cortisol growth hormone and prolactin secretion in cluster headache. *Cephalalgia*. 1984;4:213–220.
17. Martelli P, Granata M, Marante A, Rordorf-Adam C, Giacobazzi M. Lymphokine pattern in cluster headache. In: Clifford R, ed. New Advances in Headache Research: 3. London: Smith-Gordon, Nishimura; 1994:225–231.
18. Barna BP, Rogers LR, Thomassen MJ, Barnett GH, Estes ML. Monocyte tumoricidal activity and tumor necrosis factor production in patients with malignant brain tumors. *Cancer Immunol Immunother*. 1991;33:314–318.