

tasks. We monitored concentration changes of oxy-Hb, deoxy-Hb, and total-Hb, using an NIRO-500 instrument (Hamamatsu Photonics KK, Japan). The optodes were placed at an interoptode distance of 3.5 cm on the left forehead so that the centre of the two optodes was placed on the centre of the tumour. With an optode distance of 4 cm, correlations of oxy-Hb and total-Hb measured by NIRS and rCBF measured by PET suggested that the reliable penetration depth of near infrared light into brain tissue is about 1.3 cm³; thus the present NIRS measurement area was restricted in the tumour. The patient was seated and had his eyes open during the NIRS measurement. Informed consent was obtained from the patient.

To activate the left frontal lobe, we used the following four tasks: (1) semantic verbal fluency, which entails naming as many items in a semantic category (for example, animals) as possible; (2) confrontational naming, which involves naming ordinary items presented by the tester; (3) backward digit span, a working memory task which involves reporting of digits (2 to 8) in the reverse order; (4) reading, which entails reading a short descriptive passage aloud. The speech responses of the patient to the tasks were normal.

Figure B shows an example of changes in NIRS during the naming task. After the beginning of the task, oxy-Hb and total-Hb decreased to negative values during the task, and deoxy-Hb also decreased. These changes returned to the control level gradually after the end of the task. The other tasks also caused similar changes of oxy-Hb, total-Hb, and deoxy-Hb.

The rCBF in the left frontal lobe is generally increased by all the tasks used in the present study.^{3,5} Indeed, our NIRS activation study using the cognitive tasks showed increases in oxy-Hb and total-Hb in the left frontal lobe in most normal adults—for example, increases in oxy-Hb and total-Hb—were found in 92.3% of young adult subjects (mean (SD) 28.8 (4.4) years) during the word fluency task (unpublished data). Therefore, although we could not measure the changes in rCBF in the left frontal lobe of the patient, the evidence from our previous studies strongly suggests that the tasks caused an increase in rCBF in the left frontal lobe of the patient.

The decrease in oxy-Hb and total-Hb recorded from the brain tumour indicates a decrease of local blood flow in the tumour because the NIRS measurement area was restricted to the brain tumour.³ The decreases in oxy-Hb and total-Hb were found only during the tasks; consequently, these changes were probably not due to changes in systemic blood pressure, which can alter tumour blood flow.¹ Based on these assumptions, we suggest that the increase of rCBF in the left frontal lobe induced by the tasks stole the local blood flow of the brain tumour through the cortical branches, leading to the decrease of local blood flow in the tumour.

The present report suggests that activity dependent increase in rCBF can steal blood flow from the adjacent tissues including non-activating cortex. Recent NIRS activation studies have shown that cognitive tasks cause decreases in oxy-Hb and total-Hb in the left frontal lobe in some normal subjects^{4,5}; these decreases indicate a decrease in rCBF.³ Although the physiological mechanisms of the decrease in rCBF during neuronal activity have not yet been elucidated, we hypothesise

that a stealing of blood flow is one of the mechanisms.¹ The present report supports this hypothesis.

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Migraine aura masquerading as Balint's syndrome

Migraine is a common neurological disorder with a prevalence of 0.5% to 2% in the general population.¹ In one fourth of total migraineurs, headache is preceded by an aura.² We describe a patient with recurrent episodes of migraine in whom headache was preceded by a constellation of visual symptomatology which constituted salient components of Balint's syndrome. This syndrome, consisting of a triad of simultagnosia, optic ataxia, and oculomotor apraxia, is seen with bilateral lesions of occipitoparietal cortices affecting connections between visual cortical regions and the frontal eye field.³

A 29 year old female teacher presented with an 8 year history of paroxysmal alternating hemicranial and throbbing headache which was often associated with nausea and photophobia. Patients fulfilled the requisite criteria for establishing the diagnosis of migraine with aura as devised by the International Headache Society (1988).⁴ She used to have six to eight episodes of headache a month. There was no history of status migranosus during these years. On several occasions, headache was preceded by a peculiar constellation of visual symptomatology comprising distortion of visual images followed by inability to perceive simultaneously objects in the visual field and touch an object under direct visual guidance. However, she could see the component parts of objects during the episode. These visual symptoms

lasted for about 10–25 minutes and were followed by a hemicranial, throbbing headache which was often associated with nausea, photophobia, and occasionally vomiting. Headache used to last for about 4 to 18 hours and would respond to either ergot drugs or sumatriptan, especially if taken at the beginning of the episode. Occasionally these visual symptoms were not followed by headache. The patient would not lose contact with the environment during or after the visual symptoms. Her mother and two younger sisters were also having paroxysmal episodes of common migraine.

Her general physical and neurological examination in between the episodes was unremarkable. Neurological examination during the aura symptoms disclosed that she was unable to see simultaneously all the objects in the visual field (simultagnosia). She did omit several words while reading a paragraph. However, she could comprehend and read each and every word individually. On being shown a complex picture comprising multiple subunits she was not able to comprehend and perceive the entire picture but was able to perceive all the components of the picture individually (seeing in piecemeal). These aforementioned features were consistent with simultagnosia. Besides simultagnosia, she had optic ataxia as evidenced by her inability to coordinate hand and eye movements. Optic ataxia was tested as follows: each eye was tested separately and the hand ipsilateral to the eye being tested was used. The target stimulus was a 5 mm long pin with a white head placed at preselected locations. The patient was asked to touch this pin with her index finger without shifting her gaze from the fixation point. The patient had difficulty in performing this test but had no problems in reaching out to her own body parts or an auditory stimulus with her eyes closed. These features were consistent with optic ataxia. Moreover, gaze apraxia was evident by her inability to look at an object on command. However, she could do it spontaneously. In addition, she had impaired smooth pursuit and voluntary saccades in all directions. Reflex eye movements were normal. Visual acuity during the episode was 6/6 bilaterally. Visual fields were also normal during the episode as demonstrated by the confrontation method. Ophthalmological examination, including perimetry performed during a symptom free period, was normal. There was no clinical evidence of Gerstmann syndrome, prosopagnosia, object agnosia, or colour agnosia. Her cranial CT and magnetic resonance angiography were unremarkable.

Electroencephalography was also non-contributory. The frequency of visual aura symptoms and headache decreased considerably after the patient was started on flunarizine at a daily dosage of 10 mg at bed time.

The visual impulses, after being received by the primary visual cortex (Brodmann area 17), are interpreted and integrated in visual association areas 18 and 19. Brodmann area 19, in turn, is connected with the angular gyrus and frontal eye field by virtue of association fibres. Any lesion in the visual association areas or their connections would result in impaired integration of visual impulses despite normal visual acuity.

The visual symptom complex in this case possibly represents an aura of migraine. The pathogenesis of migraine aura has been a debatable issue.⁵ In this case it is suggested that the pathophysiological process of migraine aura results in a disconnection syndrome by

involving visual association areas and their association pathways. Optic ataxia, gaze apraxia, and simultagnosia seem to represent a dissociation of visual information from the frontal eye field and dorsal parietal regions.

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"Can't you use another vaccine"? postrabies vaccination encephalitis

A healthy 39 year old man was bitten on the ankle by his own apparently normal dog. After the incident the dog disappeared into the forest and was not seen again. Three days later the patient was seen at a provincial hospital in Vietnam and started on an alternate day regimen of suckling mouse brain postrabies exposure vaccination (SMBV). After the second dose, he felt unusually lethargic although he was still able to work. After the third dose, he became unrousable, and was transferred to the Centre for Tropical Diseases, Ho Chi Minh City, the referral hospital for infectious diseases in southern Vietnam. On admission, he was afebrile, confused, had slurred speech, and his Glasgow coma score was 13. He had mild spastic weakness of his left face, left arm, and both legs. Full blood count and results from routine biochemistry and chest radiography were all normal. The CSF: blood glucose ratio was 0.47 (63/140 mg%), the protein content was raised (78 mg/dl), and there was one lymphocyte/ml in the CSF. Screens for malaria toxoplasmosis, cryptococcus, and neurocysticercosis were negative, as was a CSF gram stain. The CSF was sterile after 2 weeks of culture. Brain MRI (Access Toshiba LPT 6.0Ip, 0.064 Tesla) showed areas of high signal throughout the white matter, and cystic-like change in the basal ganglion and right cerebellar hemisphere (figure A). These variably sized lesions were bilateral, widely distributed, asymmetric, and showed no evidence of haemorrhage or mass effect.

As paralytic rabies could not be excluded he was managed conservatively and the SMBV course was continued. On the 4th day after admission he deteriorated with a Glasgow coma score of 10, and was incontinent of urine and faeces with generalised spastic paraparesis. Methylprednisolone (500 mg/ day) was given for 5 days followed by a reducing course of prednisone for a presumptive diagnosis of postvaccination encephalitis. The SMBV was stopped. Within 72 hours of starting steroids there was a dramatic improvement in his neurological state. An MRI examination performed 4 weeks later showed a marked decrease in both size and number of brain lesions and no new lesions (figure B). After 6 weeks he was discharged talking, eat-

ing, walking, and continent but with some persistent emotional lability and mild memory impairment. A follow up MRI examination 5 weeks after discharge showed further improvement, apart from minor abnormalities in the basal ganglion, and generalised increase in ventricular size, consistent with residual cerebral atrophy.

Rabies is caused by an RNA virus, a member of the *Rhabdoviridae* family, it infects mammals and can be transmitted to humans by contact, generally from an animal excreting the virus in the saliva. Rabies manifests as an acute encephalomyelitis, the development of which is almost invariably fatal. The distinction between rabies and postvaccine encephalitis is difficult and may be helped by antigen detection via a skin biopsy; however, this technique is not available in Vietnam.¹ Paralytic rabies could not be excluded in this patient and hence steroids were not used initially. Steroids have been reported to increase mortality in experimental animals with rabies, and it has been suggested that they may abrogate the immune response to the postexposure vaccine, thus precipitating uncontrolled rabies.²

There are three types of postexposure vaccine in use world wide. The Semple type (STV) is obtained from inactivated virus prepared on adult animal nerve tissue; it is inexpensive and relatively easy to produce. In India 3 million people receive postexposure courses of STV (phenolised sheep brain) antirabies vaccine each year.¹ These produce

neurological reactions, including postvaccination encephalomyelitis, in up to 1 in 220 courses, with a 3% mortality.³ Clinical forms include a reversible mononeuritis multiplex, and meningoencephalitic and encephalomyelitic reactions. Myelin basic protein and related neural proteins from the nervous tissue of the animal on which the virus was cultivated stimulate an autoimmune reaction in the human nervous system.

Tolerance has been improved by the development of the suckling mouse brain vaccine (SMBV). The attenuated virus is cultured on immature mouse brain tissue, which contains little myelin, thus reducing the risk of complications. SMBV is inexpensive (US\$1.5 per treatment course) and easily manufactured locally; it is the most widely used postexposure vaccine in Vietnam. Rare neurological reactions do occur with SMBV, Complications of the CNS have been reported to occur after vaccination with an incidence of 1:27000 treated people, with a 22% mortality⁴ The mortality was particularly high (90%) if there was extensive CNS involvement. The third type of vaccine available is the human diploid cell tissue culture vaccine (HDCV), which is both safe and efficacious. However, the recommended regimen is not affordable in most developing countries.

When we approached the Rabies Laboratory, Ministry of Agriculture and Fisheries, United Kingdom for advice in this case their comment was "why do you use the SMBV, can't you use another vaccine". Worldwide about 10 million people each year receive rabies vaccine after exposure; at the Centre for Tropical Diseases we treat 3000 people with dog bites annually. The cost of an HDCV in Vietnam, administered in its present regimen (1ml given for 5 days on days 0, 3, 7, 14, and 28 with an optional booster on day 90) is US\$ 125, making the use of this vaccine unaffordable.

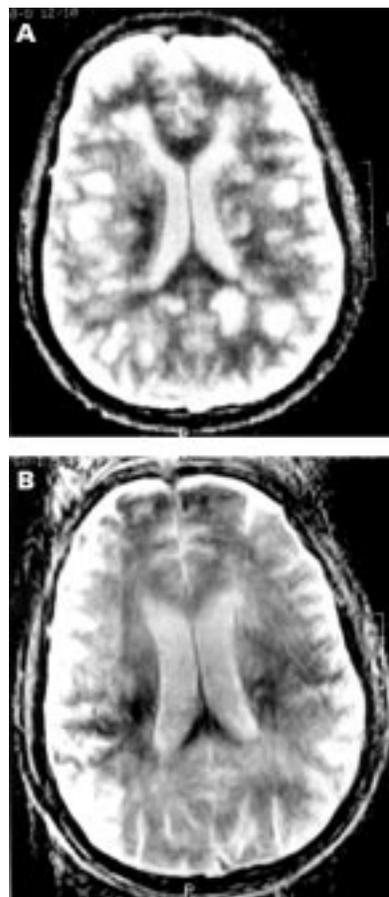
This is the first report to show the demyelinating CNS lesions on MRI, and their resolution after steroid therapy. It is relatively rare for patients to survive if they develop severe CNS effects after postexposure rabies vaccination. Although the incidence of reactions to SMBV is very much lower than STV, this report confirms that it does still occur. Both SMBV and STV are widely used throughout the developing world, and would be the vaccine administered to travellers exposed to animal bites in such countries. This case stresses the need for high dose steroids in postexposure vaccine encephalitis and the urgent need for the development and deployment of a safe, and critically, affordable postrabies exposure vaccine regimen. The economic low dose multisite intradermal regimen using the HDCV provides an example of how this goal may be achieved although it is not yet widely accepted. Such a vaccine regimen (0.1 ml HDCV given at multisite injections on days 0, 7, 28, and 90) could be made affordable, and offers excellent protection without the risks of postexposure immune mediated encephalitis.⁵

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Brain MRI in May 1997. (A) T2 weighted image showing multiple areas of high signal in the cerebral white matter. Bilateral subcortical and periventricular lesions are seen. (B) Brain MRI in July 1997. T2 weighted image shows resolution of the white matter lesions.