TEST YOURSELF

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Dot-to-dot

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A 34 year-old, right-handed, mother of two was at home one evening when she walked into a door-frame, hitting her left temple. The next morning she continued to bump in to objects on her left and was beginning to drag her left leg. She noticed she was dropping items and that her right arm was clumsier than normal. As the day progressed her left leg became weaker as well. There was no headache, vomiting or malaise but she had recently recovered from a minor viral illness. She had worked as a hairdresser, but retired to care for her eldest child who has cerebral palsy. Her only regular prescribed medication was citalopram for depression.

On examination she had corticobulbar dysarthria, left hemiparesis, left homonymous hemianopia and left visual inattention. There was ataxia of the right upper limb. There were no other abnormalities on examination; in particular she did not have optic atrophy nor an internuclear ophthalmoplegia.

Question 1

Where is the lesion?

COMMENT

Many of her signs suggest a right hemisphere process; the left hemiparesis, homonymous hemianopia and visual inattention are all consistent with this. But is this a diffuse cortical lesion or a more localised thalamic lesion? The thalamus is recognised as producing pseudo-cortical symptoms and signs. And is the lesion entirely consigned to the right hemisphere? How could a single right cortical lesion produce a right-sided ataxia without extension into the brain stem? Perhaps there are two lesions, or more?

MR imaging of the brain confirmed a large subcortical parieto-occipital hyperintense lesion in the right hemisphere (fig 1) involving the right lateral thalamus, compatible with demyelination. The lesion appears to creep across the corpus callosum, hinted at in fig 1A.

Question 2

What caused her clinical presentation and scan findings?

COMMENT

She had had a preceding viral infection, raising the possibility of viral encephalitis; however she was afebrile, alert, and there were no seizures—all of which militate against an infection. The MR imaging does not suggest an abscess. Was this a swiftly evolving malignant process? Lymphoma as well as primary and secondary malignancies can produce rapidly evolving signs when associated with a great deal of surrounding oedema or haemorrhage.

Although her symptoms progressed during the first 36 hours and she did not have vascular risk factors, we could not completely

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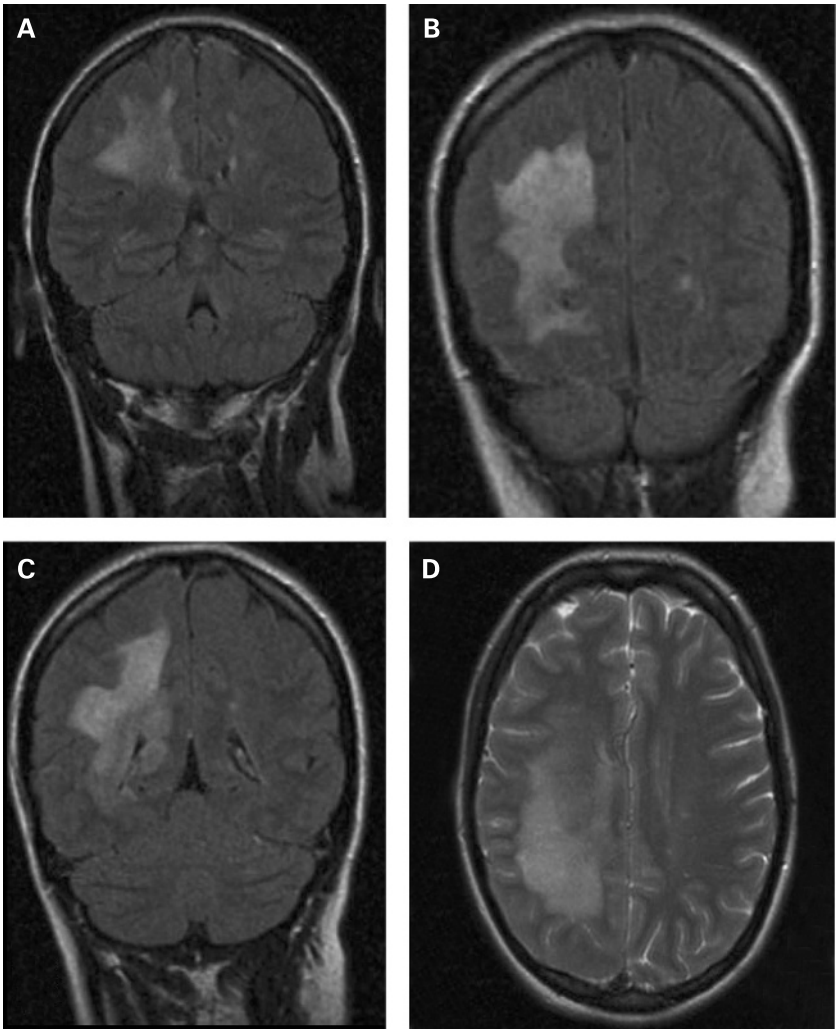

Figure 1
(A–C) Coronal MR FLAIR images demonstrating a confluent subcortical white matter lesion predominantly in the right hemisphere but involving the lateral thalamus and crossing the corpus callosum. (D) T2 weighted axial image demonstrating the posterior distribution of the lesion.

exclude a vascular event on the basis of her history and clinical signs—but the MR scan did not look stroke-like. Therefore, on the basis of the history, signs and MRI pictures, we thought that acute disseminated encephalomyelitis (ADEM) was the most likely diagnosis. ADEM is a para- or post-infectious autoimmune demyelinating disease of the central nervous system and by definition has a monophasic course; any further episodes would suggest other inflammatory conditions such as multiple sclerosis. The condition is usually precipitated by a viral infection or vaccination. The presenting features typically include acute encephalopathy with concomitant, multifocal, neurological deficits. Children are more often affected than adults.[1, 2] "Stroke-like" demyelinating disease is uncommon but recognised.[3]

We then requested further investigations. Her cerebrospinal fluid (CSF) was clear and colourless with the following findings: glucose 2.8 mmol/l, protein 0.44 g/l, red blood cells 405/mm^3, white blood cells 4/mm^3, no organisms, no malignant cells and no bacterial growth. Cerebrospinal fluid PCR for Herpes simplex, Herpes zoster and JC virus was negative. Oligoclonal bands were present and unmatched in the serum. The following were normal or negative: full blood count, erythrocyte sedimentation rate, liver function, renal function, lactate dehydrogenase, human immunodeficiency virus serology, antinuclear factor, anti-double stranded-DNA, anti-cardiolipin antibodies and paraneoplastic antibodies. She had an atypical weakly positive antineutrophil cytoplasmic antibody test but this was both MPO and PR3 negative. Visual evoked potentials were abnormal with a degraded wave form and a delayed P100 from the left eye.

Six months later she developed vestibular symptoms that were not resolving with vestibular sedatives. A repeat MR scan showed new high signal intensity in the right side of the medulla, pons and midbrain and new lesions in the white matter anterior to the right temporal horn and in the deep white matter of the left cerebral hemisphere (fig 2), raising the possibility of multiple sclerosis.

On the basis of the clinical history and the changes in the MR scan we made a diagnosis of multiple sclerosis. We then referred her for neuropsychological testing.

Question 3

What do you think the neuropsychological tests showed?

COMMENT

She scored 70/100 on the Addenbrooke's cognitive examination (ACE-R), failing predominantly on visuospatial areas. Her WAIS III scores were 79 for verbal (8th percentile, bottom of low average) and 64 for performance (1st percentile, very impaired). When testing shape and spatial perception she scored 11/20 on both the incomplete letters test and dot position test, even when in the vertical plane to allow for any neglect. She could not copy a complex 2D figure, but face perception was intact. There were exclusively left-sided errors on cancellation tasks and consistent failure to read the first syllables of

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words. When asked to name a picture of a squirrel, she said "feather", only visually processing the rodent's bushy tail.

To exercise her mind, she started to complete her young son's dot-to-dot pictures. The images were consistently incomplete on the left, despite being completed accurately on the right (fig 3). It also appears that she overlooked the numeric cues.

Question 4

Do the changes seen on MRI explain the visual neglect?

COMMENT

Neglect is almost exclusively a right hemisphere phenomenon. It occurs in up to two thirds of right hemisphere stroke patients; it has been described in multiple sclerosis, but rarely in ADEM.[4] Anatomically it is classically linked to *cortical* damage in the non-dominant parietal lobe or temporo-parietal junction, particularly the angular gyrus and superior temporal gyrus. Focal frontal lobe lesions may also cause transient neglect.[5]

In papers speculating on causes of neglect in stroke syndromes (for example, posterior cerebral artery ischaemic stroke) the buzz phrase is "disconnection". Parietal lobe (para-angular gyrus) disconnection due to a lesion in the right thalamus (paramedian and tuberothalamic lesions including the ventro-lateral nucleus) is recognised as a cause of cortical type neglect. The right lateral thalamus appears to be affected in our patient.

Question 4

Can you be certain that she has genuine visual neglect and not simply a hemianopia?

COMMENT

Object copying and clock-drawing tests have been used as screening tests for neglect, but their sensitivity as isolated tests is poor and they can be difficult to score. As a result neuropsychological assessment relies on the use of test batteries that may include word cancellation tests (mentioned above) and line bisection tests (fig 4).

If a patient has a hemianopic field defect, it can be difficult to definitively prove that there is coexistent neglect. In addition to cancellation tasks and the failure to copy the left part of drawings,[6] line bisection has been used as a useful tool. Line bisection tests have been studied in the German literature since the late 19th century.[7] Patients with a left hemianopia but no neglect deviate slightly leftwards when asked to bisect the line. Patients with a right-hemisphere syndrome and left neglect are seen to bisect rightwards. This effect is more marked the longer the line used. With very

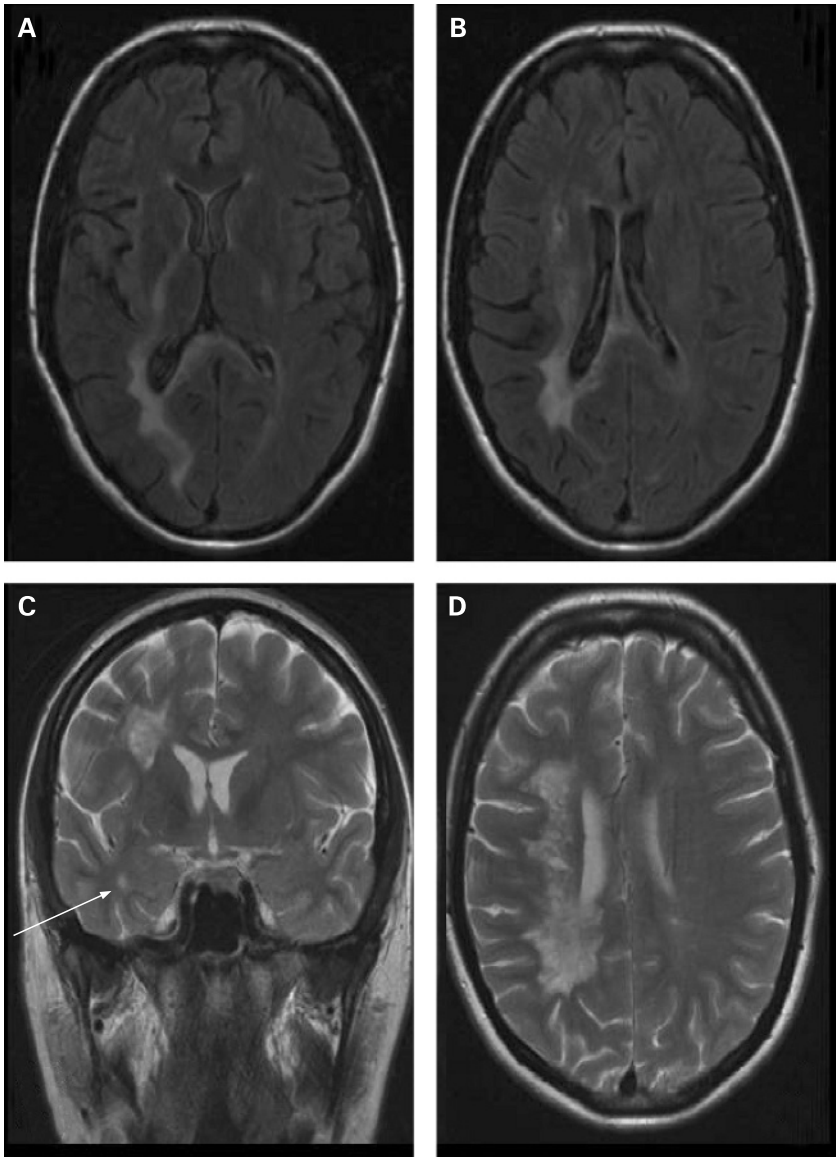

Figure 2
MR images performed six months after presentation. The T2 FLAIR images (A and B) confirm that although the lesion is predominantly right-sided it does cross into the left. (C) T2 weighted coronal view, shows a new lesion in the right temporal lobe (arrow), whilst the original subcortical lesion is still clearly visible (T2 axial, D). There were also high signal foci seen in the right medulla, pons and midbrain (not shown).

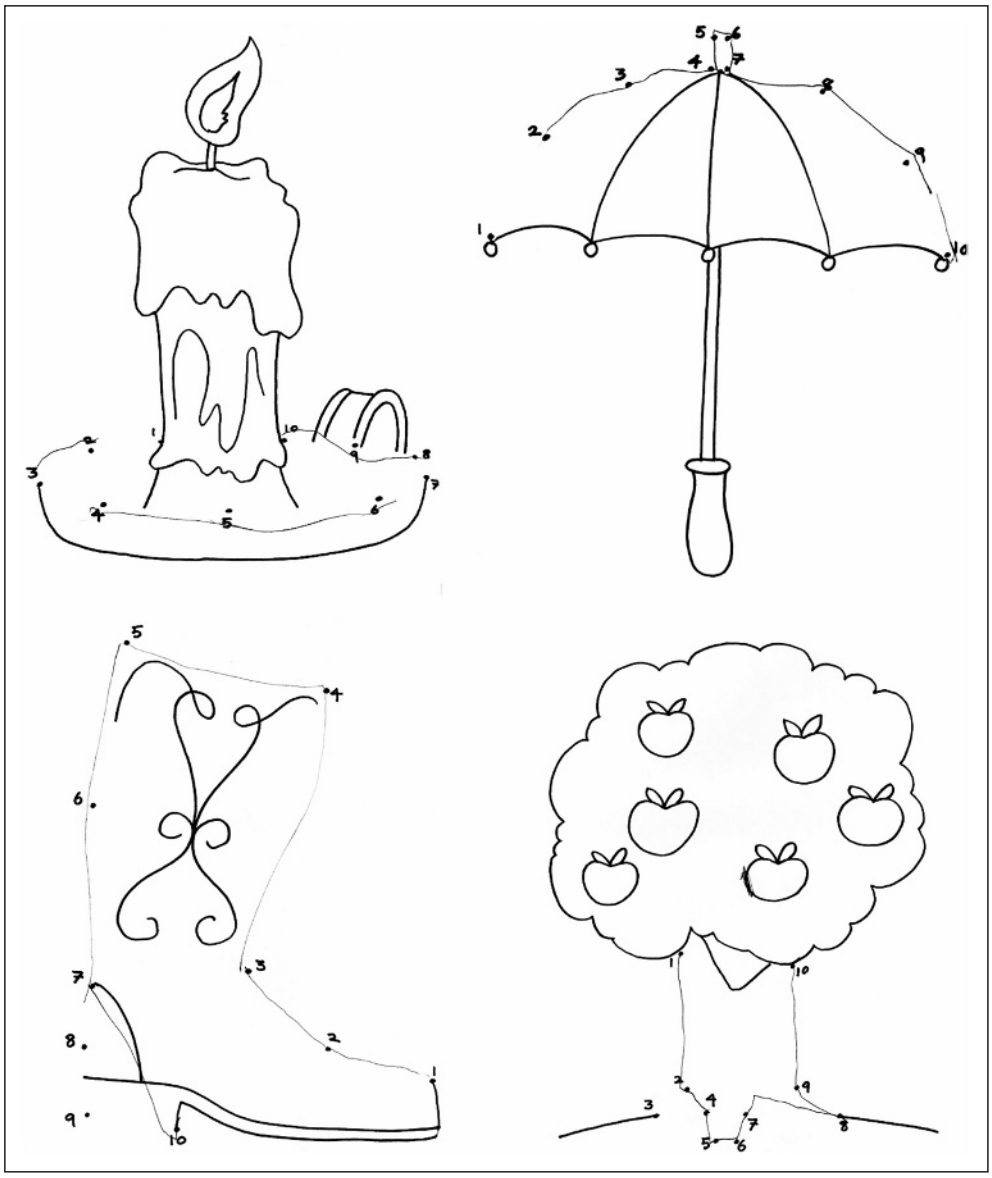

Figure 3
Dot-to-dot pictures.

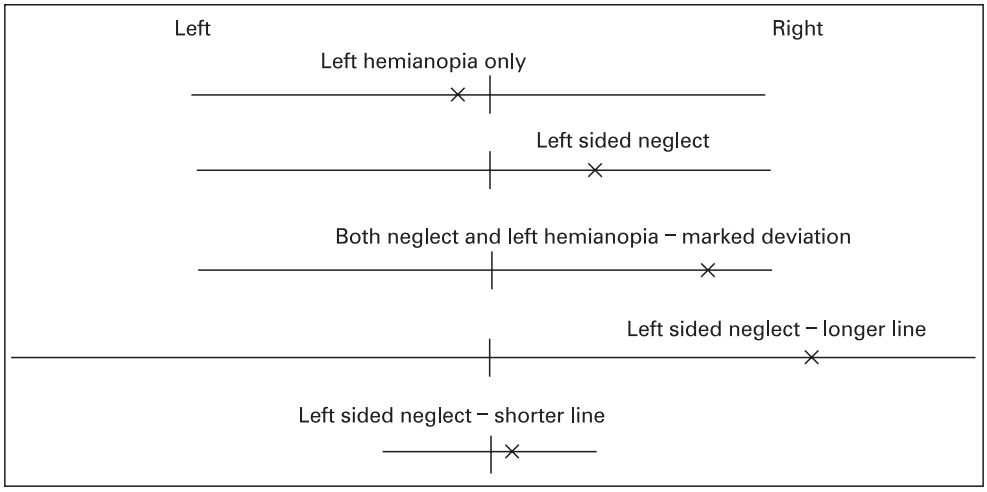

Figure 4
Pictorial representation of the effect of hemianopia, neglect and line length on line bisection. This is not to scale—the variable relative deviation from the true centre is for illustrative purposes.

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short lines the bisection bias reverses from the right to left side of the line physical centre (the so-called crossover effect). When hemianopia and neglect are both present however, a marked rightwards deviation is seen.[5, 8]

An alternative strategy for separating the two is to ask the patient to visualise an area well known to them (for example their local high street) and to describe what they see as they walk forwards. If left-sided neglect is suspected then right-sided objects and shops would be remembered. You then ask the patient to mentally walk to the end of their high street and turn around, walking back down the street the other way. Now shops on the other side of the road would be mentioned, not on the left.

Awareness of her left-sided inattention allowed our patient to implement strategies to overcome this disability. She was able to complete further dot-to-dot pictures accurately, in addition to more functionally important tasks.

PRACTICE POINTS

- Neglect is usually due to a lesion in the non-dominant cerebral cortex.
- Neglect is seen in up to two thirds of people with right hemisphere stroke, but is less well recognised in demyelinating disease.
- Thalamic lesions can cause neglect due to disconnection of the non-dominant parietal lobe.
- Simple bedside tests of cognitive function can be very revealing, including children's dot-to-dot pictures.

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