ORIGINAL ARTICLE

Functional Magnetic Resonance Imaging (MRI) and MRI Tractography in Progressive Supranuclear Palsy-Like Syndrome

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ABSTRACT

An 18-year-old woman underwent an uneventful ascending aortic aneurysm repair then developed progressive supranuclear palsy-like syndrome. Extensive neuroimaging including contrasted fat-suppressed cranial and orbital magnetic resonance imaging (MRI), MRI tractography, and functional MRI (fMRI) revealed no clear radiographic involvement except for a single tiny hypoechoic midbrain dot on the T2*-weighted gradient-echo imaging, which is not considered sufficient to account for the patient's deficits. This case attests to the occult nature of this rare and devastating syndrome.

Keywords: fMRI, gradient-echo imaging, MRI tractography, progressive supranuclear palsy

INTRODUCTION

Progressive supranuclear palsy (PSP)-like syndrome is a rare disorder that occurs most commonly following aortic aneurysm repair, but may occur after other cardiac procedures.^{1–7} We present a young woman who developed this syndrome following ascending aortic aneurysm repair, with devastating consequences. We also provide a video of her illustrating how profound these deficits are. Given the degree of her neurologic impairment, we thought advanced neuroimaging would be abnormal. To our surprise, it was only the T2*-weighted gradient-echo (GE) imaging that showed a single tiny hypoechoic midbrain dot; otherwise, the neuroimaging we employed was completely normal. This may shed light on the anatomic substrate involved, as highlighted in the discussion.

CASE REPORT

An 18-year-old woman was incidentally noted to have a 3-mm ascending aortic aneurysm 1 year after a motor vehicle accident. She presented with chest pain and CT (computed tomography) of the chest demonstrated dilation of the aneurysm. She subsequently underwent an uneventful ascending aortic aneurysm repair. She was normal after surgery for 48 hours, and then she developed dysarthria, dysphagia (requiring a gastric tube), emotional lability, and ophthalmoplegia. Prior to surgery, she had no significant medical history. Examination showed normal orientation and memory but emotionally labile; she had spastic dysarthria but she did not have masked facies. Strength and sensation were normal, as was tone. Gait was narrow based but slightly ataxic. Finger-to-nose testing showed mild

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FIGURE 1 Axial MRI tractography showing intact corticobulbar and corticospinal tracts (vertical tracts) and posterior visual pathways (horizontal tracts).

dysmetria. Postural reflexes were impaired. Visual acuity was 20/20 in each eye with normal colour vision and full confrontation visual fields. Pupils were isocoric at 5 mm with normal reactivity and no relative afferent pupillary defect. The patient was orthophoric in primary gaze, but the ocular motility showed complete ophthalmoplegia, which could be overcome horizontally and vertically with the oculocephalic manoeuvre. Trigeminal and facial nerve functions were normal. Anterior segment and fundoscopic examinations showed no abnormality. Contrasted cranial and orbital fat-suppressed magnetic resonance imaging (MRI), including diffusion-weighted imaging (DWI), MRI tractography, and functional MRI (fMRI), were all normal. It was only the T2*-weighted GE imaging that showed a single tiny hypoechoic midbrain dot (see Figures 1–4).

DISCUSSION

Progressive supranuclear palsy (PSP)-like syndrome, which may manifest immediately after surgery or hours or days later, usually includes supranuclear gaze palsy, dysarthria, emotional lability, and gait ataxia mimicking PSP.^{1–7} However, it should be noted that some truly isolated saccadic palsy patients do exist.⁸ Mokri and colleagues noted a biphasic distribution in his patients consisting of an immediate phase of a supranuclear gaze palsy (most common) that initially improved then presented a latent progressive phase occurring in several weeks to months of a PSP-like syndrome.¹ A syndrome of ocular motility dysfunction, usually involving volitional saccades, has been reported in association with cardiac surgery. However, upon review, most of these patients had other neurologic dysfunction and the cases likely represented the PSP-like syndrome.^{4,5,7}

Patients have been reported with infarcts in the pons, substantia nigra, centrum semiovale, frontal subcortex, striatum, corona radiata, internal capsule, and basal ganglia.^{3,4,6} Nandipati *et al.* recently published two cases of a PSP-like syndrome after aortic aneurysm repair and reviewed the literature.⁶ Of 26 cases including their two, 9 had normal neuroimaging, 7 of which had a cranial MRI, and 2 had a cranial CT.⁶ Interestingly, none of the patients in this literature review had abnormalities on T2*-weighted GE imaging.⁶ Given this extensive review and other papers in the literature reviewed via PubMed, our patient may be the youngest reported case with a PSP-like syndrome following aortic aneurysm repair.^{1–7} Conventional MRI often does not reveal an abnormality, but fMRI and MRI tractography have not previously been reported in these patients until this case report. These imaging modalities may be able to identify irregularities in white matter tracts or in the recruitment of neural activity for task performance.⁹ The mechanism of injury in these patients remains unclear; however, a perioperative ischaemic stroke from embolism, hypothermia protocol, hypotension, hyperviscosity, or cardiopulmonary bypass has been postulated.^{4,7} The recent finding of absent or fractionated perineuronal nets around omnipause neurons (OPNs) and excitatory burst neurons (EBNs) in an autopsy brainstem immunostaining analysis of one of these patients may suggest a radiographically occult mechanism (personal communication with Drs. Eggers, Horn, and Leigh, article in press).¹⁰ These perineuronal nets are aggregates of chondroitin sulfate proteoglycans that form a supporting lattice-like network around neurons with high firing rates, such as OPNs and EBNs involved in saccadic control. They may have a lower threshold of injury due to ischaemia, and injury to these structures may not be evident on conventional cranial MRI.¹¹

Our patient had extensive neuroimaging, including contrasted fat-suppressed cranial and orbital MRI, fMRI, and MRI tractography using diffusion tensor imaging (DTI), and the findings were normal. It was only the T2*-weighted GE imaging that showed a single tiny hypoechoic midbrain dot. Our patient's deficits clinically far outweighed the size of the abnormality detected on GE imaging. The value of T2*-weighted GE imaging has been studied in parkinsonian disorders and does not appear to have findings specific for PSP¹²; yet, our patient has a PSP-like syndrome acquired after surgery, rather than a neurodegenerative tauopathy.

This case further attests to the occult nature of this rare and devastating syndrome and perhaps supports Eggers *et al.*'s contention¹⁰ that the dysfunction is microscopic in nature. The abnormality detected on T2*-weighted GE imaging may be indicative of microbleeding at the site of midbrain indicating neuronal or axonal injury,¹³ but it seems to be only

FIGURE 2 fMRI coronal (A), sagittal (B), and axial (C) slices are shown through a location in dorsal anterior cingulate cortex (crosshair). A supplementary coronal image (D), highlighting superior parietal lobule, is also shown. Colours represent functional MRI activity representing the difference between task performance and rest. The contrast of interest was the eye movement task, shown in green. Despite the fact that the participant was unable to actually produce eye movements, there was strong activity in several regions that are classically associated with eye movements, based on a large number of previous studies.^{14–18} The data from our patient look qualitatively very similar to standard data reported in the literature, suggesting that her cortical circuitry is intact. Eye movement associated areas include bilateral frontal eye fields (see anterior green areas in image C) and bilateral superior parietal lobule (see posterior green areas in image C and superior green areas in image D).^{19,20} The finger tapping task (orange) and verb generation task (blue) served as controls, as the patient's ability to perform these tasks is not significantly affected. Consistent with this, neural activity associated with each task was consistent with expected data. Orange represents magnitude of activity during the finger tapping task during which the patient tapped the index fingers of both hands at her own pace. Pictures on a monitor, visible to the patient, instructed her about when to tap fingers and when to lie quietly. Finger tapping showed strong activations in a swath of cortex consistent with finger sensory motor strip and supplementary motor area (see image C); additionally, the task activated bilateral cerebellum (image D). Blue represents strongest activity during the verb generation task during which nouns were presented on the screen and the patient was instructed to think about a verb that would go well with that noun. For example, during the verb generation task, after presentation of the word "BOOK," the word "read" might be an appropriate response. During the resting period, the visual display showed "#####" in order to roughly equate the visual input during both eyes open rest and the task. The verb generation task also activated a network of regions classically associated with this task.^{21,22} These are shown in blue and in the slices shown include dorsal anterior cingulate cortex and bilateral (but stronger on the left) anterior insula. Slices not shown also indicate strong activations in posterior temporal regions and left frontal cortex. Light green and dark green represent the first and second trials of the eye movement task. The visual display for this task was identical to the verb generation task. Here, during the resting periods (when "#####" was shown on the display, the participant was instructed to lie quietly resting with eyes open). During the presentation of words, she was instructed to attempt to move her eyes from one corner of the screen to another, moving in a clockwise motion, while keeping her head still. Because of her deficit, she was unable to do this, but reported that she was able to imagine moving her eyes in this way. Note that generally, each task shows strong neural responses in brain regions associated with that task.

FIGURE 3 MRI tractography. 3D overhead (A) and a coronal slice (B) are shown through a putative frontal eye field's location, defined as the magenta box in both A and B. Colours represent the direction of anisotropy, and red lines show the tracts defined from the frontal eye field's location. MRI tractography allows measurements of the integrity of white matter tracts that project from a particular location in the brain (in this case, the frontal eye fields). Other imaging modalities do not allow assessment of whether two areas are connected, but rather examine tissue in a particular location. Note that connections to frontal eye fields appear robust by this metric, and tracts descend toward the midbrain. If the deficit had arisen because of a problem in connectivity between frontal eye fields and midbrain, we would expect to see weak or absent tracts between the two. Instead, we observed strong evidence of tracts between them.

FIGURE 4 T2*-weighted gradient-echo imaging showing a hypoechoic dot at the right medial ventral midbrain next to substantia nigra (arrow), which may be indicative of neuronal or axonal injury (micro-bleed).

the “tip of the iceberg” in terms of correlating the patient's neurologic dysfunction with the extent of brain involvement. Interestingly, the other more advanced MRI neuroimaging methods employed showed no abnormality.

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Note: A supplemental video is available online at <http://informahealthcare.com/oph>.

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