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Case Report

A novel degenerative process of the thalamus, red nucleus and connecting pathways

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ABSTRACT

A 51-year-old man presented with 7 year slowly progressive focal tremor affecting the left hand and arm. There were no associated neurological findings and no biochemical or genetic cause could be identified. Magnetic resonance imaging (MRI) demonstrated extensive symmetrical abnormality involving the thalamus, red nuclei and associated pathways. This appearance has not, to our knowledge, been previously reported. We discuss the neuroanatomy involved and the possible aetiology for the MRI abnormalities. © **Neuroanatomy. 2008; 7: 12–14.**

Key words [tremor] [red nucleus] [thalamus] [MRI]

Introduction

The role of the red nucleus and thalamic connections are incompletely understood and these pathways are poorly visualised on conventional cross sectional imaging. In this case report, we describe a patient with a movement disorder and magnetic resonance imaging (MRI) abnormalities that involved these structures.

Case Report

A 51-year-old left handed gentleman presented to the neurology outpatient clinic complaining of a tremor affecting his left hand and arm, such that he was no longer able to work. Further questioning revealed that the tremor had been present for approximately 7 years and was static or extremely slowly progressive. He denied any abnormality of the right hand, speech disturbance or unsteadiness. He had previously been prescribed both propranolol and benzhexol (without any improvement in the tremor) and was currently taking no medication. There was no family history of tremor.

On examination he had a focal dystonia of the left upper limb with tremor exacerbated by complex, controlled movements such as writing. Equivocal cerebellar signs were elicited, but no bradykinesia, altered muscle tone, or abnormality of reflexes or power. There was no impairment of autonomic function, and no sensory changes.

Biochemical profiling was entirely normal, including iron, copper, caeruloplasmin, vitamin B12 and autoantibody screen. Referral for genetic screening was performed, with assessment for primary torsion dystonia (GAG deletion within the DYT1 gene, found in 60% of cases with the typical phenotype), spinocerebellar ataxia types 1,2,3,6,7 and 17 (ATXN1, ATXN2, ATXN3, CACNA1A and ATXN7 genes) and dentate-rubral-pallidluysian atrophy (DRPLA, atrophin-1 gene). All were negative.

Magnetic resonance imaging of the brain was performed using sagittal T2-weighted, axial T2 and FLAIR, and coronal T1 and FLAIR sequences. The findings were unexpected (Figures 1, 2) consisting of bilateral symmetrical signal change within the entire thalamus. The abnormal signal was most markedly in the lateral nuclei including the ventralis posterior lateralis (VPL), lateralis posterior (NLP), and the pulvinar. Smaller foci of abnormal signal were present in the ventralis posterior medialis (VPM). The red nuclei, substantia nigra, subthalamic nuclei and possibly the medial lemniscus demonstrated abnormal signal. In the brainstem, transverse pontine fibres, rubrothalamic and rubrospinal tracts appeared abnormal, suggesting involvement of the dentate-thalamo-rubral pathways. The dentate nuclei themselves appeared normal, however. These abnormalities are bilateral and symmetrical. More superiorly there are foci of abnormal signal in the subinsular region in the region of the claustrum bilaterally but more marked on the right and in the peritrigonal white matter predominantly on the left.

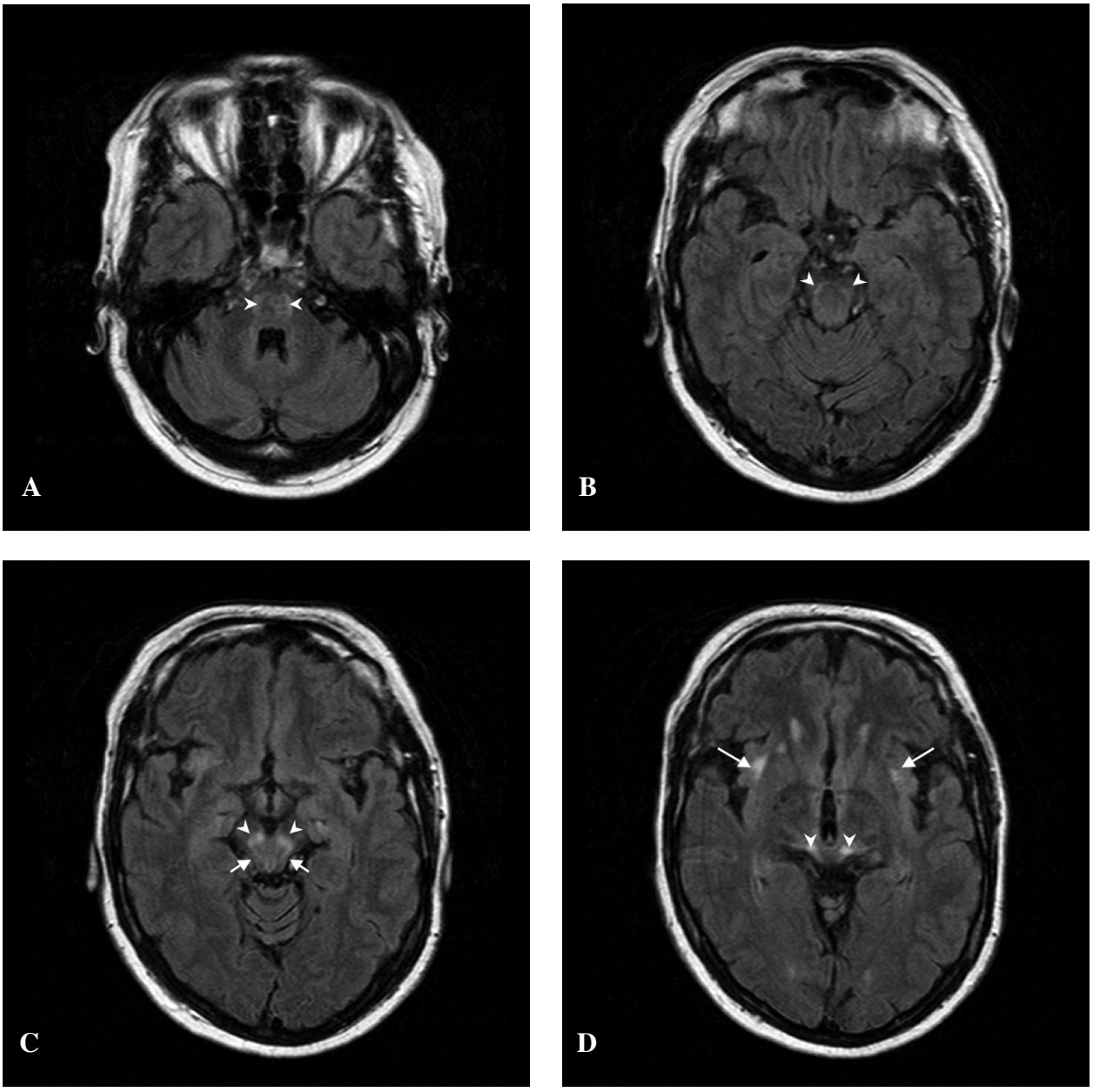

Figure 1. A: Axial FLAIR at the level of brachium pontis. Abnormal high signal in traversing dentate-thalamic-rubral fibres (***arrowheads***); **B:** Axial FLAIR at the level of the midbrain demonstrates abnormal high signal in the rubrospinal tracts and medial lemisci (***arrowheads***); **C:** Axial FLAIR at the level of the cerebral peduncles demonstrates abnormal high signal in the red nuclei and substantia nigra (***arrowheads***) and subthalamic nuclei (***arrows***) bilaterally; **D:** Axial FLAIR at the level of the anterior commisure showing abnormal high signal in the red nuclei (***arrowheads***) and claustrum (***arrows***) bilaterally.

Discussion

To our knowledge this pattern of signal abnormality has not been previously reported in cases of movement disorder. Clinically this patient had signs and symptoms of a focal dystonia, rather than a more generalised disorder such as Parkinson's disease or Huntington's chorea (and the MRI findings are not supportive of either of these diagnoses). MRI in focal dystonia and benign essential tremor is usually unremarkable and neuroimaging is typically used to exclude a focal lesion as a cause of any movement disorder.

Corticobasal degeneration may present with asymmetrical or unilateral upper limb movement disorder, but MRI findings are of frontoparietal cortical atrophy rather than thalamic degeneration [1]. It is well known, however, that lesions in the region of the red nucleus and thalamus may cause movement disorders. Rubral lesions may cause contralateral limb motor abnormalities, and thalamic lesions may result in a wide range of choreiform and dystonic movement abnormalities. A series of 62 cases with thalamic/subthalamic lesions did not produce any cases of isolated tremor, however [2]. The underlying pathology of focal dystonia remains unclear, but

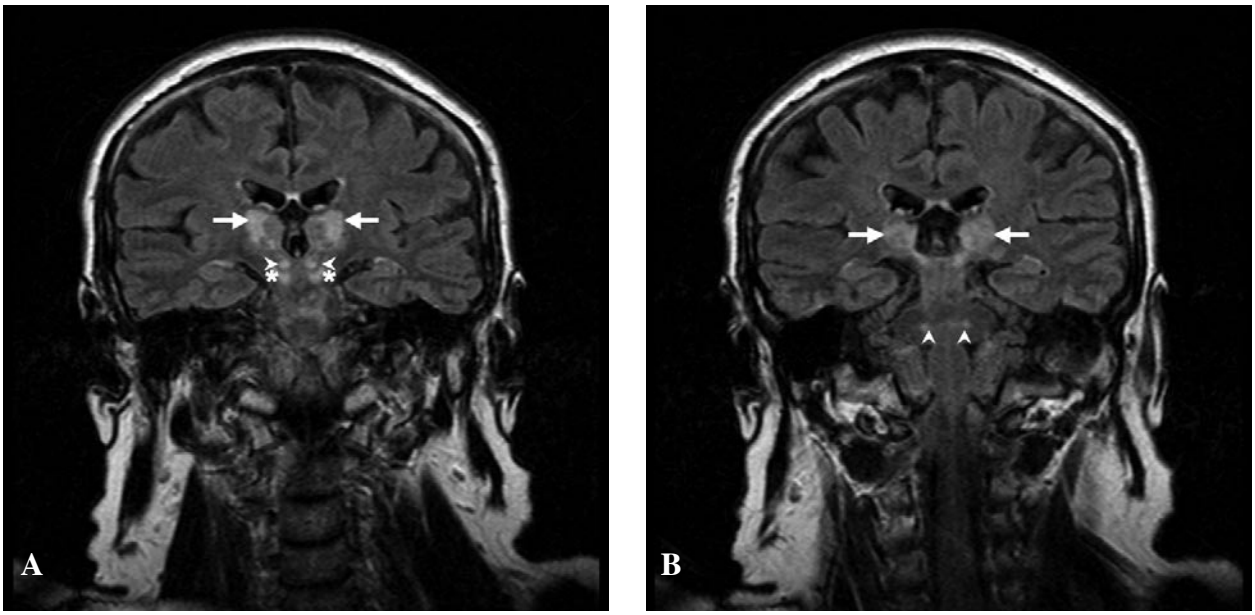

Figure 2. A: Coronal FLAIR demonstrates abnormal high signal through the VPL and VPM (***arrows***), red nuclei (***arrowheads***) and subthalamic nuclei (***asterisks***)*;* **B:** Coronal FLAIR demonstrates high signal within the rubrothalamic tracts and VPL bilaterally (***arrows***) and in the crossing fibres of the dentate-thalamo-rubral tract (***arrowheads***).

functional imaging and stereotactic neuronal recording suggest that functional abnormality of the basal ganglia results in altered thalamic control of cortical motor areas, with a lack of motor inhibition. There is also altered descending control of brainstem and spinal cord inhibitory interneuronal mechanisms [3]. Thalamotomy and, more recently, stereotactic deep brain stimulation of the thalamic nucleus ventralis intermedius are used to treat disabling and medically intractable tremor in Parkinson's disease and benign essential tremor [4].

This case showed significant bilaterally symmetrical changes predominantly involving the thalamus and its connections, and it is perhaps surprising that there was so little in the way of symptomatic neurology. The thalami are complex structures with multiple nuclei, and extensive connections both between the various thalamic nuclei, and with extra-thalamic grey matter. They function predominantly to modulate the vast majority of neural activity projecting to and from the cerebral cortex. Connections between the thalamus and the claustrum have not been described in man, although they have been described in other mammals [5] and it is possible that signal changes in these subinsular areas may represent incidental non-specific parenchymal ischaemic changes. The majority of the structures and pathways that demonstrate abnormal signal in this patient are involved in the control of limb movement. The medial lemniscus conveys information from contralateral proprioception in the upper body whilst the red nucleus and its connections are involved in relaying cortico-cerebellar feedback pathways via the thalamus. The ventral lateral nucleus has input form the globus pallidus, pars reticulata of the substantia nigra and cerebellar nuclei, spinothalamic tract, vestibular nuclei and primary motor cortex to its anterior, medial and posterior divisions respectively. Output from the ventral lateral nucleus extends to the premotor and supplementary motor areas, dorsolateral and medial frontal lobe and primary motor cortex. The subthalamic nuclei and substantial nigra have extensive reciprocal connections principally with the basal ganglia.

It seems likely that this clinico-radiological picture represents the sequelae of the degeneration of a specific set of thalamic nuclei and their connections, possibly those containing a specific cell population. Given that functional studies can demonstrate neuronal functional abnormalities, it is possible that there is abnormal function within the striatum and other areas involved in motor control, despite these areas appearing normal on this conventional MRI. The aetiology of this abnormality remains unclear from the history and imaging: possible causes include exogenous factors such as toxins or viral infection, endogenous genetic factors or combination of the two.

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