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Short communication

Thalamic cramplike pain

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ABSTRACT

Importance: We describe a case of cramplike pain after a left thalamic ischemic stroke, a neglected type of central post-stroke pain and we describe its neuroanatomical correlates.
Observations: A 68-year-old right-handed man presented with right arm, leg, and flank cramplike pain noted upon awakening. Neurological examination was normal, with no evidence of objective sensory abnormalities. Because of the nature of the pain and the preserved sensory function, we first did not consider stroke as a potential cause, and suspected that pain was related to the combined effect of intense physical exercising on the right side and the use of statins. Diffusion-weighted magnetic resonance imaging showed an acute ischemic infarction within the left thalamus. By registering high-resolution 3 T T1-weighted and T2-weighted magnetic resonance images to the Talairach atlas, we showed the infarction is within the border between the pulvinar and the ventral posterior medial nuclei. Brodmann's areas 3, 1, 2, 4 and 6 were identified as the cortical correlates of the ischemic lesion by diffusion tensor tractography.
Conclusions and relevance: Thalamic cramplike pain should be recognized as a type of central post-stroke pain, probably produced by lesions localized to the border between the ventral posterior and pulvinar nuclei and connected to the ipsilateral primary somatosensory cortex and primary and secondary motor cortices.

1. Introduction

Central post stroke pain can arise from lesions anywhere along the spinothalamic and thalamocortical pathways and constitutes an unusual consequence of ischemic stroke. The estimated incidence of pain after stroke ranges between 1 and 12%, but when the thalamus is affected, it may occur in up to 1 of every 6 patients [1,2].

We herein report a case of isolated thalamic cramplike pain without objective sensory abnormalities in a patient with an acute ischemic stroke affecting the left thalamus. We also describe the anatomical topography of the infarct and the cortical projections associated with the thalamic lesion.

2. Report of a case

A 68-year-old right-handed man presented with right thigh pain that was present upon awakening. The same day, he noted a similar pain in the right arm. He described the pain as cramps or as if the muscles were in permanent contraction. The patient did not report any other symptoms. He was seen at the emergency department and subsequently admitted. Physical examination was unremarkable, with no evident sensory or motor abnormalities. A computed tomography (CT) brain scan ruled out acute ischemic and hemorrhagic lesions, and showed mild volume loss and scattered subcortical and deep white matter hypodensities. A subsequent brain magnetic resonance imaging (MRI) was performed three days after admission and he was discharged home.

His medical history was relevant for hypertension, hyperlipidemia, obstructive sleep apnea, a non-ST myocardial infarction when he was 63 years-old, and a probable transient ischemic attack 23 years earlier, characterized by a left facial droop lasting less than 24 h. His medications comprised aspirin 81 mg/daily and rosuvastatin 40 mg/daily. Twelve days later he developed a severe "crampy" (sic) right lower quadrant pain and was admitted again with unremarkable abdominal CT and ultrasound results.

We assessed the patient at the TIA/Stroke Clinic 16 days after symptom onset. He was still suffering intermittent right arm, leg, and flank cramps during the daytime and in sleep. Cramps presented intermittently, as 3 to 5 episodes/h lasting approximately 3 min, with a maximum intensity of 9/10 and fading rapidly into less severe background pain (5/10). He reported that the day before the symptom onset he had been exercising predominantly with his right arm and leg. General and neurological examination including sensory examination (light touch, pain, temperature, joint position, graphesthesia, stereognosis and vibration sensation), were unremarkable. As the brain MRI was performed elsewhere, we were not aware of the results. We first suspected that symptoms could be related to the combined effect of high-dose statins and the predominantly right sided physical

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exercise done the day before awakening with cramps [3]. For this reason, we ordered a serum creatine kinase determination and we asked the patient to exercise predominantly on his left extremities to see if we could reproduce symptoms. Creatine kinase was 126 U/L (normal value ≤ 190 U/L) and vigorous exercising did not elicit any new symptoms.

A few days later we were able to review the brain MRI, which disclosed a 0.8 × 0.5 cm area of restricted diffusion within the left posterolateral thalamus (Fig. 1).

In a follow-up visit six weeks after the stroke, cramps were still present and there were no changes on neurological examination. A needle electromyogram of the muscles indicated by the patient as being the most painful was performed on the same day, without electrophysiological evidence of cramps. Almost 6 months after the stroke, and after 4 weeks of treatment with increasing but still low doses of gabapentin (1800 mg/daily) the patient was still suffering from pain, but the cramps were less frequent (approximately one every 2 h) and the intensity of the background pain had increased to 8/10.

A 3 T MRI was performed seven weeks after symptom onset using a Siemens TIM Trio MRI system with a 32-channel head coil (Siemens, Erlangen, Germany). A magnetization-prepared rapid acquisition with gradient echo (MPRAGE) sagittal T1-weighted scan was acquired in sagittal orientation with the following parameters: repetition time = 1900 ms, echo time = 2.32 ms, and voxel size 1 mm isometric. A diffusion weighted echo-planar imaging (EPI) series was also acquired with the following parameters: repetition time = 7600 ms, echo time = 79 ms, gradient directions = 64, b-value = 1000 s/mm^2, voxel size 2 mm isometric, matrix size 128 × 128, and number of excitations (NEX) = 1. The MR acquisition was performed with Generalized Autocalibrating Partially Parallel Acquisition (GRAPPA) with a parallel factor of 2 (iPAT = 2).

Both anatomical and diffusion weighted images were imported into Brainvoyager QX software (Brain Innovation BV, Maastricht, The Netherlands) for analysis. High-resolution T1-weighted images were registered to the Talairach atlas (non-rigid registration) [4]. The lesion coordinates were mapped from the FSL MNI152 space to the Talairach space using the correction provided by Lancaster et al. [5]: center of gravity (x, y, z): −17.61, −25.56, and 5.31; X extents (min x, max x): −23.87 and −12.51; Y extents (min y, max y): −30.90 and −18.69; and Z extents (min z, max z): −4.25 and 14.56. With these labels we identified the border between the pulvinar and the ventral posterior medial nuclei as the region affected by the left thalamic infarction (Fig. 2). Diffusion scans were corrected for eddy currents and then processed for tractography. The seed point was chosen in the hypointense lesion in the thalamus on T1-weighted images and was defined through a manually drawn region of interest. Fiber tracts were constructed using the seed point. The reconstructed tracts were then superimposed onto the high-resolution anatomical images by linear registration (Fig. 3 and online Supplemental videos 1 and 2). The fractional anisotropy (FA) threshold for the track termination was chosen as 0.20. The thalamic infarct had connections with Brodmann's areas (BA) 3, 1, 2, 4 and 6.

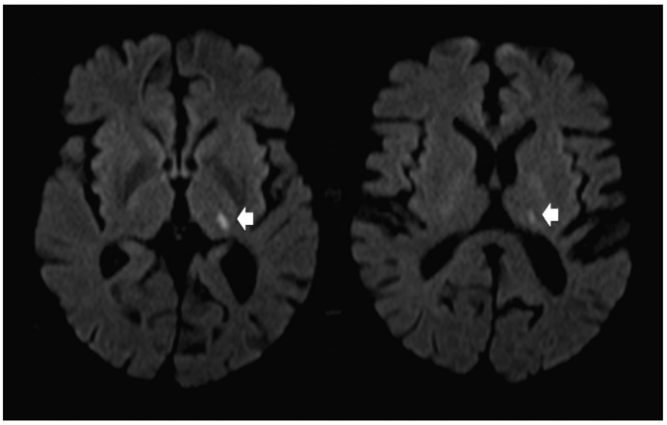

Fig. 1. Diffusion weighted MRI of the brain performed on the day of symptom onset. White arrows show restricted diffusion within the left thalamus in 2 consecutive 0.5 mm axial images.

3. Comment

We herein describe a case of thalamic cramplike pain without objective sensory abnormalities in a patient with a left thalamic acute ischemic stroke (Fig. 1). The thalamic lesion affected the border between the pulvinar and the ventral posterior medial nuclei. These nuclei were connected to BA 3, 1, 2, 4, and 6.

Cramplike pain after thalamic stroke was described more than 100 years ago [6]. However, thalamic cramps have been rarely reported in the medical literature. Because of this scarcity of reports, we suspect that this variant of central post stroke pain could be potentially neglected as a stroke symptom in clinical practice. The first descriptions of thalamic pain by Déjerine, Egger and Roussy at the beginning of the 20th Century configured a syndrome characterized by: (1) a rapidly regressive mild hemiplegia; (2) a persistent and never complete superficial hemianesthesia (i.e. "touch, pain, and temperature"), sometimes replaced by cutaneous hyperesthesia, but always accompanied by marked and persistent impairment of deep sensation (i.e. "articular, muscular, tendinous, osseous"); (3) mild hemiataxia and "more or less" complete astereognosis; (4) severe, persistent, paroxysmal, often intolerable pain on the hemiplegic side; and (5) choreoathetoid movements in the paralyzed limbs [7,8]. Pain described by Déjerine and Roussy in their 8 cases was spontaneous or evoked and portrayed as "superficial or deep burns", "twinges", "violent and painful pressure placed on the skin", and "stabbing of a dagger" [8]. Subsequent reports have categorized the nature of central post stroke pain as "burning", "aching", "pricking", "freezing", "squeezing", "lacerating", or "shooting" [1]. Despite these varied and numerous descriptions, there are very few reports defining central post stroke pain of thalamic origin as cramps. To the best of our knowledge, Head and Holmes were the first to report cramps as a variant of post-stroke thalamic pain [6]. Three of their 24 patients (cases 5, 7, and 11) had cramps along with other manifestations of Déjerine–Roussy syndrome. Mauguière and Desmedt described the pain of a subgroup of stroke patients as "cramplike" [9]. However, touch and joint position sensations were abnormal in all these cases, while in our patient sensory examination was normal; although we acknowledge that by using more sensitive sensory tests (i.e. thermal thresholds testing) we could have been able to detect some sensory abnormalities.

The use of 3 T MRI and diffusor tensor imaging (DTI) allowed us to identify the precise neuroanatomical correlate of cramplike pain. In line with our findings, the boundary between the ventral posterior and pulvinar nuclei has been identified as a specific region at a very high risk of generating central post stroke pain (odds ratio = 81) [10]. In the study of Sprenger et al., 9 out of 10 patients with central post-stroke pain of thalamic origin had a lesion within the ventral posterior nucleus, while 8 of 10 control subjects without pain also had lesions of other parts of the ventral posterior nucleus; emphasizing that this precise lesion location is the key factor for triggering central post stroke pain. In this sense, our report serves to accurately localize the boundary between the pulvinar and the ventral posterior medial nuclei of the thalamus as the region responsible for isolated thalamic cramps without objective sensory abnormalities. Our findings are further supported by previous investigations suggesting that the posterior portion of the ventral medial nucleus (VMpo) may constitute a specific relay for pain and temperature sensations in the human brain [11].

The thalamic infarct of the reported patient had connections with the ipsilateral primary somatosensory cortex, and ipsilateral primary