

## SHORT REPORT

# Vim thalamotomy for Holmes' tremor secondary to midbrain tumour

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Holmes' (rubral or midbrain) tremor is an unusual combination of 2 Hz to 5 Hz rest, postural, and kinetic tremors of an upper extremity. This tremor has been considered to result from the lesions in the vicinity of the red nucleus in the midbrain. There has been no systematic analysis of the surgical target in the Holmes' tremor so far of nucleus ventrointermedius (Vim) or globus pallidus interna. This 26 year old man gradually developed a disabling midbrain tremor involving both the distal and proximal parts of the left upper arm. Additional neurological findings included oculomotor palsy and ataxia of the left arm. On the radiological studies, a mass lesion (germinoma) was found on the midbrain tegmentum, which was treated by conventional radiation therapy. Although there was improvement in the radiological imaging, his midbrain tremor became intolerable despite medical treatment. The authors performed MR guided stereotactic Vim thalamotomy. With radiofrequency lesioning in the right Vim, his resting, postural, and action tremors were much alleviated in both the distal and proximal parts of the left upper extremity. The authors consider that Vim thalamotomy is still an effective means of controlling midbrain tremors involving the proximal upper limb.

In 1904, Holmes described a tremor of the fingers with a rotation at the wrist and elbow, which he named "rubral tremor." He believed that the rubrospinal tract was involved in the generation of this tremor based on the observation of a patient with an organic lesion in the rubrospinal tract in the pons.<sup>1</sup> Certain animal experiments have demonstrated that this tremor is caused by a combined lesion of the red nucleus and neighbouring structures.<sup>2-4</sup> However, the red nucleus itself has not been proved as the source of abnormal oscillation, and concomitant damage to the cerebellothalamic and nigrostriatal fibres may be necessary.<sup>2</sup> The term rubral tremor has been recently replaced by Holmes' tremor,<sup>5</sup> which has been associated with a variety of conditions, including cerebral haemorrhage and ischaemia,<sup>6</sup> trauma,<sup>7,8</sup> neuroleptics,<sup>9</sup> multiple sclerosis,<sup>10</sup> neoplasm,<sup>11</sup> radiation.<sup>12</sup> The Holmes' tremor is described as a combination of rest and postural and kinetic tremors. The amplitude at rest may be small, but on attempting posture it becomes uncontrollable, and attempted movement may cause a peak.<sup>13</sup> The frequency of the midbrain tremor may vary from 2 Hz to 5 Hz, may be higher still during active movement,<sup>14</sup> and disappears during sleep.<sup>5,6,12</sup> Unlike most other forms of the tremor, the proximal muscles may be affected more than the distal muscles. In addition, there are almost always other signs of midbrain damage, such as hemiparesis and cranial nerve palsy.<sup>14</sup> We report a rare case of medically intractable Holmes' tremor secondary to a midbrain germinoma, which was successfully relieved by Vim thalamotomy.

## CASE REPORT

A 22 year old right handed man gradually developed diplopia, and tremor and ataxia in the left arm over a two month period. The tremor initially affected the left forearm, but later progressed successively to the left upper arm and the left shoulder. There was no headache or any other symptoms of increased intracranial pressure. He had no significant medical history of head trauma and was taking no medication. On examination, the patient had a mild resting tremor involving the left upper limb. On attempting posture, the irregular low frequency tremor became grossly uncontrollable, and further exacerbated by any attempted movement. The tremor involved the left shoulder and the proximal and distal limb only. Ipsilateral cerebellar signs were noted in his left upper extremity, but the muscle strength and tendon reflexes were preserved.

Purposeful movements of the left hand were associated with vigorous kinetic tremor. He showed a partial right oculomotor palsy presenting mild ptosis, limitations of medial and upward gaze, and slightly dilated pupils with a preserved light reflex. There was no palatal myoclonus or any other sign of cranial nerve involvement. Magnetic resonance imaging (MRI) depicted an oval mass lesion on the right midbrain tegmentum. The isointense lesion on FLAIR image showed homogenous enhancement with gadolinium-DTPA on a T1 weighted image involving the right red nucleus (fig 1). The upper border of the lesion extended to the right thalamus, and perilesional edema was noted in the right midbrain. The tumour marker studies of serum and cerebrospinal fluid, such as placental alkaline phosphatase, human chorionic gonadotropin, and  $\alpha$  fetoprotein, were negative. Positron emission tomography (PET) detected an increased uptake of C<sup>11</sup>-methionine, but not 2-[18F]-fluoro-2-deoxy-D-glucose (18FDG), in the right midbrain lesion. Proton magnetic resonance spectroscopy (<sup>1</sup>H MRS) showed a lower ratio of N-acetylaspartate to creatine ratio and a higher ratio of choline to creatine. The MRI, C<sup>11</sup>-methionine PET and proton MRS findings indicated a tumorous lesion in the midbrain. The patient and his family refused a stereotactic biopsy because of its potential risks, so a tentative diagnosis of germinoma was made and the patient was treated with focal external radiation (total 15 Gy). As expected, the lesion regressed considerably on MRI at one month after the completion of radiation; however, the tremor worsened after the lesion completely disappeared, and was refractory to medication (clonazepam 30 mg, levodopa 1000 mg, trihexiphenidyl 17.5 mg for 10 months). Despite medical treatment the tremor considerably worsened with time so that the patient could not perform ordinary daily activities and we planned an MRI guided stereotactic thalamotomy after disappearance of mass lesion in MRI (fig 2). The stereotactic coordinates of right nucleus ventrointermedius (Vim) was 5 mm anterior to the posterior commissure, 15 mm lateral to the midline, and at the level of intercommissural line. Intraoperative stimulation (3 volts, 50 Hz, 1 ms) of the right nucleus Vim dramatically attenuated both the static and kinetic components of this tremor. After a



**Figure 1** Magnetic resonance imaging of the midbrain tumour manifesting a Holmes' tremor. An isointense mass with surrounding peritumoral edema on axial FLAIR image (left panel) was homogeneously enhanced with gadolinium-DTPA in a T1 weighted coronal (right panel) image.



**Figure 2** Postoperative magnetic resonance imaging (two weeks postoperatively) shows a successful radiofrequency lesioning in the Vim thalamic nucleus.

radiofrequency lesion (70°C 60 s and 80°C 60 s) was made, the resting and postural tremors of the proximal and distal arm markedly improved, although a mild kinetic tremor remained. The oculomotor palsy, left arm ataxia, and cerebellar signs remained unchanged and his postoperative course was uneventful. The Holmes' tremor has been continuously attenuated 14 months after the Vim thalamotomy and his neurological signs have remained stable.

## DISCUSSION

It is difficult to treat a Holmes' tremor. Though L-dopa and clonazepam have been reported to be effective,<sup>6 15 16</sup> these are single case reports and no controlled studies have been performed because of the rarity of this disorder. Generally pharmacotherapy is not effective,<sup>6 13 17 18</sup> and the surgical indication for a tumour induced tremor has not been established.

In general, the neurological deficit or the neuroendocrinological impairment attributable to direct tumour invasion can be alleviated by treating the primary lesion. In this case, the tremor was still disabling and refractory to medical treatment despite improvements in the radiological follow up, thus indicating the irreversible damage to the neuronal tracts in the upper brain stem. The surgical treatment of Holmes' tremors with stereotactic radiofrequency lesioning and high frequency radiofrequency thalamic stimulation has been reported.<sup>6 8 17-19</sup> The Vim nucleus has been reported to be the effective target of stereotactic radiofrequency lesioning in Holmes' tremors.<sup>7 17 19</sup>

Recently Miyagi *et al* reported the effectiveness of posteroventral pallidotomy for Holmes' tremor seen in the proximal segment of contralateral upper extremities.<sup>18</sup> In their intraoperative findings, Vim stimulation relieved only the postural tremor in the distal segment of the contralateral upper extremity (distal tremor), but had no effect on the vigorous action tremor (proximal tremor). They emphasised the importance of case selection, namely distal tremor compared with proximal tremor.<sup>18</sup> The selective lesions or chronic stimulation of Vim according to its somatotopy for either proximal or lower extremity tremors have been reported.<sup>20 21</sup> However, in the case of the proximal tremor, relatively larger lesions may be required because the somatotopies of the proximal or truncal muscles are poorly understood.<sup>22</sup> Therefore, a stereotaxy in the Vim for either proximal tremors or lower extremity tremors is not as popular or effective as it is for the distal tremors seen in Parkinsonian or essential tremors.

In this case, subsequent lesioning of Vim abolished the resting and postural tremor almost completely and the action tremor considerably. The tremor initially took place in the distal forearm and later extended to the proximal upper extremity. This propagation may suggest that the primary tremor mediating pathway was predominant in the pallidothalamic pathway, and it extended to involve the pallidoreticular pathway in accordance with the tumour invasion.<sup>18</sup> The effectiveness of Vim thalamotomy (especially on the distal tremor at rest and posturing) may also support this speculation. Our findings confirm the effectiveness of Vim thalamotomy as an effective surgical treatment in certain cases of Holmes' tremor.

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