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Thalamic Syndrome and Cortical Hypoperfusion on Technetium-99m HM-PAO Brain SPECT

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The six patients included in this study had painful dysesthesia, resulting from vascular lesions in or near the thalamus, confirmed by computerized tomography(CT) brain scan. Using hexamethyl propyleneamine oxime(HM-PAO) single photon emission computed tomography(SPECT) brain scanning, regional cerebral perfusion(rCP) was demonstrated. In contrast to three patients with lesions near the thalamus who showed symmetrical cortical radioactivity, the other three patients with thalamic lesions revealed decreased rCP in the ipsilateral cerebral cortex on HM-PAO brain SPECT. We thought that the loss of afferent activating stimuli from the thalamus led to decreased cortical neuronal activity and the following hypoperfusion. In patients with thalamic syndrome resulting from thalamic lesions, the role of the remote effect of the thalamic damage and consequent cortical deregulation in the development of thalamic pain and/or neuropsychological symptoms cannot be excluded completely.

Key Words: Thalamic syndrome, HM-PAO brain SPECT, cortical hypoperfusion.

Spontaneous pain and painful overreaction to external stimuli resulting from lesion confined to the central nervous system(CNS) was named as "central pain(CP)" (Riddoch 1938).

Although stroke involving ventral posterolateral thalamus is the leading cause of CP (Martin 1969), other lesions, regardless of the level, located in or very near the pain transmitting pathway could lead to CP (Riddoch 1938; Fields and Adams 1974). Since Dejerine and Roussy provided formal accounts of "Le syndrome thalamique" in 1906, many possible pathogeneses have been proposed (Fields 1987), but no one could explain all the features of the CP.

Although positron emission tomography(PET) demonstrated cortical hypometabolism and its topographical correlations in patients with thalamic infarction (Baron *et al.* 1986), the absence of cortical deregulation in a case of thalamic syndrome was reported. They concluded that deregulation of the thalamus itself, not the corticothalamic or thalamocortical loop, leads to thalamic syndrome (Laterre *et al.* 1988).

And so, we evaluated cortical perfusion with HM-PAO brain SPECT in six patients with thalamic syndrome.

PATIENTS AND METHODS

The mean age of the two men and four women included in this study was 54.5 years (range 47-64). All had spontaneous pain and painful dysesthesia opposite to the lesion side on brain CT scan, which occurred one to ten months after a stroke. At the time of the occurence of painful dysesthesia, chest x-ray, blood cell count, routine blood study, and electrocardiography showed no abnormalities.

The patients were evaluated by two neurologists and the results were summarized in Table 1. There was no evidence of peripheral neuropathy on physical and laboratory examination.

We evaluated brain CT scans, which were done at the time of the cerebrovascular accidents(CVA) and/or a few days before performing HM-PAO brain SPECT, to localize the lesion. The thalamic lesion was divided into the anterior medial part, which projects to the frontoparietal lobe, and the posterior lateral part, wich projects to the temporoparietal lobe (Fields 1987).

We performed SPECT by the following method. Eluting with 0.5 ml normal saline, (Eluent for du Pont

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Table 1. Clinical summary of the patients with thalamic syndrome

Patient	Sex/Age,yr	Character & location of the lesion		Latent period after stroke	Cutaneous hyperesthesia	Spontaneous pain	Deep sense impairment	Chorea	Dysarthria	Motor deficit	Babinski sign
Patient 1	M/51	IR	AT	few months	+	+	+	−	+	+	−
Patient 2	F/47	IR,IL,HL	PLT	few months	+	+	+	−	+	+	−
Patient 3	F/62	IL	PLT	two months	+	+	−	+	−	−	−
Patient 4	F/50	HL	IC,P	few months	+	−	+	−	+	+	−
Patient 5	M/53	HL	IC	ten months	+	+	+	+	+	+	−
Patient 6	F/64	IR	IC	one month	+	+	+	−	−	−	−

(+; Present, −; Absent, I: Infarction, H; Hemorrhage, L; Left, R; Right, PLT; Posterolateral thalamus, AT; Anterior thalamus, IC; Internal capsule, P; Putamen)

Technetium 99m Generator), a maximum of 30 mCi Technetium 99m was prepared from NEN Medical Products Technetium 99m Generator, du Pont co., and the vials containing freeze-dried HM-PAO (Ceretec®) were reconstituted. Within 10 minutes after preparation, intravenous administration of this radioactive pharmaceuticals was conducted in a quiet room with dimmed light. Twenty minutes after injection, SPECT was performed with a rotating scinticamera (MaxiCamera Autotune ZS, General Electric Co., 20 seconds 64 single scans per full rotation). Axial and coronal image reconstruction was achieved using a Star computer, General Electric Co..

After SPECT imagination, we evaluated the correlations between the location of the lesion on brain CT scan and the hypoperfused cortex on HM-PAO brain SPECT.

RESULTS

Three patients demonstrated lesions within the thalamus and the other three patients near the thalamus on brain CT scan.

Patients 1, 2, and 3, who showed lesions in the thalamus on brain CT scan, revealed decreased cerebral perfusion in the ipsilateral cortex on the axial and coronal HM-PAO SPECT image. Patient 1 has a infarction at the anterior part of the right thalamus on CT brain scan, the tuberothalamic arterial territory (Radford *et al.* 1985) (Fig. 1), demonstrated decreased cortical perfusion in the frontal, parietal, and temporal cortex (Fig. 2). Patient 2, who had suffered

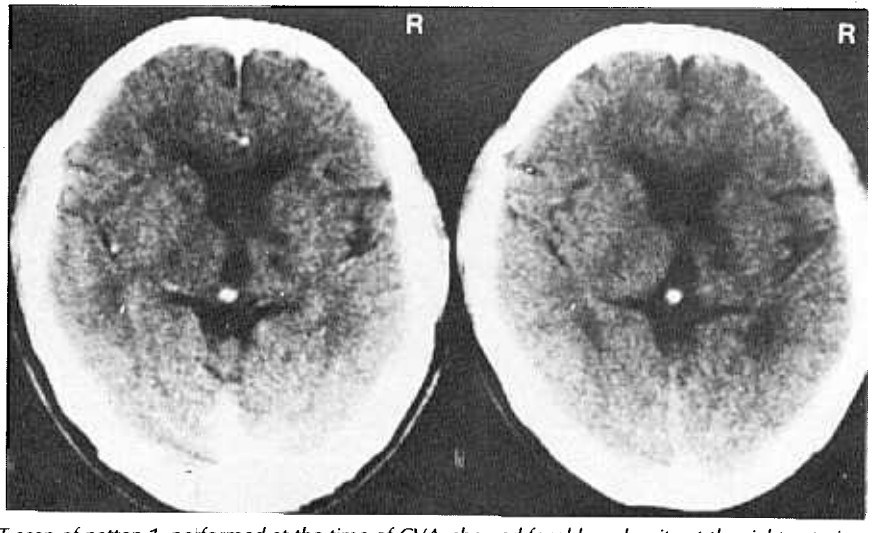

Fig. 1. *Brain CT scan of patten 1, performed at the time of CVA, showed focal low density at the right anterior thalamic area.*

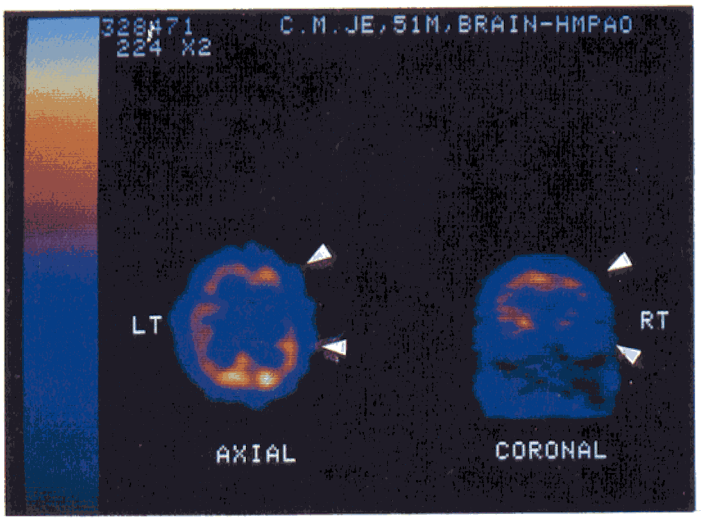

Fig. 2. HM-PAO brain SPECT image of the Patient 1 demonstrated decreased rCP in the frontal, temporal, and parietal cortex, ipsilateral to the thalmic lesion.

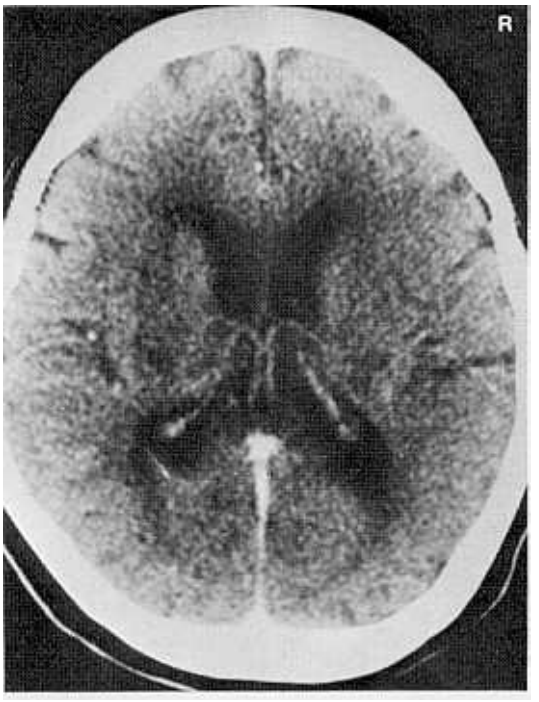

Fig. 3. Brain CT-scan of patient 2, performed one week before HM-PAO brain SPECT, showed focal low densities in the bilateral posterolateral thalamus.

recurrent infarctions and hemorrhage at both sides of the posterolateral thalamus on brain CT scans, the thalamogeniculate arterial territory (Fig. 3), demonstrated decreased cortical perfusion in the bilateral parietal and temporal cotex (Fig. 4), Patient 3, who had a infarction in the posterolateral thalmus on brain CT scan, the thalamogeniculate arterial territory (Fig. 5), demonstrated decreased cortical perfusion in the ipsilateral parietotemporal contex (Fig. 6).

In contrast to the patients with thalamic lesions, the other three patients with lesions out of the thalamus (Patient 4; hemorrhage, Patient 5; hemorrhage, Patient 6; infarction), demonstrated symmetrical cortical radioactivity. Because these three patients demonstrated similar HM-PAO SPECT images, and we showed only the brain CT scan (Fig. 7) and HM-PAO SPECT image (Fig. 8) of Patient 4.

DISCUSSION

Thalamic pain is usually described as "shooting, boring, crushing, or aching". This is usually associated with hyperpathia, which occurs suddenly after a period of latency, exploding to reach maximal intensity in the beginning. Thereafter, it spreads diffusely and persists for some time after cessation of the stimuli. In addition to sensory changes, some mood changes, choreic movements (Dejerine and Roussy 1906, Adams and Victor 1985), and autonomic and vasomotor dysfunction accompanied it (Martin 1969; Krishnan and France 1988).

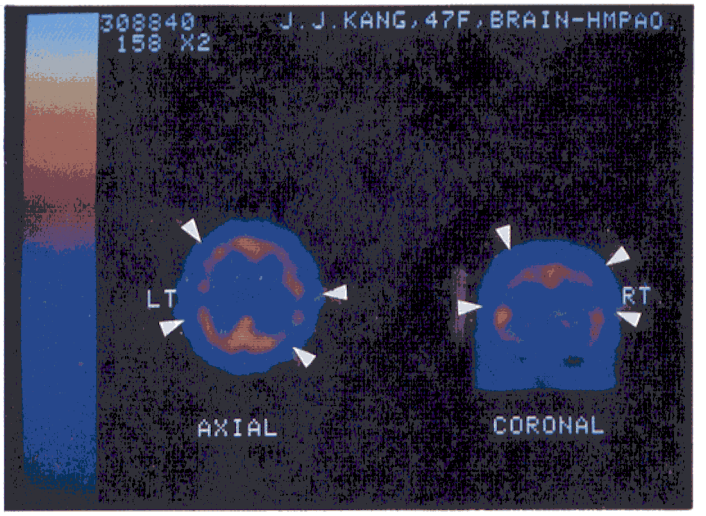

Fig. 4. HM-PAO brain SPECT image of patient 2, demonstrated bilateral hypoperfusion in the parietal and temporal cortex.

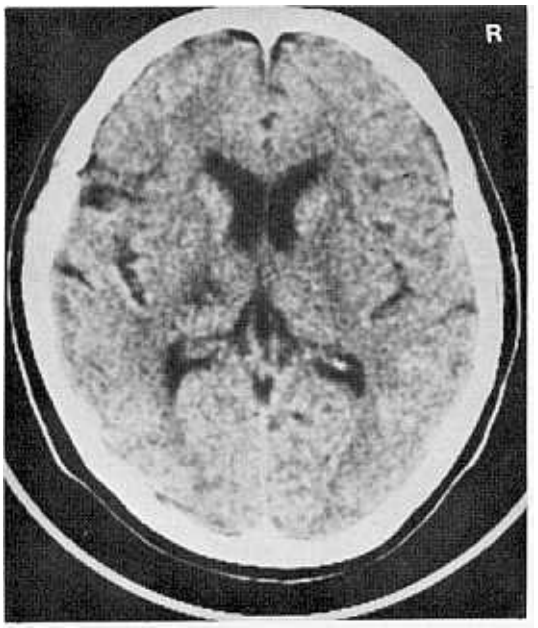

Fig. 5. Brain CT scan of patient 3 showed focal low density in the left posterolateral thalamus.

Not only the thalamic lesion, but the lesion in or around the pain transmitting pathways could lead to CP that is indistinguishable from that produced by thalamic lesions (Fields and Adams 1974).

The axons of the pain transmitting pathways, the spinothalamic tract, segregate into a medial and the lateral division as they approach the thalamus. The medial division terminate most densely in the anterior part (central lateral(CL) and submedius(SM) nucleus) and lateral division in the posterior part (ventrobasal(VB) nucleus and posterior nuclear group) of the thalamus (Fessard *et al.* 1985). And then, the nuclei give rise to cortical projection, VB to the somatosensory cortex (Melzack and Casey 1968), and CL and SM mostly to the frontal cortex and limbic system (Fessard *et al.* 1985). The former subserves the sensory-discriminative, and the latter the affective-motivational aspects of pain (Melzack and Casey 1968).

Among the arteries supplying the thalamus and its surroundings, thalamogeniculate, choroidal, and tuberothalamic arterial lesions have been established to produce thalamic pain (Martin 1969).

In addition to these anatomic considerations, many possible pathogeneses have been proposed without confirmation, such as substitution of previous inhibiting synapses by excitatory one during reinnervation (Basbaum and Wall 1976), irritation of the sympathetic system (Alajouanine and Brunelli 1935), reverberating circuit between hyperirritable cell of ventral posterolateral and the medial nucleus (Sano 1977), and loss of pain inhibiting mechanisms contained in the cortex (Head and Holmes 1911), striopallidal system (Foerster 1927), thalamus (Lhemitte 1933), lemniscal system (Riddoch 1938) or any level of CNS (Wall 1980). Central pain is not due to a unique pathophysiological mechanism, and the above

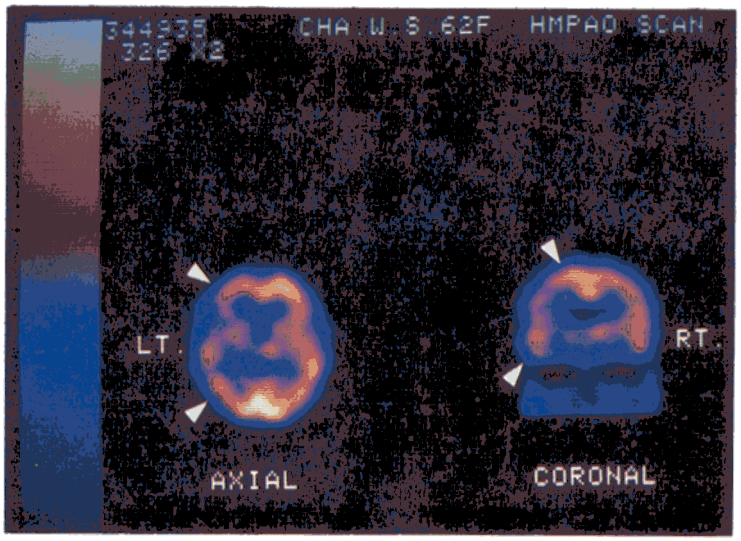

Fig. 6. HM-PAO SPECT image of the patient 3 demonstrated decreased rCP in the parietotemporal cortex ipsilateral to the thalamic lesion.

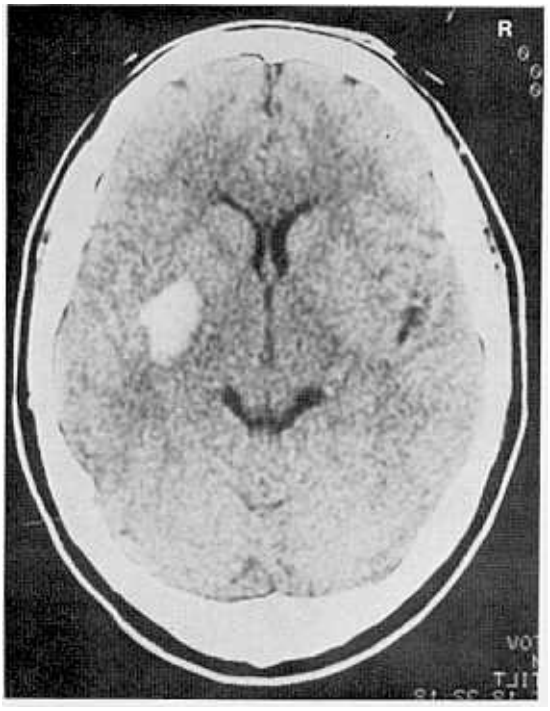

Fig. 7. Brain CT scans of Patient 4, performed at the time of CVA showed a small hematoma at the left putamen and internal capsule.

mechanisms are probably simultaneously at work and combine to give rise to the whole spectrum of CP.

With respect to cortical alterations, Head and Holmes proposed that injury of the cerebral cortex, which exerts through corticothalamic fibers a damping influence of the thalamic nuclei, resulted in hyperactivity of the thalamus so that afferent impulses evoked exaggerated response and heightened sensation. Although it is uncertain whether the thalamocortical and corticothalmic loops are involved in thalamic syndrome, ipsilateral cortical and subcortical atrophy have been reported in six patients with thalamic tumor. The authors proposed that disappearance of thalamic ganglion cells and nerve fibers, leads to secondary Wallerian degeneration of the projecting fiber from the thalamus and retrograde degeneration of the efferent fibers to the thalamus (Kawk *et al.* 1978).

Recently, PET gave a fresh impulse to a study on such functional alteration. In 1986, Baron *et al.* reported decreased cortical metabolism following thalamic infarction, and they proposed that the cortical hypometabolism was due to one or other of the following: (1) anterograde Wallerian degeneration of the thalamocortical terminals, (2) retrograde degeneration of the corticothalmic neurons, secondary to a lesion of the thalamocortical terminals, (3) transsynaptic degeneration of the cortical neurons, secondary to a lesion of the thalamocortical synapsis, (4) reduced functional activity of the cortical neurons (without actual degeneration), secondary to the loss of activating afference from the thalamus. Although confirmative measurements were not made, there were some

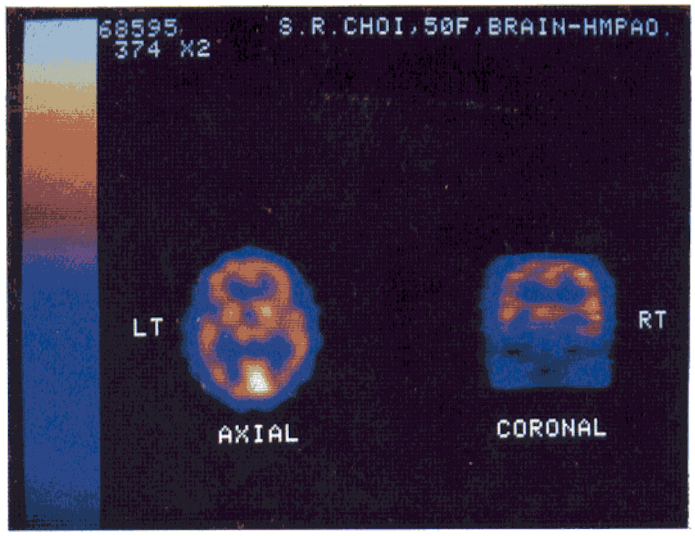

Fig. 8. HM-PAO brain SPECT image of patient 4 demonstrated symmetric cortical rCP.

topographical correlations between the location of the vascular thalamic lesion and hypometabolic cortex. They concluded that reduced functional activity of the cortical neurons secondary to the loss of activating afferences from the thalamus lead to cortical hypometabolism.

But in 1988. Laterre *et al.* reported thalamic hypometabolism and cortical sparing on PET study in a case of thalamic syndrome, resulting from laminar infarction confined to the putamen and posterior limb of the internal capsule. They thought that thalamic pain originated from deregulated processing of pain related-information at the thalamic level.

We had some questions about the cortical sparing. And so, we evaluated cortical perfusion using Technetium-99m-HM-PAO that was reported to cross the intact blood brain barrier and distribute in the brain in proportion to regional blood flow (Sharp *et al.* 1986). It had been proved that HM-PAO brain SPECT was an appropriate method for the detection of diaschisis (neuronal death by deafferentation) (Leonard *et al.* 1986; Biersack *et al.* 1987).

Considering the cause of cortical hypoperfusion demonstrated in this study, the possibility of cortical ischemia due to a vascular lesion at the cortex may be rejected since the involved vascular territories are different. And in patients with hemorrhage, considering the time interval between stroke and HM-PAO brain SPECT imagination, a direct consequence of mass effect could be ruled out (Baron *et al.* 1986).

Thus, we thought that sequential occurrences of loss of afferent activating stimuli from the thalamus to cortex, cortical neuronal deregulation, decreased cortical neuronal activity, decreased demand, and decreased rCP might be the causes of demonstrated cortical hypoperfusion (Lou *et al.* 1987). But we could not say so conclusively, because there was a small number of patients included in this study, HM-PAO SPECT has limited resolution (Kung *et al.* 1983), and no trial had been made to define the correlation between neuropsychological deficits and cortical hypoperfusion.

Further evaluation, including a greater number of patients and the use of imaging with good resolution, is needed to define the topographical correlations and the role of cortical hypoperfusion in the development of thalamic syndrome.

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