

# Slowly progressive limb-kinetic apraxia with a decrease in unilateral cerebral blood flow

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We report two patients with slowly progressive motor disorders, whose principal manifestations were asymmetric limb-kinetic apraxia and muscle rigidity. In both patients MRI revealed no responsible lesion, whereas single photon emission computed tomography (SPECT) showed a decrease in cerebral blood flow (CBF) in the unilateral hemisphere. One patient with mainly right-sided apraxia had a decreased CBF in the left central region between the frontal and parietal cortices, and the other patient with left-sided apraxia in the right parietal cortex. In agreement with asymmetric clinical symptoms, the regional CBF decrease in the unilateral cortical areas including the frontal and parietal cortices may suggest a degenerative disease, presumably diagnosed as having corticobasal degeneration.

**B. Okuda, H. Tachibana, K. Kawabata, M. Takeda, M. Sugita**

Fifth Department of Internal Medicine, Hyogo College of Medicine, Japan

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B. Okuda, Fifth Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya 663, Japan

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Limb apraxia is divided into three subgroups consisting of limb-kinetic apraxia (LKA), ideomotor apraxia and ideational apraxia (1). While ideomotor apraxia and ideational apraxia have been well explored, LKA remains to be elucidated (2, 3). We present two patients with slowly progressive limb apraxia, mainly LKA, in combination with extrapyramidal symptoms. CBF measurement by using SPECT and N-isopropyl-p[<sup>123</sup>I]iodoamphetamine (<sup>123</sup>I-IMP) as a tracer in both patients showed a decreased perfusion in the frontal cortex and/or the parietal cortex on the side contralateral to the greater apraxia. The unique combination of asymmetric LKA and unilateral CBF decrease is distinct from the dementing diseases such as Alzheimer's disease or Pick's disease, and appears to be the early manifestations of a degenerative disease, called corticobasal degeneration.

## Case report

### Case 1

A 72-year-old right-handed man without a personal or familial history of neurologic disease was admitted to our hospital due to progressive limb-clumsiness. He initially noticed difficulty in using the right hand, especially in manipulating objects, three years before admission. One year later clumsiness developed in the right lower limb, and he suffered from gait disturbance: Movement disturbance grad-

ually progressed, and then he became unable to write letters or pick up an object, and frequently fell to the right side. Recently, he found clumsiness in the left hand. Since he was diagnosed as having cervical spondylosis, he underwent laminectomy of the cervical spine two months before admission to our department. Limb-clumsiness, however, persisted. On admission, he was neither demented nor aphasic (Mini-Mental State Score 28/30, WAIS verbal IQ 99). He presented with bilateral limb apraxia predominating on the right side and constructional apraxia. He had difficulty making fine finger movements such as tapping, picking up a coin and imitating finger patterns, especially with the right hand (Fig. 1 A,B). He had also clumsiness in gestures such as waving goodbye in response to verbal command and imitation, and clumsiness in object manipulation such as using scissors. Voluntary movements of the right leg were also difficult when initiating gait and putting on shoes. Alien hand sign was not seen. Eye movements were preserved except for saccadic pursuit. He was mildly bradykinetic, and muscle tone was rigid in the right upper limb and paratonic in the other limbs. Muscle strength was normally preserved in all limbs. Involuntary movements were undetected. Deep tendon reflexes were brisk on both sides without Babinski reflex. Limb-coordination was clumsy on the right side, but not ataxic. Superficial and deep sensations were normal. Cortical sensation such as two-point discrimination

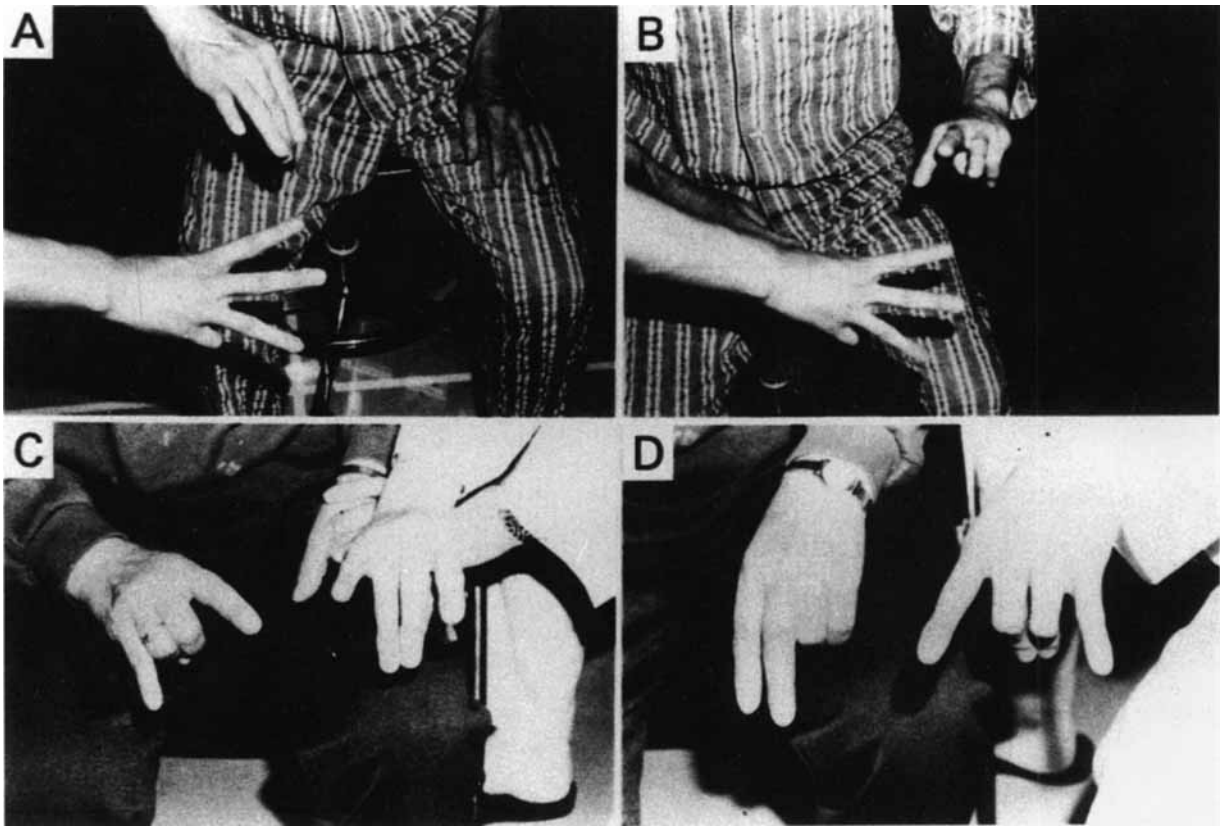


Fig. 1. Imitation of finger patterns in two patients. Patient 1 has bilateral apraxia predominating on the right side (A, B). Patient 2 had apraxia in the left hand, but imitation is correctly performed by the right hand (C,D).

and stereognosis was preserved. He walked with small steps, but neither pulsion phenomenon nor kinesie paradoxale was observed. T2-weighted MRI showed atrophic change in the left hemisphere, and a high intensity spot in the right subcortical white matter (Fig. 2). SPECT using  $^{123}\text{I}$ -IMP ( $^{123}\text{I}$ -IMP SPECT) demonstrated decreased  $^{123}\text{I}$ -uptake in the left hemisphere, especially in the central region between the frontal and parietal cortices (Fig. 3). Intravenous digital subtraction angiogram (IV-DSA) denoted no remarkable change of the main vessels. EEG revealed no significant abnormality except sporadic theta waves in the left frontal leads. Levodopa was administrated, but motor disorders remained unchanged.

#### Case 2

A 64-year-old right-handed woman without a personal or familial history of neurologic disease was admitted to our hospital because of progressive gait disturbance. She started having difficulty in moving the left leg three years before admission. She often fell to the left side. She became incapable of going up the stairs or putting on shoes. Several months later she found clumsiness in the left hand. She had difficulty in getting up and picking up an object with

the left hand. A family member noticed a decrease in her speech a year before admission. She was diagnosed as having Parkinson's disease in another hospital. On admission to our hospital, she was not aphasic but moderately demented (Mini-Mental State Score 16/30, WAIS was not performed). Limb apraxia was revealed on the left side. She had difficulty making precise finger movements of the left hand such as tapping and imitating finger patterns (Fig. 1 C,D). Manipulating objects of the left hand was difficult when picking up a coin, putting on gloves and buttoning. Gestures such as waving goodbye and saluting were clumsy on the left side in response to verbal command and imitation. Movements of the right hand were slow but correctly performed. Voluntary movements of the left leg were also difficult when initiating gait and kicking a ball. Constructional ability was disturbed. Alien hand sign was absent. Cortical sense such as two-point discrimination, stereognosis and graphesthesia was preserved. She presented with bilateral upward gaze palsy with preserved Bell's phenomenon. Muscle strength was normal in all limbs. She was bradykinetic, and muscle tone of the limbs was rigid predominating on the left side. Deep tendon reflexes were normal without Babinski reflex. Neither involuntary movements nor cerebellar ataxia was de-

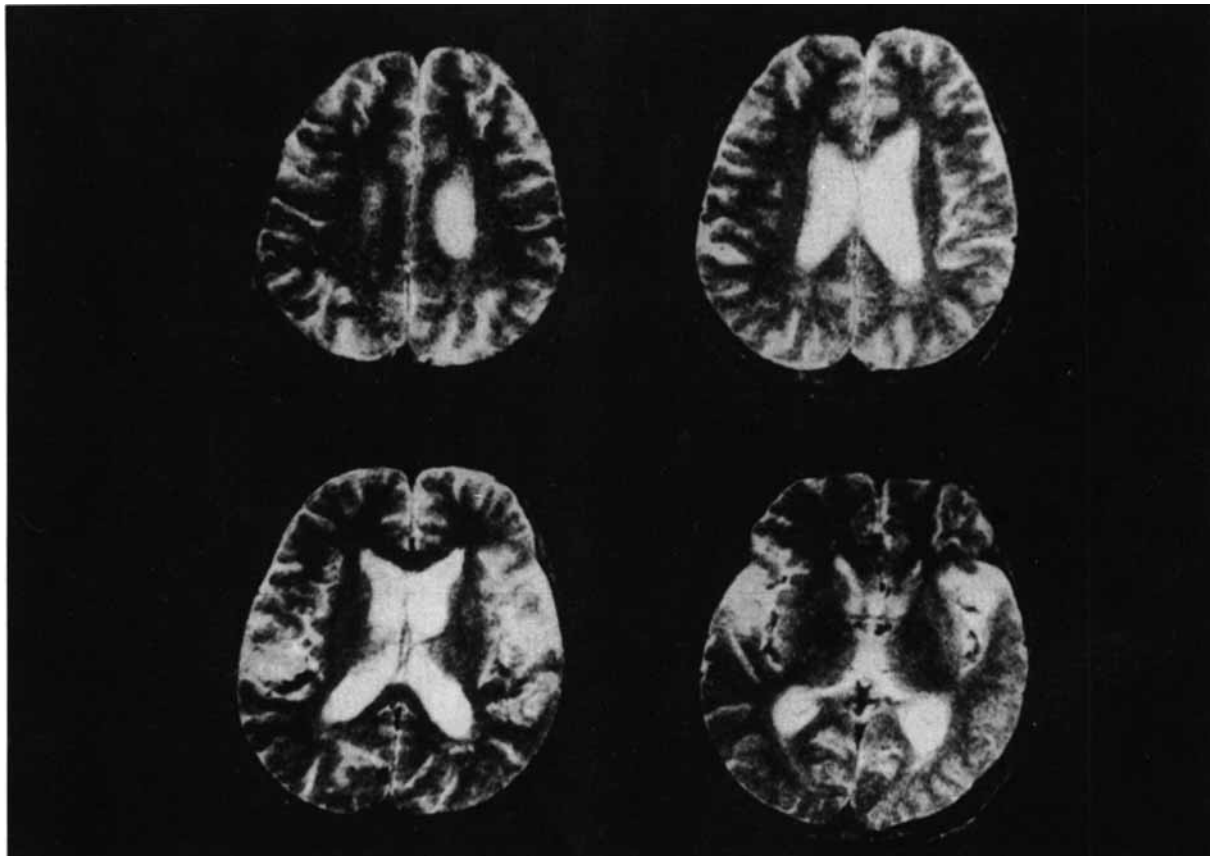


Fig. 2. T2-weighted MRI (Spin echo, TR 2000 ms, TE 120 ms) in Patient 1. A high intensity spot in the right subcortical white matter is seen, and there is atrophic change in the left hemisphere.

tected. T2-weighted MRI showed high intensity spots in the periventricular region, but no cortical lesion was seen (Fig. 4). IMP-SPECT disclosed a decrease in  $^{123}\text{I}$ -uptake in the right parietal cortex (Fig. 5). IV-DSA revealed no remarkable change of the main vessels. EEG gave normal findings. Levodopa was administered, but motor disorders did not improve.

#### Discussion

Ideomotor apraxia and ideational apraxia are generally defined as a disorder of symbolic action such as gesture and a disorder of a series of acts such as object handling, respectively (1, 4). Unlike ideomotor apraxia and ideational apraxia, LKA is defined as a breakdown of previously skillful movements, manifested by difficulty making fine precise movements (3, 4). The disorder is more obvious when testing finger movements and can be evident when making gestures, imitating postures, and using objects (1). Liepmann postulated that a lesion in the sensory motor cortex induced LKA on the contralateral side (3). While the status of LKA remains disputable, several cases have been reported to have

motor clumsiness of this type (4–6). The responsible lesion is considered to be located in the central region between the frontal and parietal cortices (precentral gyrus and postcentral gyrus) (5, 6). It is hypothesized that LKA is induced by impaired organization for motor control involving interaction between the motor cortex and the somatosensory cortex (7, 8). Our two patients had disorders of gesture and object handling, but more prominent disorder was difficulty making fine finger movements. Accordingly, the apraxic disorders in these patients were mostly ascribed to LKA rather than ideomotor apraxia or ideational apraxia. Muscle rigidity may play a role in difficulty in performing voluntary movements. Patients with parkinsonism often have slowness in limb movements but can correctly perform purposeful movements or finger imitation until becoming severely rigid and akinetic. Thus, motor clumsiness in our patients cannot be attributed to muscle rigidity. Patient 1 had bilateral LKA with predominance on the right side, and Patient 2 had left-sided LKA. A decrease in CBF suggested by IMP-SPECT, in the left central region in patient 1 and in the right parietal region in Patient 2, may account for LKA on the contralateral side respec-

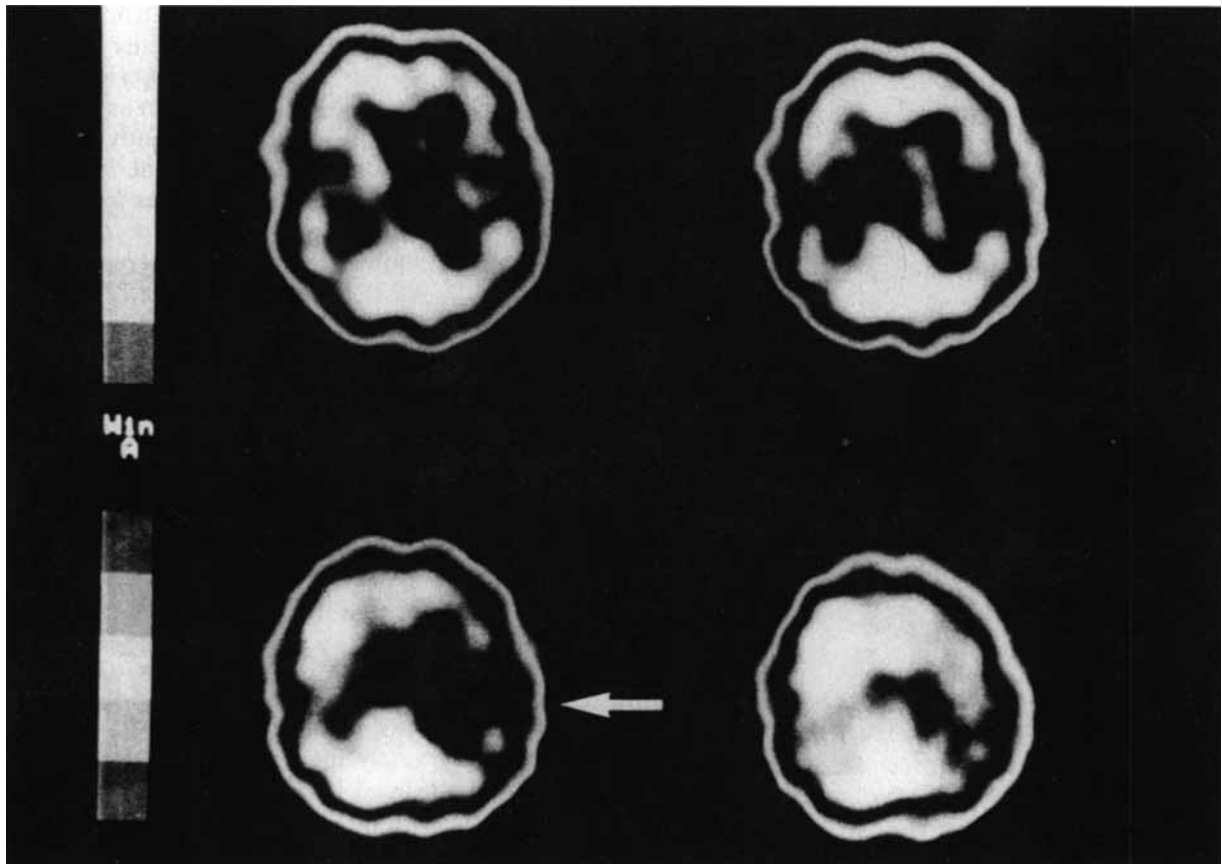


Fig. 3.  $^{123}\text{I}$ -IMP SPECT axial view performed 30 min after administration of  $^{123}\text{I}$ -IMP (early image) in Patient 1. In comparison to the right hemisphere,  $^{123}\text{I}$ -uptake in the left hemisphere is decreased, especially in the central region (arrow).

tively. Furthermore, a decreased CBF in the left central region in Patient 1 may be related to bilateral LKA, because the dominant hemisphere lesion can induce bilateral clumsiness (9).

Since Mesulam's report (10), diseases causing progressive impairment of higher cortical function have been discussed in connection with Pick's disease, Alzheimer's disease, or Creutzfeldt-Jacob disease (11–13). Slowly progressive apraxia combined with extrapyramidal signs has been reported in patients with degenerative diseases, called corticobasal degeneration (14) or cortical-basal ganglionic degeneration (CBD) (15). In these cases reported, the usual age of onset was in the sixth and seventh decades, and limb-clumsiness gradually developed with asymmetric features. Cerebral cortical signs consisted of apraxia, cortical sensory loss, constructional disability and alien hand signs, suggesting dysfunction of the frontal and parietal cortices. The other main clinical features were extrapyramidal signs such as akinesia, rigidity and involuntary movements. Dementia, pyramidal signs and supranuclear oculomotor palsy were sometimes seen. The common neuropathological findings of autopsied cases were degenerative changes consisting of gliosis and neu-

ronal achromasia in both the cerebral cortex, mainly the frontal and parietal cortices, and the basal ganglia, mainly the substantia nigra.

The clinical features of our two cases appear to be compatible with CBD. Patient 1 had typical clinical features common to CBD described above. The patient had cervical spondylois, but no improvement of the motor disorders could be obtained following laminectomy. The apraxic disorders with rigidity cannot be ascribed to cervical spondylosis. Since Patient 2 was demented, this case raises a possibility of the other dementing diseases, including Pick's disease, Alzheimer's disease, progressive supranuclear palsy, Parkinson's disease, or diffuse Lewy body disease. The patient's initial and principal symptoms, however, were motor disturbance comprising left-sided apraxia and parkinsonism, which were unusual in Pick's disease or Alzheimer's disease. Furthermore, cortical signs such as limb apraxia and constructional disability cannot occur in progressive supranuclear palsy, Parkinson's disease or diffuse Lewy body disease. To our knowledge, LKA has not been reported in the above diseases. The other possibility is that a vascular disorder may play a role in the motor disorders. While MRI revealed

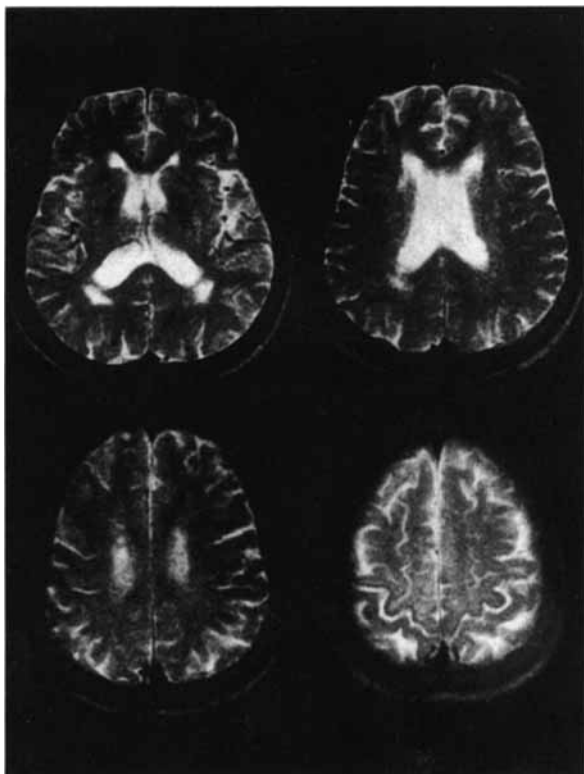


Fig. 4. T2-weighted MRI (Spin echo, TR 2000 ms, TE 120 ms) in Patient 2. High intensity spots in the periventricular area are seen, but no cortical lesion is noted.

no responsible lesion, IMP-SPECT suggested the regional hypoperfusion in both patients. A vascular insufficiency may be associated with a degenerative process. A few cases of CBD presented with mild vessel disorders in pathological examinations (15). Our two patients, however, had no risk factors for stroke, and IV-DSA showed no significant changes of the main vessels in both patients. Above all, a vascular insufficiency can hardly cause the slow progression of both higher cortical and basal ganglionic dysfunctions. The unique combination of asymmetric LKA and extrapyramidal signs favor the diagnosis of CBD. Therefore, we presented two cases as slowly progressive LKA, presumably diagnosed as having CBD. However, the possibility of a distinct entity with focal cortical degeneration cannot be excluded (16, 17). Moreover, CBD has not been recognized fully as a clinical entity. Further clinicopathological studies are required to make a distinction between CBD and the other disorders causing progressive deterioration of cerebral cortical or subcortical functions such as Pick's disease, Alzheimer's disease or progressive supranuclear palsy.

In the present series, a hemispheric decrease in CBF corresponded to neuropathological findings of CBD, which revealed degenerative changes in the cerebral cortex, mainly in the frontal and parietal

cortices. Sawle et al. reported positron emission tomography (PET) findings in clinically diagnosed CBD (18). PET showed that fluorodopa uptake was asymmetrically reduced in the striatum and that cortical oxygen metabolism was significantly depressed in the superior and posterior temporal, inferior parietal and occipital association cortices as well as in the posterior frontal cortex. In the present study, IMP-SPECT showed a unilateral decrease in  $^{123}\text{I}$ -uptake in the basal ganglia in Patient 1, but asymmetric uptake in the basal ganglia was undetectable in Patient 2. The cortical hypometabolic areas demonstrated by PET are larger than the cortical regions where  $^{123}\text{I}$ -uptake was decreased in the present study. The inconsistent results may be explained by the difference in duration of patient's illness studied in both series. Both patients in the present study had a history of three years, whereas most patients studied by Sawle et al. had a history of more than four years. Moreover, patients of the latter groups presented with supranuclear gaze palsies, myoclonus, or alien limb sign together with clinical features seen in the former group. These findings suggest that either the frontal or parietal cortex or both cortices may be unilaterally involved in the early stage of CBD, accompanied by asymmetric involvement of the basal ganglia, and that the degenerative process may extend to the other cortical areas in the later stage. Thus, a regional CBF decrease in the unilateral frontal or parietal cortex or both cortices may aid the clinical diagnosis of CBD, especially in the early stage.

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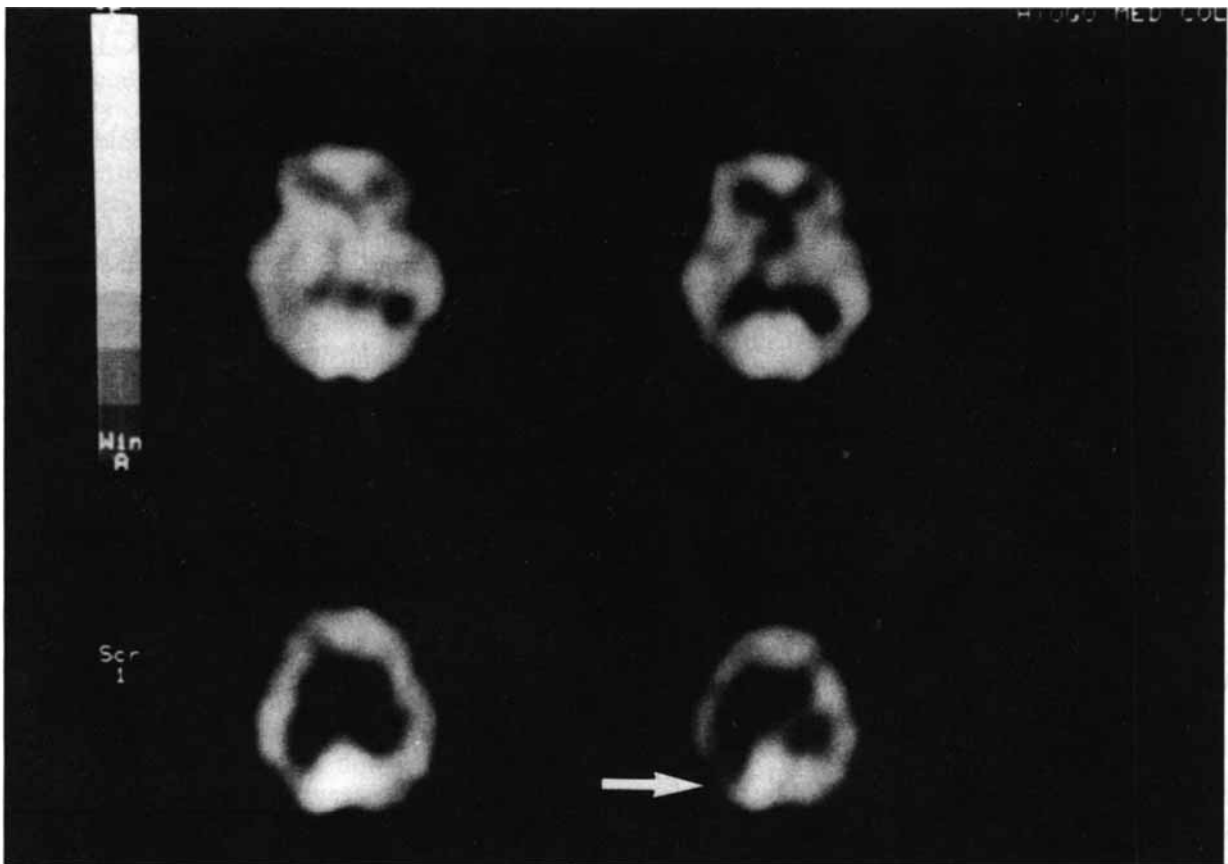


Fig. 5.  $^{123}\text{I}$ -IMP SPECT axial view performed 30 min after administration of  $^{123}\text{I}$ -IMP (early image) in Patient 2.  $^{123}\text{I}$ -uptake is reduced in the right parietal region (arrow).

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