Cenesthetic hallucinations in a patient with Parkinson's disease

Hallucinations are a side effect of treatment with levodopa and dopamine agonists. They are more common in patients with Parkinson's disease with advanced age and cognitive impairment.¹⁻³ Hallucinations secondary to dopaminergic drugs are usually visual, and less often, auditory.⁴ We describe a patient who developed cenesthetic hallucinations during pergolide and levodopa treatment.

A 66 year old woman with Parkinson's disease, predominantly rigid akinetic, had been treated with carbidopa-levodopa since the age of 55 in 1984. When she was evaluated for the first time in our hospital in 1991, she was treated with 62.5/625 mg/day of carbidopa/levodopa divided into five doses, 5 mg/day selegiline, and 7.5 mg/day bromocriptine. She had motor fluctuations and mild peak dose dyskinesias. Pergolide was introduced in gradually increasing doses up to 3 mg/day as replacement for bromocriptine, with a good initial response. However, in 1992, the parkinsonian symptoms had worsened progressively, and she spent around 60% of the day in "off" periods. Pergolide was increased up to 5 mg/day with a good response. In October 1993, standard levodopa was changed to a controlled release preparation of carbidopa/levodopa, up to 1400 mg/day divided into seven doses, and pergolide was reduced to 3 mg/day because of dyskinesias. On this combination, the parkinsonian symptoms remained stabilised until July 1995, the "off" time being about 20% of the day. At that time, controlled release carbidopa/levodopa needed to be increased up to 450/1800 mg/day and pergolide up to 3.5 mg/day. In September 1995, the patient developed somatic hallucinations that she described as feeling as if her bowels and bladder extruded from the distal parts of her upper limbs. She tried to avoid the extrusion of these organs by compulsively scratching her arms, up to the point of inducing erosions. Reduction of pergolide to 2.5 mg/day and of controlled release carbidopa/levodopa to 350/1400 mg/day did not control the hallucinations, but they improved greatly with clozapine in gradually increasing doses up to 150 mg/day. The somatic hallucinations remained stabilised until November 1996. At that time the dose of clozapine needed to be increased up to 200 mg/day because of worsening. In January 1997, these symptoms were again well controlled.

Somatic hallucinations are defined as false sensations of things occurring in or to the body. When they are visceral in origin they are named cenesthetic hallucinations.⁵ Our patient developed cenesthetic hallucinations that were likely to be related to the antiparkinsonian treatment and were controlled adequately with clozapine. To our knowledge, cenesthetic hallucinations had not been described in this situation previously, and should be added to the range of psychiatric side effects of antiparkinsonian drugs.

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Neuroleptic malignant syndrome-like condition in multiple system atrophy

Neuroleptic malignant syndrome (NMS) usually occurs during treatment with neuroleptic drugs, but a similar condition may occur after a sudden withdrawal of antiparkinsonian drugs or an imbalance of the monoaminergic systems in the brain. On the other hand, extrapyramidal symptoms and dysautonomia are common in multiple system atrophy, which is a disorder of the monoaminergic system, affecting dopamine, noradrenaline, and serotonin. Catecholaminergic agents are sometimes used to treat multiple system atrophy, and NMS-like conditions may also occur in patients with multiple system atrophy.^{1,2} We found six episodes of an NMS-like condition in three out of 14 patients with multiple system atrophy over a one year period (table).

Patient 1 was a 47 year old man who had been receiving antiparkinsonian drugs from the age of 45. Because the drugs did not cause much response, he needed an increasing dosage. On 12 October 1995, the daily dosage of bromocriptine was decreased from 26 mg to 8.6 mg and he was also given 6 mg trihexiphenidyl HCl.

After four days, he developed myalgia, hallucination, hyperhidrosis, and severe bradycardia. On 19 October his body temperature

was 37.7°C. He had high serum creatine kinase (5264 IU (normal <180 IU/l)) and was admitted.

Bromocriptine (26 mg/day) and dantrolene sodium produced an immediate response, but also urinary retention and orthostatic hypotension. Brain MRI suggested a diagnosis of multiple system atrophy. In February 1996, the addition of 50 mg/day trazodone HCl induced bradykinesia and rigidity. Serum creatine kinase was 2560 IU/l. Discontinuation of trazodone HCl and administration of 75 mg dantrolene sodium produced an improvement.

Patient 2 was a 58 year old man who had developed gait disturbance with parkinsonism at the age of 51 and was taking antiparkinsonian drugs. In July 1991, he received low temperature burning on his abdominal skin. After 10 days, he developed rigidity and was admitted to hospital. He had severe rigidity, pyrexia with high serum concentrations of creatine kinase (34 080 IU/l), blood urea nitrogen (51 mg/dl), and creatinine (10 mg/dl), urinary myoglobin (600 mg/day), and showed oliguria. He was diagnosed as having acute renal failure caused by myoglobinuria, and haemodialysis resulted in recovery. In January 1992, he was transferred to our hospital. In June 1993, he developed pneumonia and received antibiotics with a continuation of antiparkinsonian drugs. After recovery from pneumonia, he continued to have a pyrexia, increased rigidity, tremor, and bradykinesia. On 12 July, his temperature was 39.8°C with high serum creatine kinase (2418 IU/l). Discontinuation of L-threo-DOPS and an increase in bromocriptine (17.2 mg to 26 mg) with intravenous dantrolene sodium (40 mg/day) therapy produced improvement. Discontinuation of dantrolene led to a relapse. Increased dosage of levodopa/dopa-decarboxylase inhibitor (300/75 mg to 900/225 mg/day) produced a response. In August 1995, he had a body temperature of 40.3°C and raised creatine kinase (1200 IU/l) with no inflammation or altered medication. Treatment with intravenous dantrolene sodium (40 mg/day) induced recovery within three days.

Patient 3 was a 56 year old woman with a six year history of dysautonomia. At the age of 52, she was pyrexial in the summer. Four years later, she had severe ataxia with hypotonia and no involuntary movements. On 10 July 1987 L-threo-DOPS (600 mg/day) was added to the previous drugs to decrease

Description of patients

Patient	Illness	Sex	Age	Duration of illness	Month of NMS-like episode	Maximum body temp (°C)	Maximum serum CK (IU/l)	Cause	Course
1	SND	M	47	3	October	37.7	5264	Decrease of bromocriptine	Recovery by bromocriptine and dantrolene
			47	4	February	37.4	2560	Trazodone	Recovery by bromocriptine and withdrawal of trazodone
2	SND	M	54	3	July	>39.0	34081	Low temperature burning	Renal failure. Recovery by dialysis
			56	5	July	39.8	2518	Pneumonia	Recovery by antiparkinsonian drugs and dantrolene
			58	7	August	40.3	1200	Pyrexia	Recovery by dantrolene
3	OPCA	F	56	6	July	42.0	1500	Pyrexia + L-threo-DOPS	Died of disseminated intravascular coagulation

SND=Striatonigral degeneration; OPCA=olivopontocerebellar atrophy; CK=creatinine kinase.

autonomic failure. On 21 July, she had a low grade fever, and was transferred to Kishiwada Hospital. Her temperature was 37.5°C and she had a normal serum creatine kinase concentration. Five days later, she developed a pyrexia of 42°C with high serum creatine kinase (1500 IU/l). Intravenous dantrolene therapy produced no response and she died of disseminated intravascular coagulation two days later.

In these six episodes of an NMS-like condition, one was caused by decreased antiparkinson medication, one by an antidepressant drug, two by complications, one by hyperthermia from environmental origin, and one by hyperthermia with L-threo-DOPS. Five episodes occurred in the hot season. In Japan, we had hot days in October 1995. Two cases had multiple episodes.

A putative mechanism of pyrexia in an NMS-like condition is dopamine depletion in the extrapyramidal system causing severe rigidity, resulting in high fever and creatine kinase leakage from the muscle to the blood.¹ With antipsychotic drugs, the stronger the affinity to the D₂ receptor, the more often NMS occurs. On the other hand, some agents which do not influence the dopaminergic system also produce an NMS-like condition. An abnormal mechanism in the monoaminergic system is thought to alter the function of the thermal centre of the hypothalamus.³ The setting of body temperature becomes higher by activation of the noradrenergic system, and lower by the dopaminergic or serotonergic systems in the thermal centre.⁴ An imbalance of these systems via medication or other causes may trigger an NMS-like condition. In patient 1, an antidepressant, which influences serotonergic and noradrenergic activities, caused the second episode.

It is characteristic that five episodes were caused by somatic stresses such as infection or hyperthermia of various origins. This condition occurred during the hot season in patients with or without antiparkinson drugs. In a patient with vascular parkinsonism not receiving antiparkinsonian drugs, an NMS-like condition after typical hyperthermia⁵ was reported to be immediately alleviated by intravenous levodopa therapy. This suggests that activation of the dopaminergic system was important in the NMS-like condition even when dopamine depletion was not its cause. In patient 3, treatment of pyrexia with L-threo-DOPS, a precursor of noradrenaline, caused a further increase in body temperature and development of an NMS-like condition. This substance is effective for akinesia in Parkinson's disease and dysautonomia, and is reported to provoke an NMS-like condition by causing monoaminergic imbalance in the CNS.² A change in hypothalamic noradrenergic activity caused by L-threo-DOPS seems to precipitate an NMS-like condition.

Besides withdrawal of dopaminergic agents, administration of agents which alter monoaminergic neuron activities, stresses to the body, and heat increase from various causes tend to be triggers of an NMS-like condition. Patients with multiple system atrophy, which usually affects thermal regulation, are particularly at risk of developing the condition.

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Non-Hodgkin's lymphoma as a new cause of non-thrombotic superior sagittal sinus occlusion

The syndrome of non-thrombotic superior sagittal sinus occlusion is an uncommon complication of local neoplastic disease which presents clinically as chronic intracranial hypertension without focal signs.¹ A few cases have been reported as complications of midline tumours involving the occipital region such as Ewing's sarcoma, plasmacytoma, neuroblastoma, and disseminated carcinoma of the breast.¹⁻⁴

To our knowledge, this is the first case report in which this complication appeared secondary to a non-Hodgkin's lymphoma.

A 36 year old man presented with a subcutaneous mass in the occipital region of the scalp which had increased in size during the past year. His medical history was unremarkable.

The tumour was painless, hard, and fixed to underlying tissue. Neurological examination was normal, except for bilateral papilloedema. Visual acuity was normal. Cranial MRI disclosed an occipital subcutaneous tumour 10×8×3 cm in diameter. Surrounding bone was thickened, and part of the mass extended extradurally, causing displacement of the venous sinuses. Normal signal void in the superior sagittal sinus in T1 weighted images was replaced by a hyperintense signal (figure, A). Complete coagulation studies were normal. The tumour biopsy disclosed a non-Hodgkin's lymphoma and extension study showed a metastatic lesion in the right femur, confirmed by biopsy.

The patient was treated with local radiotherapy and chemotherapy (six sessions CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)).

The subcutaneous mass had disappeared two months later. At one year follow up the patient did not complain of neurological or ophthalmological symptoms, and recent MRI and magnetic resonance angiography showed the absence of occipital tumour and superior sagittal sinus occlusion (figure, B).

(A) Sagittal cerebral T1 weighted (TR 441, TE 15) MRI (1 tesla) showing an occipital subcutaneous tumour infiltrating bone and extending extradurally causing occlusion of superior sagittal sinus (arrow); note a retention cyst in sphenoid sinus. (B) Sagittal cerebral T1 weighted (TR 600, TE 15) MRI (1.5 tesla) one year after local radiotherapy and chemotherapy: the mass has disappeared and superior sagittal sinus has returned to normal.

The syndrome of non-thrombotic occlusion of the superior sagittal sinus, first described by Plant *et al.*¹ consists of compressive occlusion of dural venous sinuses secondary to midline tumours in the occipital region of the skull. The clinically distinctive feature is the lack of focal signs in the course of chronic intracranial hypertension.

The most common thrombotic occlusion of the superior sagittal sinus is an acute disorder, usually with disturbance of consciousness and focal signs, including seizures and paresis.⁵ Reported cases of occlusion of the superior sagittal sinus associated with neoplastic disease have usually been examples of thrombotic complications secondary to hypercoagulability states.

The syndrome of non-thrombotic occlusion of the superior sagittal sinus occurs when a tumour produces an extradural tissue mass beneath the inner table of the skull, and it is difficult to differentiate between compressive occlusion of the superior sagittal sinus or tumour invasion of the dura and sinus. Cerebral angiography may help in such differentiation, but unfortunately, this examination was not performed in our patient.

This complication has not been described in tumours that commonly give rise to bone metastases such as carcinoma of the bronchus, which develop expanding lytic lesions in the skull with minimal soft tissue involvement. Previous cases of non-thrombotic occlusion of the superior sagittal sinus have been reported secondary to solitary plasmacytoma, Ewing's sarcoma, disseminated carcinoma of the breast, and neuroblastoma,¹⁻⁴ which, as in our case, all present significant involvement of soft tissue.