Ischaemic optic neuropathy, transverse myelitis, and epilepsy in an anti-phospholipid positive patient with systemic lupus erythematosus

We report a 37 year old woman who had severe, bilateral visual loss in association with transverse myelitis, epilepsy, serological evidence of systemic lupus erythematosus, and the presence of anti-phospholipid antibodies. Recognition of a possible underlying thrombotic aetiology suggests that long term anticoagulation and immunosuppressive treatment could prevent progression and relapses of neurological and ophthalmic complications in patients with antiphospholipid related disease.

The 37 year old housewife was admitted in May 1992 with a three day history of visual loss in her right eye, preceded by a severe frontal headache lasting 24 hours. There were no associated symptoms of retro-orbital tenderness or pain on eye movement.

She had a complex history. Aged 13 months she had febrile convulsions and at 11 years of age developed epilepsy. At 16 years of age she was mildly hypertensive and developed recurrent attacks of angioneurotic oedema, Raynaud’s phenomenon, and photosensitive skin rashes. At the age of 22 she was admitted with diminished power in her right leg, bilateral extensor plantars, and a sensory loss at T2. She improved spontaneously but relapsed a month later with a positive Babinski sign and normal power in her right leg, bilateral extensor plantars, and a sensory level below T9 on the right and between C4 and T2 on the left. All investigations including a myelogram were normal apart from a mildly raised erythrocyte sedimentation rate (55 mm/hour), antinuclear antibody titre borderline at 1/40, DNA binding significantly raised at 61%, and a positive lupus band test. An atypical and probable systemic lupus erythematosus with transverse myelitis was made. Her neurological deficits improved spontaneously with residual weakness on the left. She had recurrent episodes of myelopathy, similar to those described, in the subsequent years, which resolved either spontaneously or with short courses of pulse methylprednisolone once daily and with an INR reduced to 1.9, she had a recurrence of vision loss in her right eye, which once again improved with pulse methylprednisolone and increased anticoagulation (INR > 3.0). On recovery, her visual acuity was 6/9 but there was a persistent right altitudinal field defect. She has subsequently found her vision to be more sensitive to anticoagulation and steroid treatment, stabilising at 10 mg prednisolone once daily and an INR of 3.0, with preservation of visual acuity and field.

Assessment of the differential diagnosis of this patient’s illness includes multiple sclerosis and the syndrome of lupus anticoagulant. Lupus anticoagulant can give rise to neurological disease and in such cases may be associated with systemic lupus erythematosus, as in our patient. Systemic lupus erythematosus only very rarely produces identical symptoms to typical demyelinating optic neuropathy.7 The patient’s new episode of visual loss in both of our patient’s eyes was atypical for primary demyelinating optic neuritis; in her left eye, she had the uncharacteristic features of severe visual loss with late improvement, and later pronounced retinal vascular attenuation, and in the right eye no associated optic neuritis. Repeat DNA and raised C4 concentrations were suggestive of a lupus anticoagulant. Her subsequent response and sensitivity to anticoagulation and steroids, we believe, favour the diagnosis of systemic lupus erythematosus.

Transverse myelitis and epileptiform seizures are known to occur in the presence of antiphospholipid antibodies.8 Ophthalmic veno-occlusive phenomena associated with high levels of phospholipid antibodies include anterior ischaemic optic neuropathy, branch and central retinal artery occlusions, amaurosis fugax, and venous occlusions.9 Splinter haemorrhages have previously been reported to occur in association with ocular vasculocclusive disease in the antiphospholipid syndrome.4 Oppenheimer and Hofbrand in 1986, were the first to describe the association of spinal myelopathy and optic neuritis in a case similar to ours.9 In the same paper, they reviewed 13 previously reported cases of patients with known systemic lupus erythematosus and optic neuritis: six had at some point had a spinal myelopathy and they suggested that disease in the optic nerve and spinal cord might have a common underlying aetiology. Recently, a possible relationship between the two vascular diseases in patients with stroke and antiphospholipid antibodies was reported with affected patients having human brain microvascular endothelial reactive antibodies present.10 The association of antiphospholipid antibodies with transverse myelopathy, epilepsy, and optic neuritis may be part of the spectrum of antiphospholipid antibodies.11 This has important therapeutic implications in that long term anticoagulation, reducing the incidence of vascular thromboses, possibly with immunosuppression, may prevent neurological and neuroophthalmic relapses in...
patients with systemic lupus erythematosus and antiphospholipid antibodies.

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Cocaine induced chronic tics

Since the early 1980s, cocaine misuse has rapidly become more frequent with many users chronically taking large doses of this drug. Cocaine has been increasingly associated with ischaemic stroke, subarachnoid and intracerebral haemorrhage, seizures, migraine-like headaches, toxic encephalopathy, a fatal condition resembling neuroleptic malignant syndrome, and dysautonomia during administration and after withdrawal. It is also a risk factor for neurologic induced dystonia. Some of these complications are caused by its powerful vasoconstric-
ting effect. It also exacerbates the multifocal motor and vocal tics that are part of Tourette's syndrome.1 The first two cases of transient (<4 months) new onset tic disorders were reported in 1990.1 2 We describe a third patient, with no per-
sonal or familial history of Tourette's syndrome, who developed cocaine induced tics over two years.

A 35 year old right handed woman was admitted for investigation of movement dis-
orders which had developed over the two preceding years. She had an otherwise unre-
markable medical record and no family

history of neurological disease. Her psychi-
atriic history showed a personality disorder with aggressive hyperactivity and episodes of depression with polydrug and alcohol misuse, having consumed marijuana, mescaline, LSD, and magic mushrooms from 12 to 17 years of age. There was no evidence of the focal symptoms of obsessive compulsive disorder or tran-
sient tics in childhood. She admitted to binging drinking of alcohol as well as regular and exclusive use of cocaine from the early nineties. She took cocaine intranasally from 26 to 32 years of age, then she switched to "crack" for three years. She also took benzodiazepines during periods of cocaine abstinence to suppress the intrusive route on a virtual one hour. Her first HIV serology test was negative two months previously. She came to us one month before admission. Her symptoms consisted mainly of nostril flaring, arm jerks, gri-
maces, shoulder shrugging, grunting, and head jerks that had progressively increased in frequency and severity. These move-
ments had not disappeared for more than a few hours since the onset. They were mostly brief and jerky but more prolonged move-
ments also occurred, and were exacerbated by anxiety or temporarily suppressed volun-
tarily (for example, waiting for a job interview). Neurological examination showed, in addition to the tics already
described, a mild cogwheel rigidity of the right arm. Tics were more prominent in either extremity. The patient had no other symptoms and was not taking medication. She presented an acute episode of exacerbation after her return from a weekend leave during which she misused both alcohol and cocaine. She had complex tics with coordinated abnormal movements involving her entire body, including eye deviation and rolling, facial contortions, and plaintive vocal sounds. She was also hyperactive, impulsive, and mutilated herself (right fingers).

The abnormal movements disappeared briefly (five minutes) when she ate, and decreased to the basal level after one day.

Her routine blood biochemistry was nor-
mal, as was her EEG. Her CSF proteins were slightly increased (548 ng/ml). A CSF dopamine receptor antagonist study proved negative. CSF homovanillic acid (HVA) was 26-1 ng/ml, 5-hydroxyindolacetic acid (5HIAA) was 16-9 ng/ml, and 3-methoxy-4-hydroxy-
phenyl-ethanolamine (HMPG) was 38-7 ng/ml (normal CSF values of biogenic amines were obtained in 15 age matched controls with lumbar disc herniations. These were: HVA 48-2 (SD 10-1) ng/ml, 5HIAA 22-8 (6-8) ng/ml, and HMPG 118 (5-4) ng/ml). sec-Tc-HMPAO SPECT showed focal regional cerebral blood flow hyperperfusion in the bilateral anterior parietal lobes and parieto-
cerebral cortex, left temporal and cerebellar cortex, and right basal ganglia. Brain CT showed no focal or general atrophy. The only abnormality was dilatation and elonga-
tion of the right vertebral and basilar arteries. Against medical advice, she refused treatment and hastily left the hospital two weeks after admission, during which tics were always present. Neuropsychological evaluation was incomplete and no firm conclusions could be drawn. Pascual-Leone and Dhuna reported two cases of transient new onset tic disorders after a high dose of cocaine in the habitual cocaine misusers. Neither had a personal or family history of tics. After taking an unusu-
ally high dose of cocaine, two patients both intravenously, these two patients presented multifocal motor and vocal tics. The tics resolved over several weeks to four months.2

Our patient seems to be the first case who developed tics after a new onset of cocaine misuse (not crack).3 4 Multifocal motor and vocal tics with chronic cocaine misuse. She took many other drugs from age 12 to 17, but her consumption of cocaine usually limited to three to six times from 26 to 35 (intranasally for six years and "crack"
cocaine for three years). Alcohol (which is also misused by our patient) misuse or alco-
hol withdrawal is not associated with tics in the absence of well known problems.4 5 In our patient the tics were clearly exacerbated by high dose cocaine use. The hyperactivity syndrome presented in the past by our patient could be related to Tourette's syn-
drome and could represent an alternative phenotype for the putative Tourette's syn-
drome gene that might have been predis-
posing this patient to cocaine. This remains speculative, however.

In our patient SPECT showed multifocal abnormalities of regional cerebral blood flow. This may represent the consequence of regional functional damage, directly related to the toxic effects of cocaine, potentiating the physiological response to cocaine, or subclinical cerebral vasculitis.1

Irregularity of the right vertebral artery per-
rated the second hypothesis. The discrete right extrapyramidal hypertonia may have been induced by some of these focal abnormalities. In 16 of 18 cocaine dependent polypid drug users, focal abnormal-
iens were found in the inferior parietal lobe,
in the inferior parietal cortex, temporo-
cortex, anterofrontal cortex, and basal ganglia.4

The major symptoms (multifocal tics) in our patient were not lateralised, however, and did not favour this haemodynamic or structural interpretation.

Many neurotransmitter systems have been implicated but only the dopaminergic (DAergic), noradrenergic (NAergic), opioid, and GABAergic systems have shown consis-
tent abnormalities, and no primary system has emerged in the pathophysiology of tic disorders. Imbalances within different inter-
neurotransmitter systems could account for these abnormalities.1 3 4 1 2 Cocaine is a known
reuptake blocker of the DAergic and NAergic systems. Chronic cocaine con-
sumption leads to depletion of endogenous dopamine and noradrenaline stores and may induce postsynaptic receptor hypersensitivi-
ty. Some studies have shown lower CSF HVA concentrations in patients with tics compared with controls, which return to normal with successful neuroleptic drug treatment.6

The clinical evidence in favour of the DAergic hypothesis is summarised by Lang8: (a) dopamine receptor antagonists are most effective in treating tics; (b) tics often increase with drugs that enhance dopamine neurotransmission (for example, amphetamine); (c) tics may occur as part of tardive dyskinesia (rare). CSF HVA was low in our case, indicating that the DAergic system may play a major part in this disor-
der. It is interesting to note that the use of amphetamine (which seems to cause release of dopamine as well as blocking of its activity leading also to depletion of striatal dopamine and to hypersensitivity of dopamine receptors) is known to induce repetitive stereotypic dyskinesia and may
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