SHORT REPORT

Cogan's syndrome complicated by lacunar brain infarcts

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Abstract

Cogan's syndrome, nonsyphilitic interstitial keratitis with vestibuloauditory dysfunction, is an uncommon disease of young adults, probably a manifestation of vasculitis. A 32 year old woman with this syndrome developed a thalamic syndrome with amnesia and dysphasia due to lacunar infarcts.

Cogan's syndrome, nonsyphilitic interstitial keratitis and vestibuloauditory dysfunction, is an uncommon disease of young adults. Typically it presents as episodes of interstitial keratitis closely preceded or followed by episodes of Ménière's disease-like attacks, rapidly leading to bilateral hearing loss.[1 2] Systemic manifestations are not uncommon and may dominate the clinical picture and prognosis.[1-5] Most authors have considered the disease a part of the spectrum of vasculitis though pathological and immunological evidence is inconclusive. Involvement of small and medium-sized vessels in multiple organ systems has been documented[1 3] and about 10% of patients develop aortitis with subsequent aortic insufficiency.[1 2] Elevated erythrocyte sedimentation rates (ESR), leukocytosis and an association with upper respiratory tract infection, suggest an immunological mechanism.[1-5]

Neurological symptoms and signs, mainly neuropathy and mental changes have been associated with Cogan's syndrome,[1 2 4] but to our knowledge only two cases with strokes as complications have been described, including one of Cogan's original patients.[5 6]

Case report

A 32 year old woman was admitted in January 1986 because of sudden disorientation and right-sided hemiparesis. Her medical history included a left adrenalectomy in 1978 followed by irradiation to the hypophysis because of Cushing's disease, followed by a course of o,p'-DDD (mitotane). Her endocrinological status on follow up was normal. She had been taking diuretics for mild labile hypertension since 1978, but had not used oral contraceptives and had never smoked.

In August 1985, she experienced sudden hearing loss, worse on the right, episodic vertigo and nausea and then unremitting itching pain in both eyes for a month. Mild interstitial keratitis in the right eye and left episcleritis led to the diagnosis of Cogan's syndrome. Although the patient was treated with large doses of methylprednisolone, her hearing deteriorated and she became completely deaf. A month later, corticosteroids were reinstituted because of a severe flare up of interstitial keratitis bilaterally. No systemic findings suggesting vasculitis or aortic valve disease were found. Laboratory screening for connective tissue diseases was normal but for an ESR > 100 mm.

In November 1985, while still on 30 mg/d methylprednisolone, she suffered a mild transient left hemiparesis. A month later she had a short episode of right facial paraesthesia. Neurological examination was normal but computerised tomography (CT) of the brain revealed a hypodense area in the left lateral thalamus compatible with a small infarct (fig A).

In January 1986 she presented with right hemiparesis and disorientation of sudden onset although still on 20 mg/d methylprednisolone. She exhibited a few cushingoid stigmata and was completely deaf but no evidence of active eye inflammation was found. On repeated examinations the systolic blood pressure was 130–145 mm Hg and the diastolic 80–90 mm Hg. Her temperature was normal, there were no orogenital lesions, alopecia or poliosis. She was mildly hemiparetic on the right, but all sensory modalities were intact. Visual fields and eye movements were normal.

The dominant feature of her neurological illness was an amnestic syndrome with impairment of both short and long term memory with inability to retain new information. The patient was constantly repeating orientation questions: "What happened"?; "Where am I"?; "Why can't I hear anything?" Her speech was fluent with occasional word finding difficulties, paraphasia, echolalia and perseverations. Naming was severely impaired. She had difficulties lip reading even close relatives; but reading, writing and calculation were intact. Repetition (by lip reading) was impaired, though written questions were well understood, verbal and visual memory retention tasks were impaired. Left/right orientation was normal but she could not complete a sketch of a house, or correctly place the hands of a clock (though able to read the time).

CT scan of the brain obtained on admission revealed a second hypodense area consistent with infarction in the anterolateral left thalamus (fig B). A repeat scan three weeks later, when the patient had improved considerably, revealed another discrete infarct in the area of the head of the left caudate nucleus

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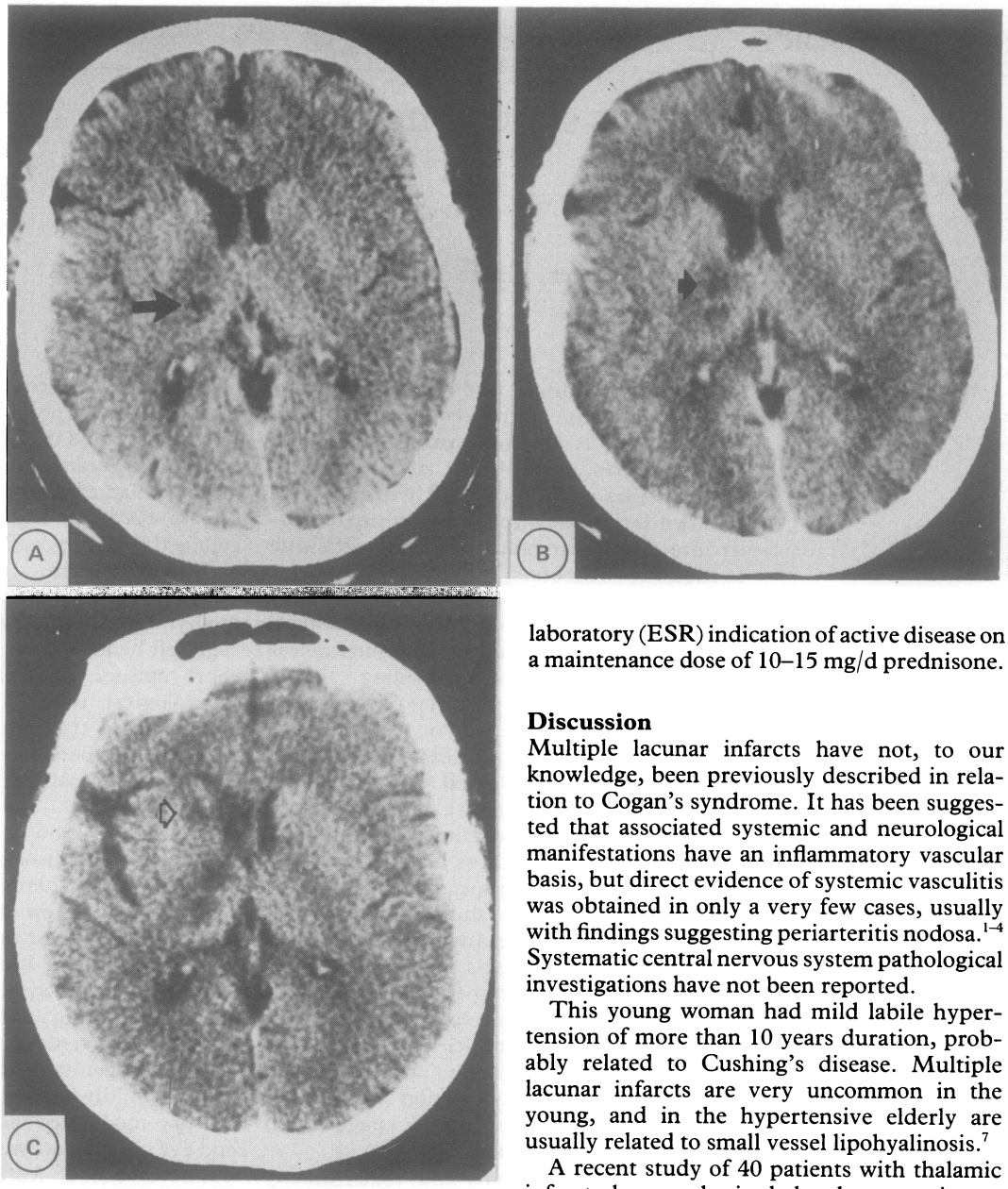

Figure A Contrast enhanced CT of brain with a hypodense lesion in the dorsolateral left thalamus in the territory of the geniculothalamic artery (arrow).

Figure B Contrast enhanced CT of brain with a new hypodense lesion in the anterolateral left thalamus in the territory of the tuberothalamic artery (arrowhead).

Figure C Contrast enhanced CT of brain shows three small infarcts. The latest one appeared at the head of the left caudate nucleus (open arrowhead).

(fig C). Laboratory screening for vasculitis and connective tissue disorders, including latex RF, antinuclear antibodies, VDRL, complement, circulating anticoagulant, cryoglobulins and serum protein immunoelectrophoresis, was again negative but the ESR was elevated (80 mm in one hour) and there was mild leukocytosis. The electrocardiogram and echocardiograph were normal. Aortic arch, bilateral carotid and vertebral arteriography showed no evidence of occlusive large vessel disease or vasculitis. A biopsy of the quadriceps muscle revealed normal blood vessels.

The dose of corticosteroids was raised to 60 mg/d prednisone and the ESR returned to normal values. The hemiparesis and naming difficulty rapidly improved as did her orientation and lip-reading, and three months later she was able to return to a part time job as an assistant accountant in spite of marked impairment of short term memory. When last seen she was normotensive and with no clinical or laboratory (ESR) indication of active disease on a maintenance dose of 10–15 mg/d prednisone.

Discussion

Multiple lacunar infarcts have not, to our knowledge, been previously described in relation to Cogan's syndrome. It has been suggested that associated systemic and neurological manifestations have an inflammatory vascular basis, but direct evidence of systemic vasculitis was obtained in only a very few cases, usually with findings suggesting periarteritis nodosa.[1-4] Systematic central nervous system pathological investigations have not been reported.

This young woman had mild labile hypertension of more than 10 years duration, probably related to Cushing's disease. Multiple lacunar infarcts are very uncommon in the young, and in the hypertensive elderly are usually related to small vessel lipohyalinosis.[7]

A recent study of 40 patients with thalamic infarcts has emphasised that hypertensive or diabetic arteriolopathy, large artery atherosclerosis, cardioembolism and migrainous stroke were the most common aetiologies.[8] Yet a few cases of lacunar infarcts in patients with SLE or periarteritis nodosa have been described, some with stroke occurring even before the systemic vasculitis became symptomatic.[8-10] Although hypertension cannot be ruled out as an aetiological factor in our patient's cerebrovascular disease, her young age and well controlled blood pressure make it unlikely. Aortic arch and cerebral angiography did not show atheromatic or occlusive lesions and the echocardiography was normal, thus a thromboembolic aetiology seems improbable. Oral contraceptives, a risk factor in young women,[8] were not used. Her blood glucose levels and lipids were within normal range. The association of the ischaemic neurological event with marked elevation of sedimentation rate responding promptly to corticosteroids, supports the idea that vasculitis related to Cogan's syndrome caused the lacunar infarctions.

The NIH group[1] has suggested that patients

with atypical Cogan's syndrome, that is, with significant inflammatory eye lesions, other than or in addition to interstitial keratitis, are more prone to develop systemic vasculitic complications. Our patient falls within this graver category as she had episcleritis.

The clinical manifestations: a retentive memory defect, disorientation, impaired comprehension and naming, paraphasic speech and a mild hemiparesis, and the CT finding (fig B) are compatible with infarction in the anterior lateral left thalamus in the territory of the tuberothalamic artery.[8 11 12] The repetition defect noted in our patient, unusual in anterior thalamic refarction,[8 11-13] resolved quite early and could be ascribed to her lip reading difficulties, especially in the light of intact reading and writing. The patient had a previous thalamic infarction visualised on her first CT scan after a short episode of right sided facial paraesthesiae (fig A). This mild clinical picture and the CT scan finding are compatible with infarction in the territory of the geniculothalamic artery.[8 10] Thus in this young woman, two thalamic syndromes were expressed together with asymptomatic involvement of the striate arteries resulting in caudate nucleus lacunar infarct (fig C). We believe that vasculitis related to Cogan's syndrome was the cause of the strokes.

While long term systemic glucocorticoid therapy for uncomplicated Cogan's syndrome is not recommended[1 2] and a short trial is usually reserved for rapidly deteriorating auditory functions,[1 2] systemic complications should be treated with early institution of 1–2 mg/kg/day of prednisone[1-3] and cautious tapering off is recommended because small changes in dose could result in systemic flare up.[3] Doses in the range of 5–20 mg prednisone per day as maintenance therapy were reported adequate.[2 3] Cytotoxic immunosuppressive agents may be useful adjuncts.[1-3] Prompt institution of adequate corticosteroid therapy whenever transient neurological impairment occurs might reduce the incidence of stroke and other systemic complications in patients with Cogan's syndrome. Careful monitoring for systemic flare up, especially routine ESR measurements,[1-3] is indicated.

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