Clinical Topics

Horner's syndrome and headache due to carotid artery disease*

T E T WEST, R J DAVIES, R E KELLY

British Medical Journal, 1976, 1, 818-820

Summary

Horner's syndrome was accompanied by ipsilateral pain in the head, face, or neck in eight patients. In all cases angiography showed narrowing of the internal carotid artery in a pattern compatible with dissection within the arterial wall. In one patient in whom this diagnosis was substantiated by surgical exploration biopsy of the arterial wall showed changes typical of cystic medial necrosis. It is suggested that this clinical presentation constitutes a distinct syndrome.

Introduction

Diseases affecting the cervical carotid artery usually present with contralateral episodic neurological symptoms and signs. We describe eight patients in whom disease of the cervical portion of the internal carotid artery was characterised by ipsilateral Horner's syndrome and pain in the head, face, or neck. In some patients contralateral neurological symptoms and signs were also present. These features constitute a recognisable clinical syndrome resulting from disease of the internal carotid artery in the neck. On angiography this is characterised by appearances compatible with dissection of the arterial wall.

Case reports

Case 1—This 46-year-old man developed dull constant left-sided headache three days before admission to hospital. On the same day he noticed that his left pupil was smaller than the right and on the next day experienced a 20-minute episode of weakness and heaviness of the right leg. Twenty-four hours later he had a further episode of weakness of the right leg, which on this occasion was accompanied by clumsiness of the hand and stiffness of the fingers. He experienced two further episodes similar to this. He had a left-sided Horner's syndrome with a minimal right facial weakness and hypertension (blood pressure 160/110 mm Hg). Left carotid angiogram (fig 1) showed prolonged narrowing of the internal carotid artery, which was maximal in the intraosseous part of the vessel. He had no further attacks, his headache resolved, and the Horner's syndrome cleared within six weeks.

Case 2—A man aged 36 developed increasing numbness of his right arm, which after two weeks was accompanied by weakness of the right hand and one week later by weakness of the right side of the face and dysarthria but no dysphasia. These symptoms were accompanied by

headache. He had a left-sided Horner's syndrome, paresis of the right arm, and hypertension (blood pressure 180/120 mm Hg). Angiography showed a tapering occlusion of the left internal carotid artery.

Case 3—A 56-year-old man gradually developed a left hemiparesis over a period of three months. This was associated with right-sided headache and tenderness over the right side of the head and face and a right Horner's syndrome. Electroencephalography showed a diffuse right hemisphere abnormality and a right carotid angiogram showed an occlusion which tapered upwards over 1 cm.

FIG 1—Case 1. Left carotid angiogram showing narrowing of left internal carotid artery.

Case 4—A woman aged 38 was admitted to hospital with a presumptive diagnosis of subarachnoid haemorrhage because of a severe headache. The ache, however, was mainly over the right side of the face and spread to the right temporoparietal region. It had not started with dramatic suddenness and fluctuated in its intensity. The only abnormal sign was a right Horner's syndrome and the patient herself had been aware of her right eyelid drooping before admission. A right carotid angiogram showed a complete occlusion of the internal carotid which tapered upwards over 1 cm. Her symptoms fluctuated over the next fortnight, when she improved and the headache disappeared but the Horner's syndrome remained.

Case 5—A man aged 48 presented with right-sided headache and right facial pain accompanied by tenderness of the upper part of the right face and head and over the carotid artery. The only abnormal physical sign was a Horner's syndrome on the right. The carotid angiogram showed narrowing of the lumen throughout the course of the cervical internal carotid artery.

Case 6—This 65-year-old man experienced in 1971 a transient episode of dysphasia, and angiography showed a narrowed left internal

*This article is partly based on a paper presented by R E Kelly at the second Pan-African Neurological Congress, 1975.

St Thomas's Hospital, London SE1 7EH

T E T WEST, MD, MRCP, lecturer in medicine

R J DAVIES, MB, MRCP, lecturer in medicine

R E KELLY, MD, FRCP, physician in charge of neurology department

carotid artery with several irregular areas. In 1972 he presented with right-sided headache which was initially paroxysmal and stabbing, and a diagnosis of trigeminal neuralgia was made. When present, this pain lasted for 30 minutes and was totally incapacitating. The pain rapidly became continuous and was associated with vomiting and with tenderness over the whole of the right side of the skull, temple, and upper face. The pain was throbbing and burning and was often eased by holding the right side of the face and head. This was associated with drooping of the right eyelid. The right carotid and temporal arteries were both tender and a diagnosis of giant cell arteritis was considered but the erythrocyte sedimentation rate was only 5 mm in the first hour and corticosteroids had no clinical effect. Right carotid angiography showed that the internal carotid artery was greatly narrowed and tortuous for most of its length. The pain, which had been severe enough to warrant pethidine, subsided over a period of two months.

FIG 2—Case 7. Left carotid angiogram showing narrowing of left internal carotid artery.

Case 7—A 43-year-old man presented with soreness in the left side of the neck spreading towards the ear. This was associated with severe frontoparietal headache on the right, but there was no visual disturbance. The next day he suddenly developed difficulty in constructing simple sentences and was unable to continue at a meeting. He noticed no limb weakness but the next morning experienced some difficulty with vision in the left eye and noticed that his eyelid had drooped. He was admitted to hospital on the same day and the left-sided Horner's syndrome was confirmed. There was no other neurological abnormality and in particular there was no evidence of a speech defect. An area of tenderness was defined below the angle of the mandible on the left but no carotid bruit could be heard. Investigations disclosed no evidence of homocystinuria or Marfan's syndrome. Angiography showed the left internal carotid artery to be narrowed throughout its extracranial course (fig 2). Three days after admission the left internal carotid artery was explored and a dissecting aneurysm of the wall of the artery found beginning 2-3 cm distal to its origin from the common carotid artery and extending cranially to the base of the skull. A tear in the intima was seen and blood clot was present in the vessel wall. The artery was ligated at its origin and as far cranially as possible. Histological examination of an excised segment of artery showed the typical changes of cystic medial necrosis. The patient made an uneventful recovery and his Horner's syndrome gradually regressed. One year later he was symptom-free and had had no further episodes of dysphasia and had no abnormal physical signs.

Case 8—A man aged 37 complained of soreness of the right side of the throat two weeks before admission to hospital. This symptom became more severe and within 24 hours was accompanied by throbbing around the right eye. Within a few hours of this new symptom developing the patient noticed his right eyelid drooping. The pain persisted and was aggravated by coughing and was associated with tenderness around the right eye which extended back on to the right side of the scalp. He had a right Horner's syndrome and tenderness

on pressure of the right globe and right common carotid artery. There were no vascular bruits and no other abnormal neurological signs. A right carotid angiogram showed considerable irregularity and narrowing of the cervical part of the internal carotid artery and very little intracerebral filling. The narrowing could be seen to extend beyond the bifurcation of the internal carotid artery. At surgical exploration the cervical portion of the internal carotid artery was narrowed and went into spasm easily but was otherwise normal externally. The artery was not opened. The Horner's syndrome and pain resolved within two months.

Discussion

All eight patients presented with pain in the head, neck, or face on one side accompanied or followed by the development of an ipsilateral Horner's syndrome. The pain, which was frequently widespread, had a burning or throbbing quality suggesting that it might have been due to dilatation of superficial vessels as suggested by Marshall.¹ The association of headache and carotid artery disease is well recognised although there has been much discussion about the mechanism of the headache. Wolff² suggested that the headache resulted from inflammation of the carotid arterial wall and that irritation near the bifurcation might reflexly start painful vasodilatation. Wells,³ on the other hand, attributed the pain to embolic distortion of the arterial wall at the base of the brain which ceased when the embolus became dislodged and moved distally, an explanation that would probably not apply in all eight cases.

In three patients (cases 1, 2, and 3) there were signs of dysfunction within the carotid territory, and a fourth patient (case 7) had had symptoms of cerebral dysfunction but no signs were present on examination. In all eight patients angiography showed narrowing of the internal carotid artery. In two patients (cases 1 and 5) narrowing was present throughout the vessel; in two (6 and 8) the lumen was irregular or tortuous; and in the remaining four (2, 3, 4, and 7) the defect began in a tapering fashion. This gradual narrowing of the arterial lumen shown on angiography is characteristic of dissecting aneurysms of the internal carotid artery.⁴ Furthermore, the angiographic findings in the other patients were quite unlike those of carotid artery stenosis or thrombosis and might also have been the result of arterial wall dissection. In the one patient in whom the vessel was opened the diagnosis of dissecting aneurysm was established and biopsy showed the presence of cystic medial necrosis of the artery wall.

Several factors have been implicated in the development of dissecting aneurysms of the internal carotid artery; these include extension of the dissecting process from larger proximal vessels such as the aorta and trauma to the neck,⁵ including angiography needle puncture.⁶ The spontaneous development of dissecting aneurysms is frequently associated with the presence of cystic medial necrosis in the artery wall.⁷ The stigmata of Marfan's syndrome are rarely present, although Austin and Schaefer⁸ reported dissection of a common carotid artery in a patient with this syndrome.

We suggest that the most likely cause of the clinical syndrome described in these eight patients was spontaneous dissection of the internal carotid artery. The sudden enlargement of the artery associated with dissection might lead to the development of a Horner's syndrome through pressure on the sympathetic fibres from the stellate ganglion, which lie in the posterior wall of the carotid sheath. The pain and tenderness felt in the neck by some of the patients probably resulted from the dissection process itself and the contralateral neurological symptoms and signs either from obstruction to blood flow in the artery or from the release of emboli from thrombus forming on the damaged arterial wall.

The reported death rate of patients with spontaneous dissecting aneurysms of the internal carotid artery is high and even those who survive may have major neurological disability despite surgery.⁹ Possibly the syndrome of pain in the neck and head with ipsilateral Horner's syndrome may represent a benign

variant of the clinical spectrum caused by spontaneous dissection of the internal carotid artery in the neck. To date the symptoms and signs in five of the eight patients have regressed completely. We suggest that patients with this clinical presentation in whom the angiographic findings are compatible with a dissection should undergo exploration of the internal carotid artery and biopsy to establish the diagnosis. It is interesting that Tews¹⁰ in a retrospective survey of patients with this syndrome could identify 10 patients who had had a dissecting aneurysm of the internal carotid artery.

The authors are indebted to Dr R W Ross Russell, Dr I R Cameron, and Professor R Gilliat for permission to study patients under their care.

References

- Marshall, J, *The Management of Cerebrovascular Disease*. London, Churchill, 1968.
- Wolff, H, *Headache and Other Head Pain*. New York, Oxford University Press, 1963.
- Wells, C, *Archives of Neurology*, 1961, **5**, 490.
- Brice, J G, and Crompton, M R, *British Medical Journal*, 1964, **3**, 790.
- Northcroft, B G, and Morgan, A D, *British Journal of Surgery*, 1945, **32**, 105.
- Crawford, T, *Journal of Neurology, Neurosurgery, and Psychiatry*, 1956, **19**, 217.
- Thapedi, I M, Ashenhurst, E M, and Rozdilsky, B, *Archives of Neurology*, 1970, **23**, 549.
- Austin, M G, and Schaefer, R F, *Archives of Pathology*, 1957, **64**, 205.
- Ojemann, R G, Fisher, C M, and Rich, J C, *Stroke*, 1972, **3**, 434.
- Tews, J, 1975, personal communication.

Cromoglycate and other antiallergic drugs: a possible mechanism of action

J C FOREMAN, L G GARLAND

British Medical Journal, 1976, **1**, 820-821

Cromoglycate represents one of the few new drugs to be introduced into clinical use this decade and several compounds are now emerging with similar activity (fig 1). Preliminary findings indicate that doxantrazole¹ and AH 7725² are effective by mouth in humans. As is often the case, new and useful drugs are in widespread use before there is any clear understanding of their mechanism of action and this is so with the antiallergic drugs. Our object is not to review all that is known about the pharmacology of cromoglycate, but to propose a hypothesis for the mechanism of action in terms of some new findings relating to the release of histamine and other mediators during immediate-type hypersensitivity reactions.

Mechanism of mediator release

Most manifestations of immediate-type hypersensitivity reactions appear to result from the release of mediators after the union of antigen with IgE antibody fixed to mast cell membranes. IgE antibody binds selectively to mast cells³ and basophil leucocytes,⁴ and when IgE combines with antigen a series of events takes place leading to the liberation of mediators such as histamine, serotonin, slow-reacting substance of anaphylaxis (SRS-A), prostaglandins, and putative mediators such as eosinophil chemotactic factor.^{5 6} The biochemical processes linking the antigen-antibody reaction on the cell membrane with the release of, for example, histamine-containing granules, is not full understood but it has been known for some years that calcium is required in the extracellular medium and that metabolic processes within the mast cell must be intact.^{7 8}

In common with many other secretory systems, the antigen-induced secretion of histamine from mast cells requires calcium ions. Using a calcium ionophore (a substance which transports

FIG 1—Structures of four new antiallergic drugs together with structure of cromoglycate for comparison.

calcium across biological membranes and other organic phases) Foreman *et al* have shown that the movement of calcium ions from the extracellular to the intracellular compartment of mast cells is sufficient to stimulate metabolically intact cells to secrete histamine.⁹ The primary event after union of antigen with mast cell-fixed antibody may therefore be an increase in the mast cell membrane permeability to calcium, which promotes entry of calcium into the cell. It is possible to show an increase in the association of 45-calcium with mast cells after antigen stimulation.^{9 10}

In addition to the requirement for calcium, histamine secretion does not proceed from antigen-stimulated cells if adenosine triphosphate (ATP) generation is blocked with inhibitors of oxidative phosphorylation and glycolysis.¹¹ ATP is utilised during the release of mediators and it appears that this ATP may be produced either by glycolysis or oxidative phosphorylation

Department of Pharmacology, University College London, London WC1E 6BT

J C FOREMAN, PHD, honorary research assistant

Pharmacology Laboratory, Wellcome Research Laboratories, Beckenham, Kent BR3 3BS

L G GARLAND, PHD, biochemical pharmacologist