Today's Treatment

Diseases of the central nervous system

Relief of pain: headache, facial neuralgia, migraine, and phantom limb

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British Medical Journal, 1975, 4, 90-92

Tension headache

Tension is probably the commonest cause of headache. Ordinary analgesics, aspirin (0·3-0·9 g) or compound preparations, should be tried first, although headache is a common cause of analgesic abuse. Chronic treatment with aspirin, phenacetin, or paracetamol may lead to nephritis or peptic ulceration. Minor tranquillisers, such as chlordiazepoxide (5-30 mg daily), diazepam (2-30 mg daily), or phenobarbitone (30-120 mg daily) occasionally relieve headaches resulting from various stresses, and tricyclic antidepressant drugs such as dothiepin (50-150 mg at night) sometimes give dramatic relief from chronic tension headache in depressed patients. Major tranquillisers and narcotic analgesics should not be used to treat patients with tension headache. A simple explanation of the cause of this is often far more effective treatment than the prescription of the latest triumph of neuropharmacological research.

Migraine

About 5% of the population suffer from migraine. The classical attack begins with a visual aura followed by unilateral headache with dilatation in the branches of the external carotid artery, scalp tenderness, and sometimes oedema, as well as nausea and vomiting. Many attacks, however, do not follow this pattern and tension headaches are common in patients with migraine. The cause of the abnormal blood vessel responses during an attack of migraine is unknown, although there are several biochemical clues and psychogenic and genetic factors are largely responsible in many patients. Some have a low plasma serotonin level during the headache; serotonin causes vasoconstriction in some, but not all, cerebral blood vessels. Tyramine, a vasoactive amine present in some foods such as dairy produce and fish, may trigger headache in 10 to 30% of patients, although avoiding these foods does not always prevent attacks.

Over 400 remedies have been proposed for migraine, but ergot derivatives are by far the most effective treatment for acute attacks. Ergotamine tartrate was first developed in 1926, and is a potent vasoconstrictor drug, and also has a powerful action on the uterus. Dihydroergotamine may cause less nausea and vomiting than ergotamine, and also has less oxytocic effect, although it is probably slightly less potent. Ergotamine is more effective in migraine than ergometrine, and other ergot derivatives such as ergocornine are useless since they cause vasodilatation rather than vasoconstriction. The earlier ergot is given during acute attacks the more effective is the treatment. Ergotamine tartrate (2 mg) can be given sublingually or swallowed, but if vomiting prevents this the same dosage can be given by suppository or 0·5 mg given intramuscularly. Liquid ergot extract rapidly loses its strength. The maximum dosage of ergot should not exceed 10 mg in one attack or one week although frequently higher dosages than this are taken. Some patients become dependent on ergotamine and develop severe symptoms on withdrawal. Nevertheless, this is sometimes necessary since chronic treatment with ergotamine alters vascular physiology and will perpetuate headache. Ergotamine tartrate has been combined with caffeine, antispasmodics, antiemetics, and sedatives. Useful preparations include an aerosol ergotamine spray (delivering 360 μg ergotamine tartrate in each dose; absorption may be erratic), Migril (ergotamine tartrate 2 mg, caffeine hydrate 100 mg, cyclizine hydrochloride 50 mg), and Cafergot (ergotamine tartrate 1 mg, caffeine 100 mg). Headache may be relieved by an ice-bag or the no-longer fashionable leech on the head. Bed rest in a quiet dark room is often necessary.

Ergot in high doses should not be used for the prophylaxis of migraine. If attacks are frequent antihistamines (prochlorperazine 15-30 mg daily), antidepressants (amitriptyline 75 mg daily), progesterone-containing preparations (flumedroxone 30 mg daily), diuretics (acetazolamide 250-500 mg daily), sedatives (phenobarbitone 30-60 mg daily), or indomethacin (25-50 mg daily) may be useful. Bellergal (ergotamine tartrate 300 μg, belladonna alkaloids, phenobarbitone 20 mg) and Bellergal Retard (equivalent to 2 Bellergal tablets) are useful alternatives. The alpha-adrenergic agonist drug clonidine given in low dosage and under the name of Dixarit (tablets each containing 25 μg; 2-6 daily) has no hypotensive effect in normal subjects and reduces the frequency of migraine attacks in about half the patients. Propranolol (30-120 mg daily in divided doses) may have a similar effect. The potent serotonin antagonist, methysergide (2-6 mg daily), is the most powerful prophylactic for migraine known, and it will reduce the frequency of attacks in about 65% of patients. Toxic effects are similar to those of ergot alkaloids, and are more frequent. The use of methysergide should be restricted to patients with frequent severe migraine, who are not helped by other treatments, since it may cause the sinister condition of retroperitoneal fibrosis. This regresses on drug withdrawal, however, and it is usually recommended that methysergide is given for six months followed by 60 days of no treatment.

MIGRAINOUS NEURALGIA

Migrainous neuralgia is a common condition in which bouts of severe retro-orbital pain lasting 20 to 60 minutes occur accom-

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panying watering of the eye and blockage of the nose. Symptoms are commonly seasonal and pain may wake the patient at night. Attacks are prevented by methysergide or, alternatively, dihydroergotamine tartrate 2 mg with promethazine 10-25 mg may be given every evening. Sir Charles Symonds recommended that this treatment was given for six consecutive nights followed by 24 hours off drugs to see whether spontaneous recovery had occurred.

Other migraine variants which occasionally are difficult to diagnose also respond to ergot. Basilar migraine is rare, occurring mostly in young women who complain of vertigo or unsteadiness with visual blurring followed by occipital headache. Hemiplegic migraine, headache being followed by a contralateral transient paralysis, is sometimes a familial disorder. Ophthalmoplegic migraine, commoner in children than adults, results in pain localised to one eye followed by double vision; an aneurysm of the internal carotid or posterior communicating artery is sometimes present. Operations done for migraine in the past, including 5th nerve sensory root section and ligation of the middle meningeal artery, are now of little more than historical interest.

Ergot derivatives are comparatively safe drugs and rarely cause ergotism. Naturally occurring outbreaks of this, due to eating contaminated rye bread, caused either limb pain; vascular damage and occasionally gangrene; or nervous symptoms—confusion, drowsiness, and convulsions. Epidemic ergotism is fortunately now a rarity, the last outbreak in this country occurring in a Manchester community of tailors, but the therapeutic use of ergot may cause similar symptoms. Vascular damage may result from a single dose and chronic treatment with ergot will produce coronary, renal, aortic, femoral, or brachial artery vasospasm resulting in myocardial infarction or limb gangrene. Ergot should not be given, therefore, to patients with peripheral, cerebral, or coronary artery disease. The symptoms of ergotism—numbness of the hands and feet; vomiting; cramps of the feet, which often become pulseless, swollen, and cyanotic —may precede gangrene, and further ergot treatment must be stopped. A vasodilator such as papaverine (30-60 mg intravenously) should be given and paravertebral sympathetic block should also be done if there is any sign of impending gangrene. Hyperbaric oxygen, nitrites, and peritoneal dialysis have also been used. Ergotamine poisoning may also follow defective hepatic detoxification, so that ergot should be avoided in patients with liver disease. Comparatively large doses are needed to cause abortion, although ergotamine should be avoided in pregnant women, in whom migraine is fortunately rare.

Temporal arteritis

Giant cell or temporal arteritis occurs most commonly in patients over the age of 55. Malaise, fever, anorexia, and weight loss occur in half the patients, and may precede signs of extracranial arterial inflammation. The diagnosis is made in the presence of headache with tenderness and oedema of the temples or occiput, and a high erythrocyte sedimentation rate. Arterial biopsy shows destruction of the vessel wall, and multinucleate giant cells may be present. Involvement of intracranial arteries is said not to occur, although the vertebral artery may be involved in the neck and the mesenteric and other vessels are sometimes affected.

Steroid treatment is mandatory, for without it 20 to 30% of patients lose vision, probably owing to involvement of ciliary arteries, and other complications such as a third or sixth nerve palsy occur less often. Pain often resolves within 24 hours of starting treatment with prednisone 60 mg/day. Dosage may be reduced to 20 mg/day after three weeks, although treatment is necessary for 6 to 12 months and occasionally longer. The presence or absence of headache and the erythrocyte sedimentation rate are useful guides to dosage and the necessity for continued treatment. All the hazards of chronic steroid treatment may occur, silent gastrointestinal perforation being particularly frightening.

Postherpetic neuralgia

Herpes zoster (shingles) is caused by the virus of varicella (chicken pox). Permanent burning aching pain develops after shingles in up to half of elderly people. It may be preventable by treating the acute attack with analgesics—aspirin, phenacetin, or codeine—and corticosteroids if not contraindicated (prednisone 30 mg daily in divided doses). Once postherpetic neuralgia is established, however, treatment is very difficult and demands great persistence and enthusiasm from the patient and also the doctor.

Treatment falls into three phases: firstly, giving analgesics, sedatives, and antidepressants; secondly, the trial of many different forms of physical treatment such as spraying the skin with ethylchloride, subcutaneous or deeper injections of local anaesthetic, vibration treatment with a Pifco massager, and even deep *x*-ray therapy; and, finally, referral to a special clinic for the treatment of pain. The antiviral drug amantadine (100 mg twice daily) possibly has a minimal effect in reducing the duration of pain, probably owing to a very mild central stimulant effect. Polyethylene or Plastazote jackets can be obtained for patients whose pain is made worse by contact with clothing. Transcutaneous electrical stimulation (Devices Stimtech Stimulator) used intelligently over long periods may replace the pain of postherpetic neuralgia by a more tolerable sensation, and very occasionally permanent pain relief is obtained.

Trigeminal neuralgia

The poisons hemlock, arsenic, hydrocyanic acid, and bee, rattlesnake, and cobra venom were all used to treat trigeminal neuralgia in the 18th century, and plunging the contralateral hand into boiling water was advised as late as 1930. The anticonvulsant drug carbamezapine (100 or 200 mg tablets; 600-800 mg daily in divided doses) has revolutionised the treatment of this distressing complaint, resulting in the relief of pain in about 70% of patients. Phenytoin sodium (150-300 mg daily) is a slightly less potent alternative, and Gower's mixture (containing gelsemium tincture *BPC*, 0·3-1 ml three times daily) is sometimes effective. The action of these drugs may be related to their ability to reduce impulse frequency in the Gasserian ganglion or modify conduction velocity in trigeminal fibres. Glossopharyngeal as well as trigeminal neuralgia respond to these treatments, although other forms of facial neuralgia do not. In patients with trigeminal neuralgia pain is almost always precipitated often with specific trigger areas.

The toxic effects of long-term treatment with carbamezapine in high dosage are dizziness, ataxia, and sometimes drowsiness. Pain relief, rather than side effects, should be used to determine dosage since ataxia is abolished on withdrawing the drug and alternatively pain may lead to suicide. Carbamezapine may also cause hypertension and should not be given to patients with heart disease. Jaundice and blood dyscrasias may be caused by carbamezapine so it is wise to do periodic liver function tests and blood counts on these patients. This is seldom done, however, since in practice a blood dyscrasia may occur overnight; fortunately this is a rare side effect. If pain continues despite medical treatment trigeminal surgery resulting in sensory denervation of the face is sometimes necessary. Complete analgesia is not essential for a good therapeutic result.

Facial neuralgias

Facial pain is a common complaint, although it is often difficult or impossible to establish the cause. Disease of the teeth, nose, sinuses, ears, and temperomandibular joints may

all cause facial pain, but there is a bewildering group of patients with episodic or persistent facial pain who have no evidence of bad teeth or chronic sinus infection and no motor or sensory abnormalities to explain their symptoms. Some patients with episodic and sometimes unilateral lower facial pain may have vascular phenomena such as flushing or abnormal heat sensitivity. Occasionally ergotamine gives pain relief.

Other patients complain of a constant dull aching deep-seated pain, often in the lower face. These symptoms may be psychogenic and many, but not all, patients have alterations in mood, attitude, or behaviour. The use of potent antidepressant drugs in high dosage is occasionally successful in the treatment of this variant of atypical facial pain.

Phantom limb pain

Many different types of pain follow injury to nerves. The immediate treatment of painful peripheral nerve lesions with analgesics and sedatives may prevent the later development of painful phenomena in the limb. Phantom limb pain is one of the most terrible of these, and occurs in about 30% of patients after amputation, being permanent in 5-10%. The most vivid phantom may be associated with the most severe pain. Sympathetic ganglia contribute to this pain in some way, but, although sympathectomy will relieve the constant severe burning pain of causalgia, this operation rarely causes lasting relief of phantom limb pain. If a tender stump is present modification of sensory input by anaesthetic block or intense stimulation occasionally causes pain relief.

The effects of drug treatment are variable, although major tranquillisers (chlorpromazine 50-500 mg daily) may be partially effective. As in the case of postherpetic neuralgia, continuous or intermittent transcutaneous electrical stimulation is occasionally successful in treating this kind of pain, as well as that due to malignant disease with root or nerve involvement. The results of surgery such as chordotomy, thalamotomy, or even cortical ablation, are inconstant and there is probably a widespread central disturbance of pain mechanisms in these patients so that at whatever level pain is attacked it often returns.

Clinical Topics

The forgotten nodule: complications of sacral nodules in rheumatoid arthritis

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British Medical Journal, 1975, 4, 92-93

Summary

Nodules commonly occur in rheumatoid arthritis and occasionally give rise to complications. The sacral nodule is easily missed and may ulcerate to produce extensive sacral sores which may lead to serious and even fatal complications in patients with rheumatoid arthritis. Seven cases are reported which illustrate some of these features.

Introduction

Most doctors are aware that subcutaneous nodules may be found over the extensor surfaces of the joints and areas of the body prone to minor trauma in patients with rheumatoid arthritis. Rheumatoid nodules over the sacrum, however, are seldom looked for, and yet in our experience these may lead to pressure sores, act as a nidus for infection, and even cause fatal septicaemia in patients debilitated by severe rheumatoid arthritis.

Recently we have seen seven patients who have suffered serious complications resulting directly from sacral nodules. The main features of the cases are outlined below, and four representative case histories (cases 1-4) are described in more detail.

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Case Reports

Case 1—A 67-year-old woman with severe rheumatoid arthritis of 30 years' duration was admitted to the Centre for Rheumatic Diseases in February. Her functional capacity was Steinbroker grade IV,[1] and she had been bedridden for four years. She was admitted with multiple nutritional deficiencies. On examination she had end-stage, destructive, nodular rheumatoid arthritis with two large ulcers over the sacrum penetrating to bone. These had begun as two small nodules on the sacral area. Haemoglobin was 10·2 g/dl, erythrocyte sedimentation rate (ESR) 92 mm, albumin 2·8 gl/, globulin 3·9 g/l, and rheumatoid factor (R3) titre 1/16. At first the ulcers were treated conservatively, but ultimately they required skin grafting, and the patient was in hospital for just over a year until her ulcers had healed.

Case 2—A 57-year-old woman, who had had rheumatoid arthritis for nine years (functional capacity grade II), was admitted for a right Macintosh knee arthroplasty, and on routine examination she was noted to have a small sacral nodule. Haemoglobin was 10·3 g/l, E.S.R. 29 mm, and rheumatoid factor titre 1/16. The sacral nodule discharged on the ninth day after operation, which resulted in a sacral sore which became infected with proteus. Blood cultures were negative and the sacral ulcer gradually healed with topical antibiotics. Her total inpatient stay as a result of this complication was three months. The sacral sore before skin grafting is shown in the fig.