Assessment of painful diabetic neuropathy

1 A DETAILED HISTORY IS THE MOST IMPORTANT ASSESSMENT.

2 THERE MAY BE SIGNIFICANT UNDERLYING PSYCHOLOGICAL PROBLEMS.

3 INVESTIGATIONS ARE GENERALLY NOT NEEDED FOR ROUTINE MANAGEMENT.

4 SKIN BIOPSY MAY BE A PROMISING NEW INVESTIGATION IN THE FUTURE.

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Introduction

Patients with diabetes can often experience pain as a predominant symptom of peripheral neuropathy. Chan et al (1990) found that 7.5% of adult patients attending a diabetes clinic complained of chronic pain mainly in the lower limbs, as a manifestation of diabetic neuropathy. The severity of pain in diabetic neuropathy is difficult to quantify. Nevertheless, proper assessment is essential to allow comparison of pain severity between different patients or even in the same patient at different times.

Assessment of painful diabetic neuropathy should consist of a detailed history and full clinical examination. Investigations are not usually necessary, but may occasionally be useful.

This review describes the clinical assessment and investigation of painful diabetic neuropathy in detail.

Clinical assessment

History

A detailed history is very important for diagnosis. It will help to exclude other causes of leg pain such as peripheral vascular disease, spinal canal stenosis, prolapsed intervertebral disc, cauda equina lesions, and arthritis affecting the ankle and foot joints (Caddick et al, 1997).

Patients should be allowed to describe their problems without too many leading questions or interruptions. The features of pain that need to be assessed are described below.

Nature of the pain

The pain of diabetic neuropathy has long been described as having a burning, sharp, shooting, stabbing or lancinating quality. Patients frequently complain of painful dysthesia (deep aching pain) and paraesthesia (pins and needles). In addition, some have 'motor symptoms' such as cramps and restless legs.

When documenting the symptoms, one should record the exact words used by the patient to describe his/her symptoms, to enable comparison with subsequent descriptions following treatment (Young and Jones, 1997).

The exact anatomical site of the pain should also be noted, as painful neuropathy usually affects the distal part of the lower limbs in a symmetrical fashion.

The time course of the pain should be obtained as acute pain with little or no demonstrable neurological or electrophysiological deficit generally gets better within one year (Archer et al, 1983), unlike the insidious pain associated with chronic sensory motor neuropathy which can persist for many years (Boulton et al, 1983).

Relation to exercise

The relationship of pain to exercise needs to be established, as neuropathic pain is often unchanged or improves with exercise, whereas pain due to peripheral vascular disease is made worse by walking.

In spinal canal stenosis there is pain and weakness of the legs on walking, which is typically improved by squatting or rest (Spivak, 1998). However, some patients with severe painful neuropathy may experience worsening of pain with exercise; the worst affected patients may thus be confined to home, unable to cope with basic daily activities such as shopping (Tesfaye et al, 1996a).

Allodynia

Some patients are abnormally sensitive to non-painful stimuli. Patients typically complain of contact hypersensitivity to the bedclothes and may sleep with a bed cradle. In severe cases, patients may not be able to wear certain types of garment because they irritate the skin and may prefer, for instance, silk pyjamas.

Nocturnal exacerbation

There is a characteristic diurnal variation in pain severity, with the pain being more pronounced at night. Nocturnal exacerbation of pain and contact hypersensitivity to bedclothes often disturb sleep (Watkins,

1984). In such patients, sleep deprivation causes tiredness throughout the day, leading to inability to cope with the pressure of work.

SEVERITY OF PAIN

The pain of diabetic neuropathy varies from mild paraesthesia in a few toes to severe, unremitting pain involving both legs (Pavy, 1985). Its severity could therefore be assessed in terms of interference with the daily life of the patient. Thus, time lost from work, curtailment of recreational activities, the number of hospital visits made as a result of the pain, the type of analgesics required and quality of life should be carefully assessed.

Assessment of pain severity is an essential prerequisite to planning treatment: mild pain does not require treatment whereas severe pain may need a combination of drugs.

HEALTH BELIEFS AND FEARS

Patients have differing beliefs about the origin of pain. Those who believe that pain is enduring and mysterious are less likely to use coping strategies than those who think their pain is due to understandable physical lesions and can be of short duration (Williams and Keefe, 1991).

Patients with painful neuropathy often feel guilty, believing that their pain may be due to their inability to achieve good metabolic control. It is essential to explore these health beliefs so that appropriate advice and counselling can be given.

Many patients also have unfounded fears (e.g. of amputation) that need to be explored: a simple explanation of their condition may relieve their anxiety.

A significant number have fears of exacerbation of painful symptoms and further deterioration in their physical state, and need to be reassured that the pain does not invariably worsen and may be adequately controlled with treatment.

Figure 1. Instruments required for neurological assessment. From the top: 128 Hz tuning fork, cotton wool, neurotip, 10g mono- filament and tendon hammer.

COPING STRATEGIES

Patients often develop coping strategies to deal with the pain (Crow et al, 1996). Some sleep with their feet uncovered and/or hanging out of bed; others walk around to relieve the pain; and some with burning pain immerse their feet in cold water (Archer et al, 1984).

Those with chronic pain often become creative in discovering which methods work for their pain in combination with their functional abilities, lifestyle needs and resources (Davis and Atwood, 1996).

Thus it is important to identify and review these coping strategies.

PSYCHOLOGICAL ASSESSMENT

Neuropathic pain is associated with significant depression (Archer et al, 1983; Tesfaye and Price, 1997), which may interfere with pain perception. Pain management in such patients may be difficult, and treatment of the underlying depression is clearly indicated (Watkins, 1984).

In a recent study, patients with chronic pain had significant psychological distress closely associated with a combination of fears about the future, regrets about the past and personal relationship problems (Walker and Sofaer, 1998).

EXAMINATION

Detailed physical examination is essential, even though there may be no abnormal signs in this condition. A careful examination may reveal signs of other diseases responsible for the pain.

GENERAL EXAMINATION

A systemic examination is essential, with particular attention paid to the lower limb. Examination should include dilated fundoscopy, blood pressure measurement and screening for other chronic complications that may coexist, as this may influence pain perception.

In the leg, the condition of the skin should be noted, as it might be dry as the result of autonomic neuropathy. If there is a coincidental skin lesion, topical treatment such as capsaicin and Opsite should be avoided.

It is also important to examine the foot joints, as the pain is often due to arthritis. The foot may also have some degree of deformity and callus over pressure points, which should alert to the future development of ulcers.

A straight leg raising test should be performed if a disc prolapse is suspected.

NEUROLOGICAL EXAMINATION

Peripheral nerve function may be completely normal in painful neuropathy, although patients usually have other features of chronic sensory motor neuropathy. In contrast, some patients with advanced

neuropathy may have an insensate leg in association with neuropathic pain, the so-called 'painful-painless foot' (Ward, 1982).

Traditionally, peripheral nerve function in diabetes is examined by testing sensation such as fine touch, vibration and pinprick, and by eliciting tendon reflexes (*Figure 1*). For the purpose of discussion, we have grouped them into tests of large myelinated fibres, small fibres and motor components of peripheral nerves.

Tests of large fibres: Large fibres carry the sensation of vibration and tactile stimulation. Vibration sensation is examined using a tuning fork of 128 Hz. A vibrating tuning fork is placed on the medial aspect of the first metatarsophalangeal joint. Tactile sensation can be tested by stroking the skin with a wisp of cotton. It is important for patients to close their eyes during this test.

Tests of small fibres: Small fibres detect sensations such as pinprick, pain, cold and heat. Pinprick sensation should be tested using a neurotip (*Figure 2*) rather than a needle or pin.

Pain sensation, which is frequently lost in these patients, can be tested by pinching the Achilles tendon.

Other functions of small fibres can be assessed by checking temperature sensation. This can be tested in the clinic by asking patients to differentiate between a cold metallic stimulus (e.g. tuning fork) and a similarly shaped warm stimulus (e.g. pen). A more accurate assessment is obtained using two tubes, one filled with warm water and the other with cold water.

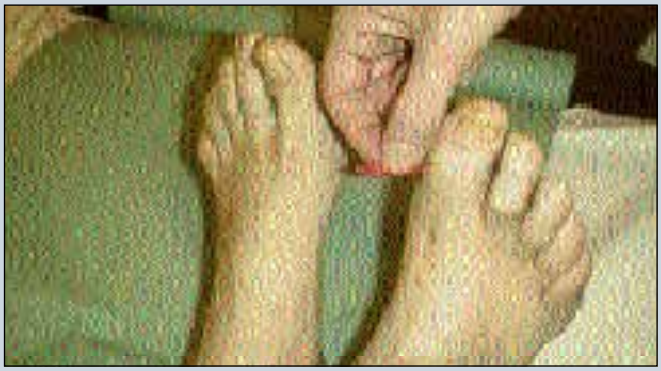

Figure 2. Assessment of pinprick sensation using a neurotip.

Tests of motor fibres: The power of different muscle groups should be tested against resistance and graded. This is usually normal in painful diabetic neuropathy, but there may be some weakness of flexors or extensors of the toe.

Ankle reflexes should be examined. These may be absent, although knee reflexes are usually present.

VASCULAR EXAMINATION

Along with neurological examination, it is very important to assess the presence of peripheral vascular disease. Pedal pulses are usually good in painful neuropathy, and their absence should alert to the possibility of vascular problems. In some patients, however, neuropathic and ischaemic pain may coexist, and it can be difficult to distinguish between the two (Ward and Boulton, 1987).

Other signs of vascular insufficiency (e.g. pale, cold feet, shiny skin with loss of hair, and poor capillary refill) should be assessed. Varicose veins can also give mild discomfort to the legs but this is usually obvious.

INVESTIGATIONS

HbA_{1c}

HbA_{1c} should be measured in all patients to assess glycaemic control. Hyperglycaemia has been shown to lower the pain threshold in human volunteers (Morley et al, 1984), although this assertion has been challenged (Chan et al, 1988).

Good glycaemic control has been shown to improve pain (Boulton et al, 1982). In contrast, there have been reports of the occurrence of neuropathic pain in chronic hyperglycaemic patients following improved glycaemic control (Tesfaye et al, 1996b).

Recent studies have shown the benefit of good glycaemic control. All patients with high HbA_{1c} should therefore be encouraged to achieve good metabolic control gradually.

ELECTROPHYSIOLOGY

Patients with painful neuropathy may have completely normal nerve conduction, despite having severe symptoms (Daube, 1987). However, most patients will have some electrophysiological changes similar to those described for moderate generalised neuropathy, with a mild reduction in sensory amplitude and mild slowing of conduction velocities (Brown et al, 1976).

This investigation may be useful in the diagnosis of more proximal disease such as nerve root lesion or sacral plexus lesion, by showing prolongation of the F-wave latencies or delayed somato-sensory evoked potential.

QUANTITATIVE SENSORY TESTING

These are groups of tests that give numerical value to a degree of sensation and make it easy to compare one with another. There are many such tests used to measure the ability of a patient to detect the threshold of vibration, tactile sensation and warm or cold sensations.

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Vibration perception threshold can be measured quantitatively using the neurothesiometer. Vibration is usually assessed at the tip of the great toe or over the lateral malleolus. The test should be performed at least three times and the amplitude of vibration is increased at different rates.

Tactile threshold can be determined using different gauges of Semmes-Weinstein monofilaments. These are pressed against the patient's skin until they buckle. A series of increasingly thick filaments is tested and the tactile threshold is the first one felt by the patient.

A vibration threshold of >25 volts and insensitivity to 10 g Semmes-Weinstein monofilament have been associated with an increased risk of foot ulceration.

Instruments such as the Thermotest and Marstock stimulator are used to measure the heat and cold sensory threshold (Fruhstorfer et al, 1976).

Computer Assisted Sensory Examination (CASE IV) has recently been developed for quantitative sensory testing. This test is reproducible and relatively easy to use (Dyck et al, 1996).

CASE IV can also be used to detect the heat–pain threshold by evaluating graduated, non-repeating ascending stimuli from a radiant heat source, which may be abnormal in painful neuropathy.

CASE IV can also be used to detect vibration perception threshold. When thermal and vibration sensory thresholds were compared, the former was more affected in painful diabetic neuropathy (Guy et al, 1985).

OTHER INVESTIGATIONS

Other investigations may sometimes be required to exclude other possible causes of the diabetic patient's pain.

Doppler flow measurement of the lower limb vessels may be indicated to exclude peripheral vascular disease. If a disc prolapse or spinal canal stenosis is suspected, a computed tomographic or magnetic resonance scan of the lumbosacral spine is indicated.

DETAILED ASSESSMENT OF PAINFUL NEUROPATHY

Some form of quantitative measurement of painful neuropathy is needed to facilitate comparison for research purposes. Thus, in addition to the tests already described, the following tests may be utilised.

PAIN QUESTIONNAIRES

The McGill pain questionnaire (*Figure 3*) was devised to enable assessment of both the quality and emotional aspects of pain. A short form has been developed for use when time is limited, and results correlate very well with those from the original questionnaire (Melzack, 1987).

The patient is asked to circle one word from a group of words that best describes their pain. It takes about 5–10 minutes to complete the questionnaire. Repetition of

McGill - SF

Some of the following words describe your present pain. Circle the one word in each group that best describes it. Mark only one word in each group. Skip the groups that do not apply.

1. Flickering, Quivering, Pulsing, Throbbing, Beating, Pounding	**2.** Jumping, Flashing, Shooting	**3.** Prickling, Boring, Drilling, Stabbing, Lancinating	**4.** Sharp, Cutting, Lacerating	**5.** Pinching, Pressing, Gnawing, Cramping, Crushing
6. Tugging, Pulling, Wrenching	**7.** Hot, Burning, Scalding, Searing	**8.** Tingling, Itching, Smarting, Stinging	**9.** Dull, Sore, Hurting, Aching, Heavy	**10.** Tender, Taut, Rasping, Splitting
11. Tiring, Exhausting	**12.** Sickening, Suffocating	**13.** Fearful, Frightful, Terrifying	**14.** Punishing, Gruelling, Cruel, Vicious, Killing	**15.** Wretched, Blinding
16. Annoying, Troublesome, Miserable, Intense, Unbearable	**17.** Spreading, Radiating, Penetrating, Piercing	**18.** Tight, Numb, Drawing, Squeezing, Tearing	**19.** Cool, Cold, Freezing	**20.** Nagging, Nauseating, Agonising, Dreadful, Torturing

Total number of words chosen:
McGill score:

Figure 3. McGill pain questionnaire.

the questionnaire following intervention can show a quantitative difference in pain.

The impact of pain on different aspects of the patient's life can be measured using the 'multidimensional pain inventory' (Kerns et al, 1985). This inventory assesses patients' appraisals of the pain problem, its impact on their life and the response of others.

VISUAL ANALOGUE SCALE

Patients can be asked to describe their pain as none, mild, moderate, or severe. However, they are not as sensitive as the visual analogue scale (VAS), where the pain experience is represented by a 100 mm linear scale.

The patient is asked to indicate his/her pain experience on a scale from 0 to 100, where 0 indicates 'no pain' and 100 indicates 'the worst pain ever'. The VAS has been well validated in chronic pain.

OTHER TESTS OF SMALL NERVE FIBRES

Current perception threshold has been used to test for hyperaesthesia (Guthrie et al, 1989), although its use for this purpose has been challenged (Veves et al, 1994).

This test has recently been shown to be useful in the diagnosis of sensory neuropathy due to diabetes (Rendell et al, 1989); the correlation was strong for numbness, but lower for pain and paraesthesia.

Other investigators have used different stimuli such as heat, cold, 'Pinchometer' or a series of weighted needles to assess small, non-myelinated C-fibre function (Watkins and Edmonds, 1997). These tests have not been well validated and are not in general use.

SKIN BIOPSY

A new technique allows the demonstration of epidermal nerve fibres (ENFs) in skin obtained by punch biopsy. ENFs are stained by immunohistochemical methods, imaged with a confocal microscope, and quantified using a neuron tracing system.

The number of ENFs was diminished in diabetic subjects with neuropathy (Kennedy et al, 1996). Holland et al (1997) found that ENFs were significantly reduced in patients with painful sensory neuropathies compared with age-matched controls.

CONCLUSION

Painful neuropathy is a common complication of diabetes, and often adversely affects the quality of life. It should be assessed appropriately in order to draw up a treatment plan tailored to the patient. A detailed history and clinical examination are usually sufficient for assessment, but other investigations may be required. For research purposes, further detailed investigations are indicated. ■

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