

Introduction

An increasing population now have 'treatable but not curable cancers' and many anticancer therapies (radiotherapy, chemotherapy or targeted therapy) can negatively impact the normal functioning of the feet and lower extremities. These podiatric adverse events (PAEs) often require podiatric treatment and, if ignored, can have a considerable impact upon the patient's mental as well as physical wellbeing (1).

The field associated with understanding the complications of anticancer therapies and implications for the podiatrist is a key growth area and much more could be done to improve awareness amongst professionals and patients. Given the wide range of PAEs linked to anticancer therapies, I have written two articles on the topic. This first article focuses on the need for improved education together with the neurological PAEs that are common side-effects of anticancer treatment, whilst my second article deals with the most common dermatological adverse events.



Need for greater awareness

Whilst covered by a number of medical papers in both cancer care and dermatology, at present there are no widely available educational tools (particularly in the UK) for patients highlighting likely PAEs and the potential consequences of failing to treat them.

There is also no lower limb screening or direct referral system into podiatry so many patients and those supporting them may be unaware of the connections between the PAEs and their anti-cancer treatment. They may therefore be relatively unprepared for them and not realise that many of these issues can be managed.

Greater awareness of these side-effects could therefore significantly help in limiting the negative impact – both through patients being able to anticipate such issues and being aware of podiatric help being available (either privately or in some cases via the NHS). By working closely with the patient and their cancer unit, podiatrists can reduce

pain, improve patients' quality of life and also reduce the chances of patients not finishing their life-enhancing anticancer therapy. After all, reducing issues, avoiding anxiety or distress, empowering them and improving their Quality of Life (QoL) have all been reported to help to improve adherence to cancer treatments^{2.}

As podiatrists we can all help to educate the wider healthcare community such as allied health professions, health care and footcare assistants as well as front line cancer staff on these effects and the valuable role podiatrists can play in treating these conditions and preventing or reducing complications. This can only lead to better outcomes for patients.

Neurological podiatric adverse events

Symptomatic podiatric adverse events (PAEs) are common in patients treated for cancer (3) and podiatric-medical intervention is key to identifying early neurological changes and help avert the rapid development of these complications.

We will discuss the details of peripheral neuropathy and chemotherapy induced peripheral neuropathy in more detail below, but from a neurological perspective, regular pedal problems include:

- Changes within the foot which can cause new footwear problems
- Painful walking and weight bearing
- Changes to tissue integrity e.g. skin and nails
- **Painful lower limb arthropathies**

From a clinical perspective, it is important to recognise PAEs and adapt our assessment and treatment protocols for cancer patients, both to reflect the specific nature of anticancer therapy and anticipate potential complications. By working in partnership with the patient and their cancer team, many problems can be minimised or avoided.

Cancer patients can often have a number of comorbidities that could put them at an increased risk of suffering from neurological PAEs. For example, 1 in 5 cancer sufferers also suffer from diabetes (4). Diabetic patients should already be encouraged to see their podiatrist regularly, however this is particularly important during, or at least early in, their anticancer treatment cycle in order to reassess their diabetic neurological foot status. Early intervention aims to reduce the risk of ulceration, infection and amputation.

Peripheral Neuropathy

Peripheral neuropathy in cancer patients manifests in two main forms, peripheral neuropathy (PN) and chemotherapy induced peripheral neuropathy (CIPN).

PN is one of the most common conditions associated with anticancer therapies and can be highly debilitating. A neurological assessment is recommended at each consultation when undergoing anticancer treatment.

How does it present?

PN normally starts after several months of anticancer treatment and patients complain of the following:

- Numbness or tingling;
- Diminished or absent temperature sensitivities;
- Reduced ability to discriminate between temperature, sharp and blunt touch, light touch, and vibration:
- Altered muscle strength which can lead to imbalance:
- An increase in falls due to loss of proprioception (balance and sense of body movement); and/or
- Changes in the foot shape or joint pain.



Symptoms can progress to a 'glove and stocking' distribution that can extend to the knee. In such cases, patients may report that they can't feel anything below the knee and a stamping gait can be seen. The severity depends on the dosage, frequency and length of each anticancer treatment cycle. PN negatively affects proprioception feedback to the brain, disrupts normal gait patterns and creates variations in the patient's movement (5).

It is also relatively common for patients to complain of a burning sensation in their hands and feet and some have found this to be so severe that they have had to take morphine to help manage the pain.

PN can lead to changes in a patient's mobility as those with numbness complain that they can't feel the ground under them whereas those with hypersensitivity on parts of their feet may find it too painful to walk. Such issues can lead to an increased risk of neuropathic ulceration and infections as pressure points on weight bearing areas are altered and abnormal friction areas will occur.



Finally, it is worth noting that patients who have other risk factors such as diabetes mellitus and obesity, as well as those with vitamin B12 anaemia are at a higher risk of developing PN. For example, some cancer drugs affect blood sugar levels, which can instigate or aggravate existing problems.

Chemotherapy induced peripheral neuropathy (CIPN)

Where PN is specifically chemotherapy induced, it is referred to as CIPN and mainly affects sensory neurones rather than motor neurones. This may be due to the lack of protection by the blood-brain barrier and less myelination of the nerves. Patients being treated for solid tumours or hematologic malignancies are particularly at risk.

Key anti-cancer drugs that can cause CIPN	
Biological agents - bortezomib (Velcade)	Thalidomide
Platinum based drugs: cisplatin, carboplatin and oxaliplatin	Taxane drugs - paclitaxel & docetaxel
Vinca alkaloids - vinblastine, vincristine, vindesine and vinorelbine	Antimetabolites - cladribine, cytosine, fludarabine and methotrexate
Procarbazine	Etoposide
Ifosfamide	Thiotepa

Patients who exhibit acute onset of CIPN (or PN) are more likely to suffer from falls and injuries as the body hasn't had time to adapt to the neurological changes. In extreme cases, the oncologist may decide it is necessary to suspend or reduce the dosage of anticancer treatment in order to mitigate the risks associated with these side effects. This is just one example of where close liaison between the podiatrist and the oncology team is important in determining the best course of action.

How can podiatrists help with PN and CIPN?

One of the key problems resulting from PN and CIPN is the development of neuropathic ulcerations. Ulceration and infection can stop treatment cycles and, due to the delayed healing time of the patient, lead to hospital admissions for treatment. In extreme cases, patients are even faced with potential amputation.

Where ulcerations have already formed, management with surgical debridement and appropriate dressings are important. However, as podiatrists we can significantly reduce the risk of patients reaching this state through regular podiatric assessment to enable early intervention, and through providing advice on areas such as footwear.

As the nerves are not providing the brain with proprioception feedback, patients may start changing their gait pattern or start tripping or falling. Many patients (but elderly patients in particular) will attribute this to their shoes and start wearing inappropriate footwear (e.g. the wrong size or shape) to minimise discomfort. This can lead to deformities developing and simply exacerbate their problems. As an example, PN patients who have reduced sensation will tend to wear shoes that are too small, in order to be able to feel the shoe is on the foot.

As a simple solution, lightweight sandals with a moulded foot bed and a tight fit can help patients' proprioception ⁽⁶⁾. However, our podiatric experience and expertise means we can offer more tailored advice, which can be invaluable to someone suffering pain due to their PN.

This will typically focus on areas such as:

- Highlighting if shoes are too tight/ loose (causing potential nail damage or ulcerations);
- Advice on different shape shoes or different depth toe box to accommodate any new deformities such as clawing or bunions;
- Checking the last (sole shape) of the shoe to ensure it is straight. Trainer-like shoes may seem more comfortable but have a growing trend of being cut on a semi-curved or curved last. This can cause the foot to form an abnormal (banana) shaped position and forces the foot into greater supinated position. This creates pressure through the arch, midfoot and lesser toes and can alter the position of the ankle and forefoot joints, impacting on knee and hip movement;
- Prescribing appropriate orthotics or insoles to add support and prevent deformities progressing.
 Incorporating a memory poron/ plastazote layer in an insole aids cushioning and reduces skin irritation.
 Of these, plastazote is particularly used in insoles for diabetic patients;
- Adding anti-shearing materials such as fleecy web on the feet (e.g. on the dorsal of the toes where clawing is present):
- Using deflective pressure padding on areas of high pressure (such as the balls of the feet) to provide additional support and pressure relief, especially where insoles are not viable;
- Providing advice on seam free shoes and hosiery (such as recommending bamboo fibre or rich cotton socks to help improve comfort and reduce shearing).

Performing regular vascular and neurological assessments will also help detect the changes quickly and allow us to monitor changes to the joints and ranges of motion. Where deformities have occurred and callus and corns have developed, regular podiatric debridement will help prevent ulcerations forming and reduce pain.

For helping to manage the pain associated with CIPN and PN, various studies have found that taking duloxetine and venlafaxine has had positive results ^(7,8) as has applying a topical application which contains a combination of baclofen 0.75%, amitriptyline 3% and ketamine 1.5% gel ^(8,9). In my experience, patients have benefited from applying three layers of Opsite film or Tegaderm to their feet to calm the sensation.

A final area where we can help patients during an appointment is by asking questions about their nutrition, since nutritional deficiencies can increase the risk of PN developing and are a known side effect from chemotherapy or radiotherapy treatment due to the associated nausea and vomiting. Reiterating the usual recommendations around eating regularly and eating a good range of fresh fruit and vegetables can be helpful, as can increasing the intake of foods rich in vitamin B12 if the patient is experiencing pain. Vitamin B12 deficiencies have been found to increase the onset and severity of CIPN (9,10) and some of my patients have anecdotally reported that they have found taking vitamin B12 is very beneficial in reducing pain. Cancer charities such as Macmillan Cancer Support also provide recipes and nutritional advice specifically aimed at helping patients on anticancer therapies.

Autonomic Neuropathy

Finally, whilst not directly podiatry related as it generally affects motor neurones, patients may also present with autonomic neuropathy. By identifying such changes and urgently reporting them to the oncologist we can contribute to earlier intervention, more rapid treatment response and better patient outcomes. This is particularly significant when airways and swallowing are affected.

Symptoms include dropping things, splaying of fingers (11) constipation (if the nerves to the bowel are affected), loss of bladder and bowel control, impotence, and difficulty chewing or swallowing (12). By asking about a patient's more general health during an appointment, or being familiar with the capabilities of patients you see more regularly, you may discover they are experiencing difficulties in these areas.

Conclusion

There are multiple podiatric adverse events (PAEs) that commonly affect cancer patients although this is still relatively poorly publicised and understood. Greater awareness of these issues, recognising them in a clinical setting, working more closely with cancer units and providing appropriate advice and treatment can be an invaluable part of supporting patients through this difficult time.

Routine podiatric care is strongly recommended from the initial diagnosis of cancer where possible as it can assist with earlier intervention and preventative actions, which help the patient maintain their independence, mobility and comfort. Symptoms from neurological PAEs such as changes in gait, increased risk of falls, general foot pain, ulcerations and infections and above all dealing with the effect of chemotherapy induced neurological changes warrants support.

Explaining likely issues to my patients at an early stage and addressing their concerns has helped them be more positive and resilient during their treatment as they are better prepared mentally for the challenges ahead. Managing many of these side effects not only reduces pain and improves their quality of life but also reduces the chances of them not finishing their life-enhancing anticancer therapy. Nevertheless, far more could be done to reach the wider population.

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About the author

Afni Shah-Hamilton runs Tiptoe Foot Care, a private pain management and podiatry practice in Barnet, London. Afni graduated from University College London in Podiatry BSc (Hons) and completed her master's degree at Kings College London. She currently sits on the Macmillan AHP advisory board and has previously been a member of the national patient safety campaign, Sign up to Safety, advisory group. Afni has worked for Southwark Foot Health Department in conjunction with Guy's and King's College Hospital as well as working for the Society of Chiropodists and Podiatrists (now the College of Podiatry) as a Union Learn Fund Project Worker, promoting learning and development across the profession.

Afni has significant experience of dealing with high risk patients through her close relationships with oncologists and a local cancer charity. She is passionate about the role that podiatrists can play in improving the quality of life for both cancer sufferers and cancer survivors.



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