

POEMS syndrome

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This Infosheet explains what POEMS syndrome is, how it is diagnosed and how it is treated and managed.

What is POEMS syndrome?

POEMS syndrome is a rare disorder that can affect multiple systems in the body. It is named after five common features of the syndrome, described below:

- **Polyneuropathy** – nerve damage to various peripheral nerves which control muscles and sensation. Also known as peripheral neuropathy
- **Organomegaly** – enlargement of organs, such as the liver, spleen or lymph nodes
- **Endocrinopathy** – abnormal function of endocrine (hormone-producing) glands
- **Monoclonal plasma cell disorder** – disorder involving abnormal plasma cells (see over)
- **Skin changes** – certain skin changes are characteristic in POEMS syndrome, such as hyperpigmentation (darkening of an area of the skin)

There are also a range of other features (“criteria”) that may occur in POEMS syndrome. However, not every patient will have them. The features include:

- Abnormal (“sclerotic”) bone growth in certain parts of the skeleton. They are typically painless but are usually visible on X-rays and scans
- Swelling of the optic nerve, the main nerve in the eye (known as papilloedema)
- Fluid build-up around the lungs, in the abdomen and/or the legs
- High red blood cell levels and/or high platelet levels in the blood
- Raised levels of a cytokine (chemical messenger) in the body known as vascular endothelial growth factor (VEGF) (occurs in most POEMS patients)
- Castleman disease (a type of lymph node disorder which causes a range of symptoms)

POEMS syndrome is also known as osteosclerotic myeloma, Takatsuki syndrome and Crow-Fukase syndrome, however, these terms are less commonly used.

What is a monoclonal plasma cell disorder?

A plasma cell disorder is the term used to describe a condition which produces abnormal plasma cells. Plasma cells are a type of white blood cell that produce antibodies (immunoglobulins). Antibodies bind to substances in the body that are recognised as foreign, such as bacteria and viruses (known as antigens), enabling other cells of the immune system to destroy and remove them.

In monoclonal plasma cell disorders, large numbers of identical plasma cells are produced. The cells produce an abnormal antibody known as paraprotein (also called monoclonal or M protein) which has no useful function. In POEMS syndrome, the abnormal plasma cells may be located in one or more specific areas of the bone marrow (termed ‘plasmacytomas’), or may be present throughout the bone marrow. The number of abnormal plasma cells in the bone marrow is generally small, and M protein levels are also generally low.

What causes POEMS syndrome?

The exact causes of POEMS syndrome are not well understood.

The paraprotein produced by the abnormal plasma cells is on its own not enough to explain the many features of POEMS syndrome.

Various cytokines are thought to play a role in causing damage to the different tissues and organs involved in the syndrome. This includes the cytokine VEGF that is found in higher levels in POEMS syndrome patients.

Who can develop POEMS syndrome?

POEMS syndrome is very rare and the incidence is not fully known. It is thought that many cases remain undiagnosed because of its rarity, the wide range of signs and symptoms that can occur, and the fact that patients may be seen by different doctors who are unfamiliar with the syndrome.

The average age of diagnosis is in people in their 50s, however this can range from 30–80 years old. POEMS syndrome is more common in men than in women.

What are the symptoms of POEMS syndrome?

The most common symptoms result from the peripheral neuropathy associated with the

syndrome. Peripheral neuropathy is often the most debilitating feature of POEMS syndrome.

The first signs of peripheral neuropathy include numbness and tingling in the hands and feet which progressively worsens over time. Pain, discomfort and weakness in the hands and feet are common features of POEMS syndrome and weakness is often an early symptom of the syndrome.

Other symptoms vary depending on the organ systems involved and can include:

- Weight loss
- Diarrhoea
- Enlargement of the lymph glands (also known as lymph nodes)
- Fluid build-up in the feet and ankles
- Increased sweating
- Skin changes, including:
 - Thickening of the skin
 - Red or purple spots on the surface on the skin
 - An increasing amount of hair on the arms and legs which is often coarse in texture
- Swelling of the fingertips and white nails (known as ‘clubbing’)

- Breathlessness
- Fatigue
- Headaches or blurred vision
- Reduced sexual function (reduced libido, loss of erections)

Patient may also be at increased risk of deep vein thrombosis (blood clots in the deep veins of the body, typically the legs). Patients may have fewer symptoms at diagnosis but develop more symptoms over time as the syndrome progresses.

How is POEMS syndrome diagnosed?

Not all of the criteria referred to in the name “POEMS” (polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder and skin changes) are always present. POEMS syndrome may be diagnosed if the patient has all of the following:

- Polyneuropathy
- Monoclonal plasma cell disorder
- One or more of the other “major criteria” of the POEMS syndrome (sclerotic bone lesions, raised VEGF and Castleman disease)
- One or more of the other criteria (such as hormone changes or skin changes).

To confirm a diagnosis, your doctor will need to perform a thorough physical examination where they will look for:

- Skin and hair changes
- Evidence of fluid build-up
- Enlargement of specific glands and organs such as lymph glands, liver and/or the spleen
- Signs of optic nerve swelling
- Signs of neuropathy by conducting a complete examination of the nervous system

Your doctor will confirm a diagnosis through a number of tests and investigations which include:

1. Blood tests, which check:
 - Your levels of white blood cells, red blood cells and platelets
 - Your liver and kidney function, and function of your endocrine glands
 - If paraprotein is present
 - The level of certain cytokines including VEGF
2. Your urine may also be tested for the presence of part of the paraprotein called light chains (also sometimes called Bence Jones Protein)

3. X-rays and scans to look for abnormal bone growth or bone damage

4. Biopsies and other tests:

- A bone marrow biopsy, or a biopsy of any individual bone lesions (plasmacytomas) identified on scans, may be performed to look for the presence of abnormal plasma cells
- A nerve conduction test may be performed to assess nerve function and damage
- A lumbar puncture may be performed to look for high levels of protein in the spinal fluid

How is POEMS syndrome treated?

It is important that treatment is started as soon as possible, because progression of the condition is rapid without treatment.

Treatment improves symptoms but may not cure the underlying condition. However, the outlook for patients with treated POEMS syndrome has improved greatly in the last few years. In a study of 100 POEMS patients in the UK, 10-year survival for patients was 82% (82 in 100 patients). Patients who relapse generally do well after further treatment.

Treatment of POEMS syndrome will depend on several factors:

- Whether the underlying plasma cell disorder is widespread in the bone marrow, or at a specific location (a plasmacytoma)
- The main symptoms present and organs affected
- Age and general fitness of the patient

Treatment may include chemotherapy and/or radiotherapy. Some patients will be given stem cell transplantation. The treatments are similar to those used in other plasma cell conditions, including solitary plasmacytoma and myeloma.

Radiotherapy

You will typically receive radiotherapy treatment if you have an abnormal bone growth in just one or two areas of the bone, but no evidence of abnormal plasma cells spread throughout your bone marrow. You will be assessed by a radiotherapy specialist who will decide on the exact amount and number of treatments needed. You may be given drug treatment in addition to radiotherapy.

Stem cell transplantation

You may be considered for high-dose therapy and stem cell transplantation (HDT-SCT) if the

abnormal plasma cells are widely spread throughout your bone marrow, and if your age and fitness make this suitable for you. You will be given high dose chemotherapy (often melphalan) before the stem cell transplant, and additional drug treatments before or afterwards. A reaction called “engraftment syndrome” can occur after HDT-SCT, with symptoms such as fever, weight gain and skin symptoms, and is treated with steroids.

Drug treatment

If the abnormal plasma cells are more widely spread throughout your bone marrow, and you are not able to undergo HDT-SCT, it is likely that you will receive a combination of different types of drugs which work together. The most common types of drugs used to treat POEMS syndrome are:

- An alkylating agent which is a type of chemotherapy drug, such as melphalan or cyclophosphamide
- A steroid, such as dexamethasone or prednisolone

These drugs may also be combined with drugs used to treat the underlying plasma cell disorder such as lenalidomide (Revlimid®), thalidomide and bortezomib (Velcade®).

The choice of treatment and dose will take into account side effects which can be problematic in POEMS syndrome (including neuropathy and increased risk of thrombosis).

Treatment is effective in the majority of patients, but improvement is normally gradual. Once there is evidence of an improvement in symptoms, quality of life and day-to-day functioning, it is recommended that patients are referred for a period of rehabilitation, preferably at a specialist rehabilitation centre, to allow nerve and muscle function to improve.

Nerve pain is common in POEMS syndrome and is often treated with drugs such as amitriptyline, gabapentin or pregabalin. Pain caused by nerve damage can be difficult to treat or manage and may require input from a pain specialist or palliative care.

How is POEMS syndrome monitored?

POEMS syndrome patients should be monitored regularly and the type of treatment they receive will determine the frequency of their hospital visits.

After initial treatment is complete, patients are seen regularly for a physical assessment and blood tests. Patients are likely to receive

other ongoing assessments such as nerve conduction tests and scans to assess any old or new abnormal bone growth.

Future directions

Ongoing research aims to better understand what causes POEMS syndrome and why only some patients with certain plasma cell disorders develop the syndrome.

Research is investigating whether new drugs treating the underlying plasma cell disorder can slow down the progression of POEMS syndrome. For example some of the newer drugs used to treat myeloma such as ixazomib (Ninlaro®) are being studied for use in POEMS syndrome.

Summary

POEMS syndrome is a rare disorder with a range of features, including peripheral neuropathy (damage to the nerves) and abnormal immune cells called plasma cells. The exact causes are not well understood. Symptoms can affect many parts of the body. Treatment will depend on how localised the abnormal plasma cells are, and may include radiotherapy, stem cell transplantation, and various drug treatments often used in

combination. Outlook for patients after treatment has increased greatly over the past few years.

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