

Patient Information

Schnitzler's Syndrome

What is Schnitzler's syndrome?

Schnitzler's syndrome is a rare condition that was first reported in 1974. The cause is unknown. Symptoms usually start in middle age, but may, rarely, appear in younger adults. The youngest reported patient was aged 13. It is commoner in men than in women, and most common in people of Caucasian ancestry.



Typical rash in Schnitzler's syndrome

Symptoms include:

- attacks of fever
- recurrent urticarial rash
- joint pain and swelling
- swollen neck glands

The symptoms are very similar to those seen in an inherited periodic fever syndrome called cryopyrin associated periodic fever syndrome (CAPS).

However, CAPS usually starts in childhood, while Schnitzler's syndrome is a disease seen in adults. Blood tests show signs of inflammation and increased quantities of a particular type of antibody produced by immune cells called plasma cells. This is known as a monoclonal gammopathy. Most patients do well over time, but some go on to develop plasma cell malignancy such as multiple myeloma.

What are the periodic fever syndromes?

These are a group of disorders in which patients experience recurrent fevers and other symptoms, although there are no signs of infection or of any other apparent cause. Many periodic fever syndromes are known to be hereditary. In recent years the precise genetic causes of most of the hereditary periodic fever syndromes have been identified so they can be diagnosed by genetic testing.

Schnitzler's syndrome is NOT amyloidosis



If you have been referred to us because of suspicion that you may have a fever syndrome such as Schnitzler's syndrome, this does NOT mean that you have amyloidosis.

Very understandably, some patients and family members may become concerned when they are referred to us, for the following reasons:

1. We are based at the National Amyloidosis Centre (NAC), at the Royal Free Hospital.
2. Our consultants are specialists in amyloidosis as well as fever syndromes.

It is true that a few patients with longstanding, untreated periodic fever syndromes may eventually, after many years, develop amyloidosis.

However for the vast majority of our patients:

1. Referral to us is for the purposes of diagnosis and treatment of a fever syndrome.
2. Amyloidosis is not suspected at any time in the course of their illness.
3. Amyloidosis can be easily prevented by appropriate treatment.

However the cause of Schnitzler's syndrome remains unknown.

Periodic fever syndromes such as Schnitzler's syndrome are all believed to be caused by overactivity of part of the body's natural defence system, the immune system. The immune system involves a wide variety of different types of blood cells and molecular messengers. These components interact together through a variety of complex mechanisms, known as pathways. The part of the immune system affected in the periodic fever syndromes is called innate immunity.

In healthy people, normal activation of the innate immune pathways occurs when the body encounters some type of tissue damage or disease. The consequent inflammation helps to fight disease and promote recovery.

In the periodic fever syndromes, some of these pathways are overactive. This leads to an overly aggressive

immune response. The body acts as if there was a serious infection even when there is no actual disease or tissue damage acting as a stimulus. There is a state of prolonged inflammation, known as auto-inflammation. Auto-inflammation itself leads to symptoms of disease and sometimes to tissue damage.

Different pathways are implicated in different types of periodic fever syndromes. Treatment aims to "switch off" the overactive inflammatory pathway and depends on precise identification of the particular syndrome, and pathway affected.

Auto-inflammation is quite different to auto-immunity. In auto-immune diseases, the body produces antibodies against its own tissues, which then cause damage. In auto-inflammatory conditions the body does not produce antibodies against its own tissues. Auto-immune diseases are far commoner than auto-inflammatory syndromes. Auto-immune diseases include conditions such as childhood diabetes and rheumatoid arthritis.

How is Schnitzler's syndrome treated?



Drugs which block the inflammatory protein, IL-1 appear promising for treating this condition, although this is an off-license use. These drugs include:

- anakinra
- canakinumab

These drugs are administered by injection under the skin. Anakinra has to be given at home every day, and canakinumab is given every month.

The side effects of these drugs include:

- stinging
- skin redness at the injection site, in some people
- increased risk of infection

In general the infections reported have been mild but we screen all patients for tuberculosis and ask about a history of other infections before starting such drugs.



Logistics

Patients with Schnitzler's syndrome may need long-term surveillance, with regular administration of medications and specialist follow up. Our consultants provide on-going direct management at the Royal Free Hospital. When patients live far away, it may be possible to arrange for some treatments to be administered at their local hospitals or at other regional centres.

In these cases, we can help by providing:

- regular advice to patients and doctors involved in their treatment
- regular reviews at the Royal Free Hospital
- arrangements for hotel accommodation during visits

Overseas and non-NHS entitled patients

The Royal Free Hospital welcomes overseas patients. European Union residents may be entitled to an NHS assessment in the UK under EU reciprocal arrangements for medical care that is not available locally (EU 112 form). Non-NHS entitled patients are welcome but are usually liable to charges.

Periodic Fever Service

The Inherited Periodic Fever Service is the only centre in the UK dedicated to the needs of patients with fever syndromes. We are based at the National Amyloidosis Centre. We have “state-of-the-art” clinical and research facilities and a team of highly qualified clinical, research and support staff. We are funded by the Department of Health to provide a diagnostic and management advice service for the UK’s national caseload of patients with inherited periodic fevers and related disorders. The clinical service includes:

- Detailed clinical assessment
- Genetic testing and counselling
- Recommendations for treatment and monitoring response
- Measurement and monitoring of specialised biochemical (blood) tests for C-reactive protein (CRP) and serum amyloid A protein (SAA)
- 3-12 monthly follow-up to assess response and further treatment requirements
- Providing information and support to fever patients, their families and health providers
- Systematic evaluation of existing and new treatments



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