PSORIATIC ARTHRITIS: A REVIEW

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ABSTRACT

Psoriatic arthritis is an inflammatory arthritis which affects the skin and musculoskeletal system. If not diagnosed early and treated effectively it can result in joint deformity and disability. Treatments such as oral disease modifying anti-rheumatic drugs and biologic therapy are effective but have side effects which could limit their use in certain individuals. Further research aimed at identifying cases earlier in order to improve outcomes is currently being conducted.

Keywords: Psoriatic arthritis (PSA), disease modifying anti-rheumatic drugs (DMARDs), biologics, the classification of psoriatic arthritis (CASPAR), dactylitis, arthritis mutilans, rheumatoid arthritis, tumour necrosis factor alpha (TNF-α).

INTRODUCTION

Psoriatic arthritis (PSA) is a chronic condition which can cause considerable disability and pain if not recognised and treated properly. Approximately 15% of patients affected by psoriasis will develop associated joint disease.[1] It was first recognised in 1964 and is now considered part of the spondyloarthropathy (SPA) group of diseases.[1] PSA can cause significant joint deformity, and can also affect the surrounding structures of joints such as tendons and ligaments. Research has shown that there is associated cardiovascular comorbidity. However, treatments have now been developed which can control the disease and achieve remission.

It is important that PSA is recognised early in order to be effectively treated. There is evidence that a proportion of PSA patients remain undiagnosed.[1] Although in most cases patients develop arthritis after having had psoriasis, there is a group of patients that develop joint symptoms prior to any skin manifestations, causing confusion and delay in diagnosis. Research has been focussed on developing scoring systems and diagnostic criteria which can identify such cases at an early stage.

GENETIC FACTORS

Psoriasis and PSA are strongly heritable conditions[2,3] when compared with other inflammatory rheumatic conditions. Family history of psoriasis/PSA (or other features of the SPA spectrum such as inflammatory bowel disease and iritis) can provide strong support for the diagnosis of PSA when assessing a patient suspected of having the disease.[3] PSA is thought to be more heritable than psoriasis.[1] Different human leukocyte antigen alleles are associated with PSA.[1] Certain gene polymorphisms are also more strongly associated with PSA, including tumour necrosis factor alpha (TNF-α) promoter, major histocompatibility complex class 1, and some interleukin (IL) receptors. The pattern of inheritance is complex and multigenic and varies from dominant in some families to recessive in others.[3]

PATHOPHYSIOLOGY

It is still not clear what exact mechanism lies behind the development of PSA. It is thought to be multifactorial and secondary to environmental, genetic, and immunological factors.[1] Over-activation of the immune system when triggered in the skin and joints causes an inflammatory cascade,

resulting in signs such as scaly skin plaques and joint synovitis in those individuals who are genetically susceptible. The synovitis which is detected in PSA can be pathologically different to that found in rheumatoid arthritis (RA).[3] In PSA the synovitis resembles more of a SPA type, with high numbers of neutrophils and greater vascularity when compared with the RA synovitis, thus suggesting that PSA is a separate condition from RA both genetically and pathologically.

Bone changes in PSA are thought to be secondary to osteoclast proliferation which are activated by cytokines. These changes include erosions, osteolysis, and new bone formation.[1] Inflammation in PSA can also affect surrounding tissue such as ligaments and tendons, which is more uncommon in RA. Inflammatory cells infiltrate the entheseal and ligament tissues causing subsequent pain and swelling. Imaging studies have shown that joint capsules and tenosynovial tissues can also be affected by inflammation in PSA. Thus in clinical assessment, it is important to focus on other sites of inflammation and not just concentrate on how many tender or swollen joints the patient has.

Pro-inflammatory cytokines such as TNF-α are present in psoriatic plaques and synovial fluid in large amounts.[1] TNF-α is also found in many other arthropathies and biologic drugs which are aimed at blocking TNF-α have been effective therapies for such conditions. Although they are useful in PSA, other therapies such as the B cell-depleting rituximab is not as effective in PSA when compared with RA.[3] Thus there are still distinct cell lines that are unique to the inflammation found in PSA and which need further research for therapeutic purposes. In particular, T helper cell 17, IL-17, and IL-23 are inflammatory mediators which have a significant role in the disease process of PSA, and research is aimed at targeting these cells.

CLINICAL FEATURES

PSA is considered an inflammatory arthritis and part of the SPA group of diseases. Its clinical features can vary from causing mild joint pains to presenting as a rapidly erosive debilitating illness causing lasting joint damage. It can affect both the axial and peripheral joints, commonly presenting in an oligoarticular pattern. Two features which are hallmarks of PSA are the presence of dactylitis and enthesitis.

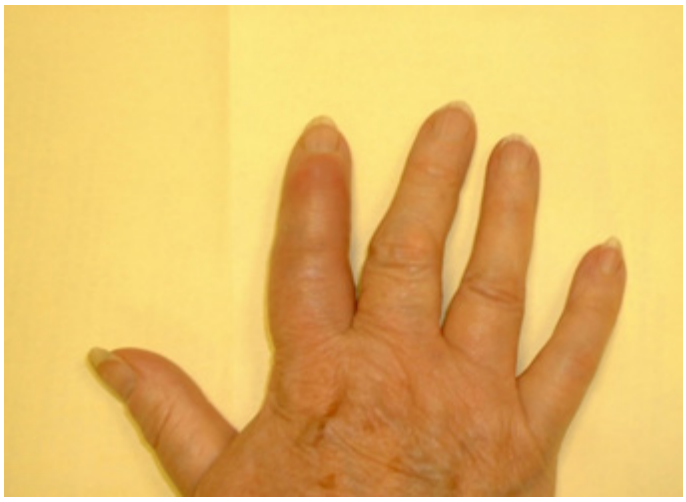

Figure 1: Patient presenting with dactylitis.

Dactylitis is inflammation of an entire digit (Figure 1). It can affect up to 40% of patients with PSA.[4] It occurs secondary to inflammation of the digital flexor tendon sheaths. Some studies have shown that it is associated with erosive joint damage. It commonly occurs in the feet; most often in the fourth toe. The presence of dactylitis could indicate overall disease severity.[4] Enthesitis is inflammation of tendon/ligament insertions into the joint,[5] and is a common feature of PSA and the other SPAs. Patients are usually tender over the tendon insertion sites in the elbows, heels, and iliac crest. The achilles tendon is most commonly affected.

Patients with PSA can also develop extra-articular signs, most frequently in the nails. The close anatomical association between the nail and the distal interphalangeal joint is perhaps why the nail is so often affected in PSA.[6] Typical changes include nail pitting and onycholysis. Splinter haemorrhages and hyperkeratosis can also occur. Nail pitting can be used as part of diagnostic criteria for PSA. If PSA is left untreated then it can lead to a condition known as arthritis mutilans. This manifests as a shortening of the digits with severe osteolysis,[7] and can cause considerable pain and discomfort for the patient. It can also result in significant functional disability.

Classification for Psoriatic Arthritis (CASPAR) Criteria

Scoring systems have been developed to try and identify PSA at an early stage and criteria have been developed to aid in classification of the

disease from the other SPAs and inflammatory arthritides. Not only are they useful for identifying PSA earlier, they can also help identify cases of PSA which do not present in the typical manner. Some criteria include PSA with the SPA group. The classification for psoriatic arthritis (CASPAR) criteria was developed specifically for PSA.[1] It has good sensitivity and specificity for those presenting with disease of <2 years' duration.[1] Although primarily used for classification, it can be used for diagnostic purposes.[8]

The CASPAR criteria consists of established inflammatory articular disease (joint, spine, or entheseal) with at least three points from the following features:

a) Current psoriasis (assigned a score of 2; all other features are assigned a score of 1): skin or scalp disease as evidenced by a rheumatologist or dermatologist
b) A personal history of psoriasis (unless current psoriasis is present): can be obtained from any healthcare professional
c) A family history of psoriasis (unless current psoriasis is present or there is a personal history of psoriasis): first or second degree relatives
d) Current dactylitis or history of dactylitis recorded by a rheumatologist
e) Juxta-articular new bone formation: as evidenced on radiographs
f) Rheumatoid factor negativity: can be by any laboratory method
g) Typical psoriatic nail dystrophy including onycholysis, pitting, and hyperkeratosis

INVESTIGATIONS

A diagnostic test for PSA does not exist[3,9] unlike in RA which is cyclic citrullinated peptide and rheumatoid factor positive. As in other inflammatory conditions, markers such as erythrocyte sedimentation rate and C-reactive protein can be raised in PSA. Immunoglobulin A can be elevated in a proportion of patients. Joint aspirate can be inflammatory, with an increase in white cell count and polymorphs.[9]

Radiographic changes can be more diagnostic of PSA and help to differentiate it from other inflammatory arthropathies. As well as bony erosions, other signs on radiography include ankyloses, joint space narrowing, and osteolysis.[3] The 'pencil-in-cup' deformity is characteristic of PSA.[3] It results from peri-articular erosions leading to the appearance of a pencil in a cup, most often affecting the distal interphalangeal joints. Bony growths over tendon and ligament attachments can also be seen. However, it is important to note that these changes can be non-specific[3] and are not present in all patients.

Further imaging such as magnetic resonance imaging (MRI) can help to identify soft tissue involvement in further detail, particularly when a patient is suffering from enthesitis.[10] Ultrasound has also become a useful tool in the investigation of arthritis; it can help to identify bony erosions in those patients where synovitis or dactylitis is not always evident clinically. Studies have shown that ultrasound scan and MRI are more sensitive for detecting inflammation than plain radiographs in PSA.

TREATMENT

As discussed, PSA can be debilitating for the patient if not adequately treated. Fortunately, treatments have been developed which can help to halt disease progression and maintain function for the individual affected, as well as alleviate any pain the patient may suffer from. A multidisciplinary approach between rheumatology and dermatology is often necessary in order to maximally treat the condition.[11]

Corticosteroids are used in PSA and in many other inflammatory arthropathies in order to provide immediate symptom relief. They can rapidly diminish the inflammatory response seen in these conditions, causing a reduction in swelling and stiffness in the joints. They can be given as an intramuscular injection for general widespread relief or directly injected into the affected joint for a more targeted response.[1] Long-term steroid use should be avoided due to the side effect profile which includes diabetes, hypertension, osteoporosis, and immunosuppression. There is also a risk of skin psoriasis flares after intramuscular injections.[12] In most cases steroids are used for short-term relief and occasionally as bridging therapy while establishing the patient on more long-term immunosuppressants.

Disease modifying anti-rheumatic drugs (DMARDs) are used in PSA as in other inflammatory conditions. They are a group of drugs which can help to reduce inflammation as well as to slow disease progression to prevent joint damage, as opposed to nonsteroidal anti-inflammatory drugs

and steroids which treat the inflammation but not the underlying cause. However, evidence behind their use in PSA is not as robust as in RA. Use of DMARDs is mostly based on a clinician's experience rather than evidence.[1] Methotrexate can cause improvement in both the skin and peripheral joints. Sulfasalazine is useful for peripheral arthropathy although only with weak evidence. Cyclosporine has beneficial effects on the skin. Small studies have shown that leflunomide has similar efficacy for use in PSA as compared with RA. The main side effect with DMARDs is their immunosuppression, which can expose the patient to potentially serious infections such as neutropenic sepsis. Methotrexate also commonly causes nausea and gastrointestinal disturbance which can be severe and unpleasant. Liver function has to be closely monitored with methotrexate and leflunomide due to the risk of liver toxicity.

Biologic therapies that have been developed in the last 20 years have been shown to be effective treatments for inflammatory conditions. Some biologics target TNF-α, a pro-inflammatory cytokine, which is involved in both the skin and joint manifestations of the disease. These drugs are expensive and are usually used when other therapies have failed. In most cases treatment failure would be considered when patients have failed two or more DMARDs used in combination and still have evidence of active disease. Biologics have been proven to reduce disease activity and improve quality of life, but their side effects include increased risk of infection, reactivation of tuberculosis, worsening of congestive cardiac failure, and demyelination syndromes.

Emerging Therapies

Recently ustekinumab has been licensed for PSA.[1] It is a human monoclonal antibody which blocks a signalling pathway in the disease by preventing IL-12 and IL-23 from binding to IL-12Rβ1. In addition, apremilast, a new oral, targeted, synthetic DMARD has been licensed, which targets phosphodiesterase 4. Apremilast offers a number of advantages over conventional DMARDs such as low toxicity and lack of monitoring need, but its efficacy in practice has yet to be fully evaluated. Further studies are researching other cytokines that can be targeted such as IL-17.[1]

SUMMARY

PSA is a complex autoimmune disorder which affects a number of sites within the body. Clinically distinct from RA, significant advances have been made in understanding the pathogenesis of the disease and a number of therapies have been shown to be effective treatments. However, a diagnostic test for the condition still does not exist, and further research is being conducted in order to develop a robust diagnostic model which can be used to identify and treat PSA as early as possible, as well as to develop new therapies.

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