

MUSCULOSKELETAL BLOCK: LECTURE FOUR

NON-INFECTIOUS ARTHRITIS

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STRUCTURE AND FUNCTION OF JOINTS

Joints are of two types:

- **Solid joints** – these joints are fixed and rigid and allow only minimal movement. Examples of solid joints include the skull sutures (where the skull bones are bridged by fibrous tissue) and the symphysis pubis (where the bones are joined by cartilage).
- **Synovial joints** – these joints have a joint space, which allows a wide range of movement. The articular cartilage in synovial joints is a specialized hyaline cartilage which is an excellent shock absorber. The synovial membrane secretes synovial fluid into the joint space. Synovial fluid acts as a lubricant and provides nutrients for the reticular hyaline cartilage.

OSTEOARTHRITIS (DEGENERATIVE JOINT DISEASE)

This is the most common type of joint disease and is characterized by the progressive erosion of articular cartilage in weight-bearing joints. The incidence increases with age. Osteoarthritis can be primary or secondary to other bone or joint disease, systemic diseases such as diabetes, a

congenital or developmental deformity of a joint, or previous trauma including repetitive minor trauma.

PATHOLOGY AND PATHOGENESIS

In the early stages of osteoarthritis, the articular cartilage becomes eroded and fragmented (fibrillated) and portions of the cartilage flake off. In contrast with joints affected by simple wear and tear, these changes occur well away from the articular margins and there is eventual full thickness loss of cartilage with the underlying bone becoming exposed and developing a polished ivory appearance (eburnation). Loss of articular cartilage stimulates thickening of the subchondral plate and the adjacent cancellous bone which impairs the ability of the joint to act as a shock absorber and results in increased damage to the residual cartilage.

Small fractures develop in the now articulating bone, allowing synovial fluid to enter the subchondral regions with resultant formation of subchondral pseudocysts. Fragments of cartilage and bone fall into the joint space forming loose bodies (joint mice). Bony outgrowths, known as **osteophytes**, form at the margin of the articular cartilage. The articular surfaces become increasingly deformed.

The reason why the articular cartilage becomes predispose to this damage appears to be related to biochemical alterations in the hyaline. In hyaline cartilage affected by osteoarthritis, the water content is increased and the proteoglycan content is decreased. The elasticity and compliance of the cartilage is, therefore, reduced. The very first change seen in osteoarthritis is proliferation of chondroblasts, and it has been proposed that these cells produce enzymes that induce these biochemical changes in the hyaline cartilage.

Clinical features

The most frequently affected joints are the hips, the knees, the cervical and lumbar vertebrae, the proximal and distal interphalangeal (PIP and DIP) joint of the hands, the first metacarpophalangeal joint and the first metatarsophalangeal joint. Osteophytes at the DIP joints produce nodular swellings called Heberden's nodes. With increasing deformity of the joint the typical symptoms develop, which are pain (which is worse with use), morning stiffness and limitation in joint movement. With involvement of the cervical and lumbar spine, osteophytes may impinge on the nerve roots causing symptoms such as pain and pins and needles in the arms or legs. The overall result is disability. The process cannot be halted.

RHEUMATOID ARTHRITIS

Rheumatoid arthritis is a chronic inflammatory multisystem disorders (hence rheumatoid disease), but the joints are invariably involved. The condition can affect all age groups. When children are affected, the condition is designated **Still's disease**. Females are affected more often than males.

The pathogenesis is not well understood, but it is thought that an initiating agent, possibly an organism, triggers immunological dysfunction resulting in persistent chronic inflammation in generatically susceptible individuals. In the joints, the ongoing inflammation causes destruction of the articular cartilage. Circulating autoantibodies (rheumatoid factors) which are directed against autologous IgG immunoglobulins, can be detected in the serum of around 80% of affected individuals. The exact role of these autoantibodies is uncertain.

PATHOLOGICAL FEATURES

Joints

The most severe morphological changes of rheumatoid arthritis are manifest in the joints. In the early stages, the synovium becomes thickened, edematous and hyperplastic. With ongoing inflammation, a

pannus is formed. A pannus is a chronically inflamed fibrocellular mass of synovium and synovial stroma which develops over the articular cartilage. As the pannus slowly spreads, it degrades the underlying cartilage and erosions and subchondral cysts develop in the underlying bone. Small detached fragments fall into the joint space and are called **rice bodies**. Localized osteoporosis may also occur. The fibrous pannus eventually bridges the opposing bones causing limitation of movement, and ossification of this fibrous tissue leads to bony ankylosis. The inflammation also affects the joint capsule, tendons and ligaments causing characteristic deformities.

Skin

The most common cutaneous lesions are **rheumatoid nodules** which arise in areas exposed to pressure, e.g. the extensor surfaces of the arms and the elbows. They are seen in ~30% of patients. They arise in the subcutaneous tissue and manifest as firm, non-tender skin nodules. Microscopically, they consist of a central area of fibrinoid necrosis surrounded by a palisade of histiocytes and fibroblasts.

Blood vessels

Patients with severe disease may develop a rheumatoid vasculitis. Peripheral neuropathy, skin ulceration, gangrene and nail-bed infarcts may develop. Impairment of blood supply to vital organs can be fatal.

Lungs

Parenchymal rheumatoid nodules (usually asymptomatic), chronic interstitial fibrosis and pleurisy can occur.

Eyes

Scleritis and uveitis can develop.

Heart

The development of rheumatoid nodules in the conduction system may occur and coronary artery vasculitis may result in myocardial ischaemia. Pericarditis can also be a feature.

Bones

Patients are at increased risk of localized and generalized osteoporosis.

Lymphoreticular

Patients may develop lymphadenopathy with or without splenomegaly. The combination of rheumatoid arthritis, splenomegaly and neutropenia is called **Felty's syndrome**. Approximately, 50% of patients with Felty's syndrome develop secondary Sjogren's syndrome. Patients may have a normocytic normochromic anaemia.

Miscellaneous

Patients are at an increased risk of developing amyloidosis.

CLINICAL FEATURES

The clinical course of rheumatoid arthritis is very variable. Some patients have mild disease, whereas others have severe progressive disease quickly leading to disability. Initially, patients may suffer constitutional symptoms and only after a few weeks or months do the joints become involved. Generally, the small joints (especially those in the hands) are affected before the large joints. The affected joints are swollen, painful and stiff following a period of inactivity. Symptoms may improve with the administration of anti-inflammatory drugs or immunosuppressants. As a result of the pathological processes within the

articular and periarticular tissues, characteristic deformities develop.

These include:

- Radial deviation at the wrists.
- Ulnar deviation at the fingers.
- Flexion and hyperextension deformities of the fingers (swan neck and boutonniere deformities).

Typical X-ray changes include:

- Loss of articular cartilage leading to narrowing of the joint space.
- Joint effusions.
- Localized osteoporosis.
- Erosions.

Fatalities are usually the result of complications such as amyloidosis, vasculitis or the iatrogenic effects of therapy (e.g. gastrointestinal bleed secondary to non-steroidal anti-inflammatory drugs (NSAIDs), infections secondary to steroids).

CRYSTAL ARTHROPATHIES

Crystal arthropathies are a group of disorders caused by the deposition of crystals within the joint resulting in an acute and chronic

arthritis. Such crystals may be endogenous or exogenous. The most common crystal arthropathies, gout and calcium pyrophosphate arthropathy, are due to endogenous crystal deposition.

GOUT

Gout occurs due to the crystallization of monosodium urate within a joint, resulting in an acute (gouty) arthritis, which is characterized by extreme localized pain, erythema and exquisite tenderness of the affected joint. The most commonly affected joint is the metatarsophalangeal joint of the great toe, followed in decreasing frequency by the ankle and the knee. The disorder is due primarily to raised serum uric acid levels, but only around 3% of people with hyperuricaemia will develop gout. Uric acid is the end product of purine metabolism and is excreted by the kidneys. Purines can either be derived from the breakdown of nucleic acid or synthesized de novo. Hyperuricaemia has several causes:

- Idiopathic (80% of cases).
- Overproduction of uric acid due to increased purine turnover (e.g. due to leukemia) or an enzyme defect.
- Decreased excretion of uric acid (e.g. chronic renal failure, thiazide diuretics).

- High dietary purine intake.

The events which lead to the deposition of urate crystals in the joint are uncertain, but possible triggers include alcohol, trauma, surgery and infection. The presence of urate crystals within the joint causes the accumulation of numerous inflammatory cells. The resulting arthritis remits after a few days of weeks, even without treatment. The diagnosis can be confirmed by aspirating the joint fluid and using polarizing microscopy to detect the needle-shaped crystals, which exhibit negative birefringence with a red filter.

Repeated attacks of acute gouty arthritis eventually lead to chronic tophaceous gouty arthritis, where the affected joint is damaged and function is impaired. **Tophi** are large aggregates of urate crystals which are visible with the naked eye. They occur in the joints and soft tissues of people with persistent hyperuricaemia. A common site for tophi is the pinna of the ear.

Urate crystals can also become deposited in the kidney, resulting in acute uric acid nephropathy, chronic renal disease, or uric acid stones causing renal colic.

CALCIUM PYROPHOSPHATE ATHROPATHY (PSEUDOGOUT, CHONDROCALCINOSIS)

This condition is due to the deposition of calcium pyrophosphate crystals in the synovium (pseudogout) and articular cartilage (chondrocalcinosis). It can occur in three main settings:

- Sporadic (more common in the elderly).
- Hereditary.
- Secondary to other conditions, such as previous joint damage, hyperparathyroidism, hypothyroidism, haemochromatosis and diabetes.

The crystals first develop in the articular cartilage (chondrocalcinosis), which is usually asymptomatic. From here, the crystals may shed into the joint cavity resulting in an acute arthritis, which mimics gout and is therefore called pseudogout. Pseudogout can be differentiated from gout in three ways:

- The knee is most commonly involved.
- X-rays show the characteristic line of calcification of the articular cartilage.

- The crystals look different under polarizing microscopy, they are rhomboid in shape and exhibit positive birefringence with a red filter.