The pathology of joint replacement and tissue engineering

Anthony Freemont

Abstract

Joint replacement is very common and undertaken in most hospitals in one form or another. Tissue engineering of connective tissues generally, and joints in particular, is becoming more common. With increased usage, these techniques generate iatrogenic morbidity. The diagnosis and exclusion of iatrogenic disease is an increasingly important area of pathologists' working lives. This article discusses the disorders that can arise in association with joint replacement and tissue engineering of joints and describes a relatively new disease (Adverse Reaction to Metal Debris [ARMD]) the first of what may become many new disorders associated with the new therapeutics covered in this article.

Keywords infection; joint replacement; osteoarticular; pathology; tissue engineering

Background

The pioneering research of John Charnley is generally considered to have triggered the revolution that led to modern joint replacement surgery.[1] Charnley's work laid the practical foundations for the use of inorganic engineered materials, such as metals and plastics, to restore joint function by replacing malfunctioning articular surfaces. These new techniques were not without their problems. More recently two new branches of connective tissue medicine, tissue engineering and regenerative medicine, have focused minds on the possibility of replacing damaged tissue with new.

As with all medical innovations, problems are recognized that with time change the practice of pathology. The problems associated with the pathology of joint tissue replacement and regeneration can be considered under four headings:

- Replacement of articular surfaces
- Replacement of non-articulating intra-articular structures
- Intra-articular injectable agents
- Tissue engineering/regeneration

Replacement of articular surfaces

Background

The purpose of joint replacement (arthroplasty) is to improve the limited movement and reduce pain caused by damage to articular surfaces. This is achieved by either replacing diseased articulating surfaces with artificial ones (e.g. hip replacements) or by replacing the entire joint with a prosthesis (e.g. finger joints).

Artificial articulating surfaces are usually constructed of metals, plastics or ceramics, or combinations of these materials. Some are used solely for resurfacing the joint, whilst others replace the articulating surfaces and adjacent bone. Often they are held in place using cements consisting most commonly of acrylic resins. Recently there has been a trend towards coating the stems of implants with materials such as hydroxyapatite that are said to promote bone growth into the prosthesis, with the hope of preventing loosening, a problem that requires revision and a new prosthesis.

Typically, both sides of a joint wear out together and arthroplasty surgery replaces both articular surfaces. If this is the case, the two opposing prosthetic surfaces may consist of the same or different materials. Traditionally the articulations were metal on plastic. They are highly successful but in a proportion of patients the differences in physical properties of the two surfaces leads to wear and formation of significant numbers of wear particles, which initiate a macrophage and giant cell reaction leading to bone loss and implant loosening. Advances in materials design has resulted in manufacture of articulations with reduced wear particle production. Of these the combination of metal articulating on crosslinked polyethylene (PE), metal on metal, and ceramic-on-ceramic articulations have all demonstrated lower rates of in vivo wear particle generation than the original metal-on-plastic ones.

The properties of wear particles derived from inorganic materials used in joint replacement

Cross-linked polyethylene: ultrahigh molecular weight polyethylene.

(UHMWPE) is the most commonly used material for acetabular and tibial prostheses.[2] It has good biocompatibility but it does undergo wear. The wear particles vary in size from a few to several hundred micrometres long. The particles are intensely birefringent and remain in tissue after conventional processing (Figure 1a).

Metals: the most common metals used for articulations are low carbon stainless steels and cobalt-chrome. Metals may be scratched, particularly during implantation, which initiates wear.

Many stems of knee and hip implants are made of alloys of titanium, vanadium and aluminium. This material can also wear. There is evidence that titanium can preferentially elute from the alloy. Although inert, titanium can disseminate widely throughout the body.[3]

Metal wear particles show up as tiny dark flecks, usually within macrophages in tissue sections of synovium (Figure 1b) or the soft tissue membranes that develop between implants and surrounding bone.

Ceramics: these (e.g. alumina [Al_2O_3]) are harder than the equivalent metals and can produce very smooth surfaces that are extremely unlikely to wear. They are, however, more brittle and more likely to fracture (in practice this occurs in <1:400 cases). The fragments produced by wear and fracture have no specific

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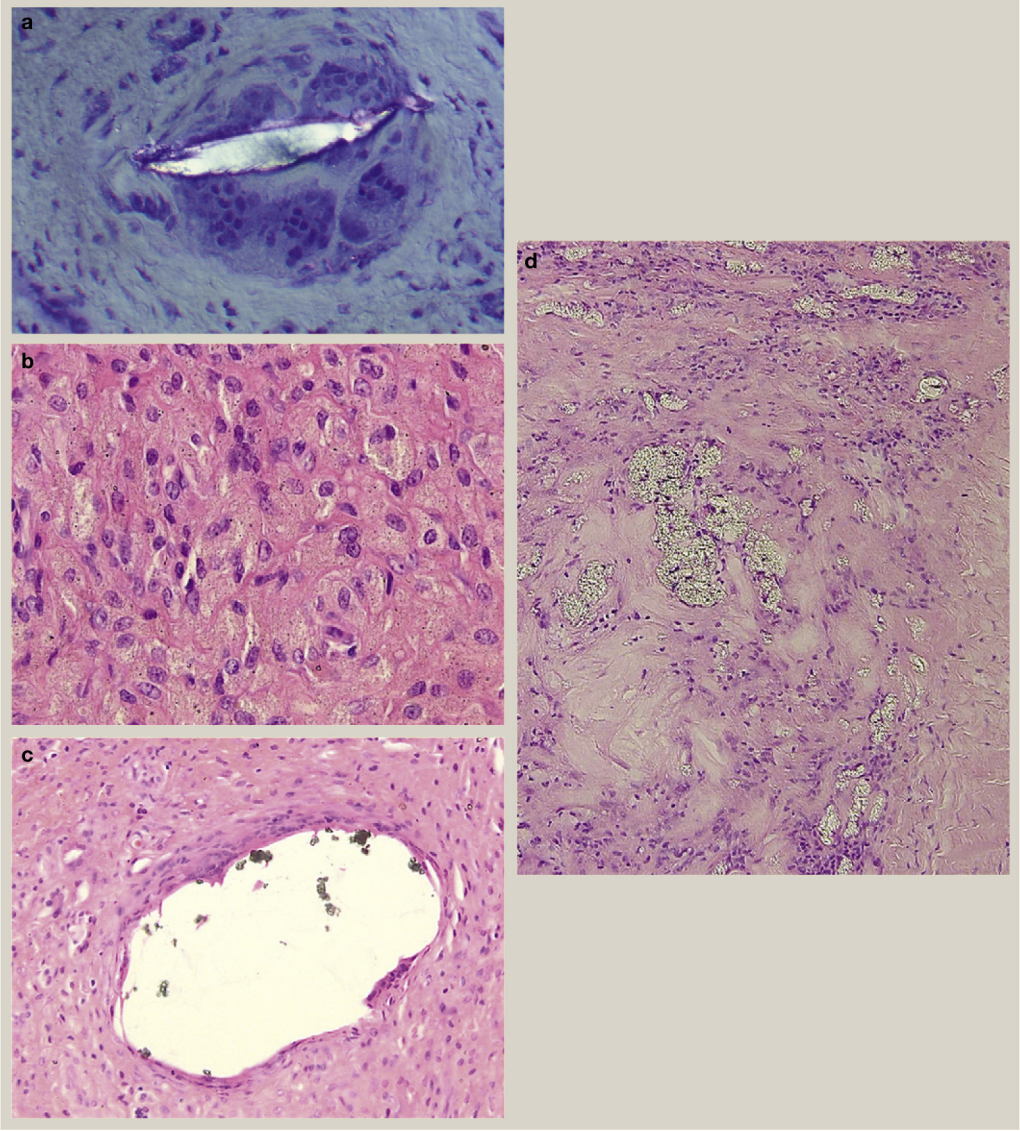

Figure 1 Examples of different materials seen in biopsies of synovium: (**a**) HMWPE. (**b**) Cement. (**c**) Silastic. (**d**) Metal particles.

features, being a granular material that resembles hydroxyapatite.[4]

Cement: most commonly cements are acrylic resins, such as polymethylmethacrylate (PMMA). PMMA forms by hyperthermic polymerization of a liquid monomer. During polymerization the cement sticks to the implant's stem and, because it is introduced into the marrow as a liquid that can permeate between bone trabeculae, when it polymerizes, it binds itself into the trabecular network, fixing the prosthesis tightly to the adjacent bone. The cement is doped with particles of metal such as barium to render the cement radiodense. Under the microscope cement appears as a large, clear, rounded nodule surrounded by macrophages and multinucleate giant cells and containing dark refractile rounded granules of the doping metal (Figure 1c).

Hinge materials: some small joints (e.g. Finger joints) are replaced by plastic hinges. The hinge materials are usually made from the silicone-based polymer, silastic. With frequent use silastic may break, releasing particulate material which can spread to other areas of the body via the lymphatics. This material is refractile, granular and usually intracellular within macrophages or synoviocytes (Figure 1d).

Complications of joint replacement surgery

Arthroplasty is a very successful procedure, however, there is a 10 year failure rate of about 2%, the major causes of which are:

- Dislocation. This is a complication that is related to the success of the surgical procedure itself and the laxity of supporting tissues.
- Damage to the prosthesis. With modern materials these events are rare.[5]
- Aseptic loosening
- Infection. This is relatively uncommon, important and dealt with later.

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