

Starch synovitis

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SUMMARY Three patients with unexplained synovial inflammation were found to have an ulcerative, granulomatous synovitis on biopsy. Maize starch was identified in giant cells within the granulomata. Starch synovitis has clinical and histological similarities to starch peritonitis, which is thought to be an example of a cell mediated immune response.

Starch, in various forms and from a number of plant species, is widely used in medical and pharmaceutical practice.¹ In particular, it is used as a dusting powder for rubber products, such as surgeons' gloves, and as a filler and disintegrant in tablet manufacture. Starch was introduced to replace talc as a glove lubricant after reports that accidental introduction of talc into wounds caused failure of wound healing, fibrosis, and sinus formation.² Contrary to initial reports³ starch is not entirely safe and reactions to it have been reported in the pulmonary parenchyma, pleura, paranasal sinuses, mastoid cavities, testes, biopsy scars, and even in the pelvic peritoneum after vaginal examination.⁴

We report three cases of synovitis in which starch appears to be the pathogenic agent.

Case reports

CASE 1

A 46 year old woman first presented in 1976 with a painful, swollen, left knee, from which fluid was aspirated but not analysed. Symptoms persisted through the ensuing four years, until she presented again in 1980 with a hot, swollen, painful left knee and additional mild swelling of the left ankle. Joint aspiration produced pale yellow, turbid fluid with fair mucin clot and a white cell count of $17.9 \times 10^9/l$ comprising 94% polymorphonuclear cells, 4% monocytes, 1% lymphocytes, and 1% synoviocytes. Cultures of the fluid and other sites were sterile for tuberculosis and gonorrhoea. Rheumatoid factors were not found and HLA tissue typing showed the presence of A1, A10, B8, and B15.

Symptoms persisted despite conventional drug treatment and so she underwent arthroscopy in May 1981; a chronic proliferative synovitis was found. The synovial fluid white cell count at this stage

was $40 \times 10^9/l$ (100% polymorphonuclear cells). Open surgical synovial biopsy was performed six weeks later, at which a grossly inflamed and thickened synovium with pannus over the articular margins was found. Other investigations at this time included an erythrocyte sedimentation rate of 33 mm in the first hour; but tests for rheumatoid factors and antinuclear antibodies and a Kveim test were all negative.

CASE 2

A registered drug addict aged 32, who admitted to injecting suspensions of crushed tablets and narcotic powders into the dorsal veins of her right foot, presented in January 1983 with pain in her right ankle. All investigations were normal with the exception of the erythrocyte sedimentation rate, which varied between 15 and 40 mm in the first hour. With conservative treatment her symptoms improved, but in July 1983 she was readmitted with a low grade fever and a swollen, hot, red ankle. Open exploration showed inflammation of the synovial sheaths of a number of extensor tendons. The synovium was biopsied.

She claimed not to have injected into the veins of the right foot since November 1982.

CASE 3

A 49 year old woman presented with symptoms of trochanteric bursitis, which responded initially to steroid injections. Her symptoms recurred one year later and she underwent synovial biopsy. Histological examination showed the bursa to have a dense fibrous wall and an inconspicuous lining layer with no evidence of inflammation or fibrin deposition. After the operation wound healing was poor and the operation site was swollen and painful. At a second operation a wide excision was performed, after which she recovered completely. All investigations including peripheral blood white cell count, erythro-

cyte sedimentation rate, and rheumatoid factor were consistently within normal limits.

Pathological examination

Tissue was fixed in 10% phosphate buffered formalin and embedded in paraffin wax. Tissue sections (4 μm) were stained with haematoxylin and eosin, periodic acid Schiff (before and after diastase), and the Ziehl-Nielson stain, using standard techniques. The sections were mounted in XAM and examined in normal transmitted and polarised light.

In addition, 4 μm sections were stained with Lugol's iodine and mounted in a water based mountant.

Results

The microscopical appearances were similar in all three cases. The normal synovial architecture was lost. No synoviocyte layer was present; instead, the surface consisted of fibrin containing a mixture of polymorphonuclear leucocytes, lymphocytes, and macrophages (Fig. 1). The subintimal layers were replaced by oedematous granulation tissue infiltrated by macrophages and occasional lymphocytes and plasma cells. Within this infiltrate ill defined, non-caseating, tuberculoid granulomata containing multinucleated giant cells and Langerhans' cells had formed (Fig. 2). The giant cells and some macrophages contained structured, doubly refractile particles, which occasionally had the typical microscopical appearances of maize starch, being polyhedral and non-striated with a central triangular hilum. In polarised light they formed

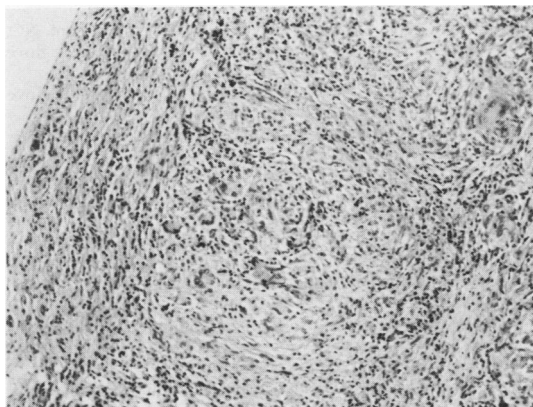


Fig. 1 The synovium from patient one. The synoviocyte layer is absent. Granulomata are present in the deeper synovium. Haematoxylin and eosin. Original magnification $\times 40$.

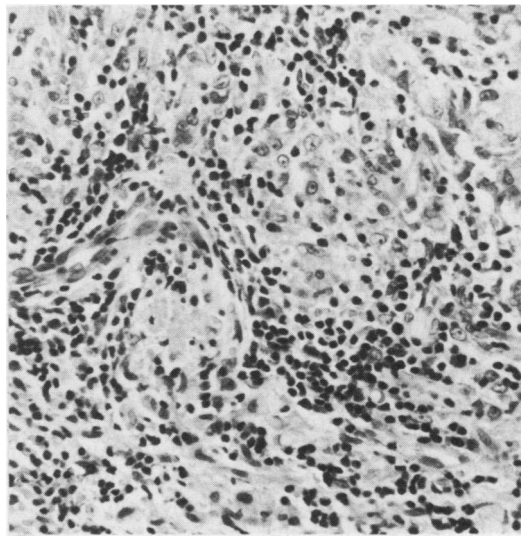


Fig. 2 Ill defined granulomata from the deeper layers of synovium. Haematoxylin and eosin $\times 100$.

“Maltese crosses” (Fig. 3). More frequently, the particles, although still recognisable as maize starch, were incomplete, suggesting partial digestion. Both intact and incomplete particles stained pink-purple with periodic acid Schiff (before and after diastase) and dark blue with iodine.

In case 3, in addition to starch granules, giant cells

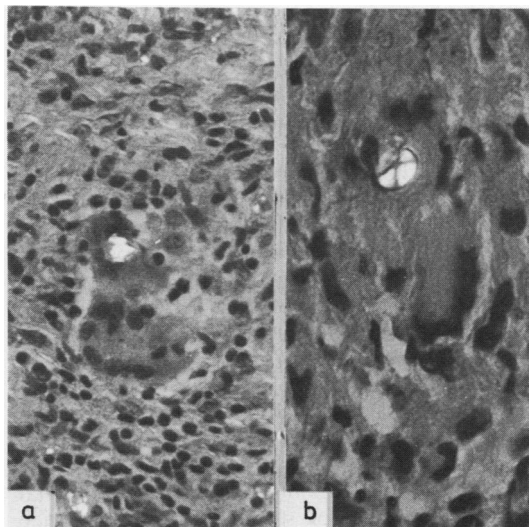


Fig. 3 Giant cells and other phagocytes contain starch granules. Under polarised light some (b) are almost complete Maltese crosses. Others (a) are less complete. All stain blue-black with Lugol's iodine. Haematoxylin and eosin, polarised light. Original magnification $\times 200$.

also contained fibrillar, doubly refractile material. There was no evidence of acid fast bacilli.

Discussion

Starch was introduced to replace talc as a lubricant after reports that it was completely absorbed from body tissues³ and therefore unlikely to induce a foreign body reaction. It is now recognised to cause rare granulomatous responses, and these have been recorded in a number of sites.⁴ In most, glove powder has been implicated as the source of the starch. Of the cases presented here glove powder introduced at a previous invasive procedure is the presumed source in two (cases 1 and 3), but in case 2 starch, derived either from crushed tablets or impurities in narcotic powders, entered the tendon sheath as a result of a misplaced injection.

Of all the reported sites the peritoneum is the most commonly affected. Extensive studies of starch peritonitis show it to have a number of characteristics, which have been interpreted as indicating a cell mediated immune disorder rather than a simple foreign body reaction.⁵⁻⁷

We believe this to be the first report of histologically proved granulomatous starch synovitis. There are both clinical and histological similarities between this disorder and starch peritonitis which suggest a similar pathogenesis. The temporal relation between probable time of starch implantation and the onset of symptoms appears variable, but in all three cases the synovium, like the peritoneum,⁸ contained ill defined granulomata in oedematous, chronically inflamed granulation tissue with undigested and partially digested starch particles within multinucleate giant cells. In case 1 it is difficult to be certain about the time of starch implantation as the joint aspirations five years and one year before biopsy could be implicated. It is more likely that the starch was introduced at the time of arthroscopy, six weeks before biopsy, a delay similar to that noted in case 2 (two months). Case 3 was different as there was no latent period after the original biopsy, and histological examination showed the presence of other foreign material in addition to the starch.

It is difficult to know why some patients develop a granulomatous response to starch whereas most do not, particularly as the risk of introduction of starch powders at operation is high. In two experimental studies, introduction of starch powder into knee joints of dogs failed to produce a granulomatous synovitis up to four weeks after its instillation.^{3,4} In one study⁴ glove powder did initially induce a severe acute inflammatory synovitis with synovial necrosis, but by four weeks, although occasional giant cells were seen containing starch particles, no

granulomata had formed and the synovium was starting to heal. This pattern of disease is similar to that reported after intradermal injection of starch into guineapig.⁹ When the starch was injected together with an adjuvant, however, a typical granulomatous response was seen. It is possible that starch is unable to stimulate a delayed hypersensitivity reaction in the absence of an adjuvant.¹⁰ Particulate adjuvants have been implicated in starch peritonitis,¹¹ and in case 3 the fibrillar foreign material seen in the synovium may have acted in this way.

In all three cases there is evidence that starch entered the joint space and there, perhaps in the presence of an adjuvant, induced a severe ulcerative, granulomatous synovitis. Although this is a rare occurrence, it could be prevented by eliminating starch powder from therapeutic and diagnostic wound sites. This may be achieved by carefully washing gloves and preventing starch becoming airborne when glove powder sachets are opened.

These three cases illustrate the need for careful examination under polarised light of biopsies from single sites of unexplained synovitis. As in many examples of synovial disease due to foreign materials, the diagnosis in these cases was not suspected clinically. Unfortunately, the task of the histopathologist is hampered by extrinsic starch, which is a frequent contaminant of tissue sections. This may result in the diagnosis being overlooked unless the presence of intrinsic starch, characterised by intracellular, often incomplete, particles, is recognised.

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