tumour with metastatic deposits in the liver and mesenteric lymph nodes. Preoperative alpha- and beta-adrenoreceptor blockade was not used, and biopsy of both primary and secondary tumour tissue produced short bursts of hypertension and extrasystoles. On her return to the intensive care unit her blood pressure rose to 240/140 mm Hg. Labetalol (50 mg), a drug with both alpha- and beta-blocking activity, was given intravenously, and continuous monitoring showed a fall in blood pressure to 75/50 mm Hg over three to four minutes. There was an increase in finger pulse volume (as detected by a Philips infrared sensor) but no change in heart rate. Pethidine 50 mg, given intravenously at this time and during two other short periods of labetalol infusion in the first 24 hours after operation, caused no change in blood pressure. It was noticed, however, on subsequent examination of the trace, that in the absence of labetalol, pethidine had produced a rise in systolic pressure of 30-80 mm Hg and in diastolic pressure of 10-30 mm Hg (see figure). The maximum pressures developed over four minutes and lasted about 10 minutes. Five episodes were recorded and in three a slight drop in blood pressure lasting 10 seconds preceded the rise. The hypertension was accompanied by a simultaneous decrease in finger pulse volume.

Comment

Pethidine and other histamine-liberating drugs should be used with caution in patients with phaeochromocytoma, as episodes of hypertension may occur. Alpha-adrenergic blockade abolished the hypertension in this patient.

I am grateful to Dr F D Thompson and Dr A M Joekes for permission to report this case and to the department of medical illustration for the figure.

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(*Accepted 27 September 1977*)

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Mixed crystal deposition disease and osteoarthritis

Deposition of calcium pyrophosphate dihydrate in articular cartilage (chondrocalcinosis) is associated with several different types of joint disease, including a chronic polyarthritis clinically indistinguishable from generalised osteoarthritis.[1] Recently hydroxyapatite crystals have also been found in the synovial fluid of some patients with typical osteoarthritis.[2] We describe six cases in which evidence of deposition of both hydroxyapatite and pyrophosphate crystals in the same joint has been found.

Patients, methods, and results

Samples of synovial fluid, synovial membrane, and cartilage were obtained at operation from six patients undergoing biopsy or prosthetic orthopaedic surgery for arthritis. Samples were prepared for routine histology and electron microscopy. Analysis of mineral deposits was carried out by infrared spectroscopy and analytical electron microscopy.[3]

All the patients presented with a chronic polyarthritis diagnosed clinically as osteoarthritis (see table). In cases 1, 2, and 3 the joint was particularly severely affected, with *x*-ray evidence of pronounced destructive changes similar to those described by Richards and Hamilton[4] in chondrocalcinosis. Four patients had spotty calcification in and around the joint, and three had chondrocalcinosis.

The histological appearances of the cartilage were compatible with osteoarthritis in all cases, with varying degrees of destructive change and clumping of chondrocytes. The synovium showed evidence of a mild inflammatory cell infiltrate in cases 1, 2, 3, and 4. Polarised light microscopy of the synovial fluid disclosed pyrophosphate crystals in all cases and other minute birefringent particles in two cases. Mineral deposits were identified in the cartilage in three cases and in the synovium and capsule in three cases. In each case analytical electron microscopy disclosed deposits with calcium:phosphorus ratios characteristic of hydroxyapatite in addition to the pyrophosphate crystals. Infrared spectroscopy showed patterns similar to those obtained with artificial mixtures of the two salts. The deposits seen were deep in the tissues, often close to cell clusters, and their morphology was quite unlike that of bone fragments.

Discussion

Clinically, these six patients were indistinguishable from others with osteoarthritis. The joint damage was severe in three cases, but these patients were clinically similar to others with advanced osteoarthritis undergoing surgery.

It is perhaps surprising that both crystals were being actively deposited in the same tissue, as conditions favouring hydroxyapatite formation inhibit pyrophosphate deposition.[5] There were possibly regional changes in the concentrations of alkaline phosphatase and inorganic pyrophosphate in our cases.

There are, however, several similarities between patients with pyrophosphate and with hydroxyapatite deposition. Osteoarthritis occurs in many people with chondrocalcinosis, and hydroxyapatite deposition often occurs in patients with osteoarthritis. The biochemical changes in articular cartilage are similar in both pyrophosphate arthropathy and osteoarthritis,[5] and the two crystals have similar inflammatory properties.

There are therefore no obvious clinical differences in patients with this type of chronic polyarthritis, whether there is evidence of pyrophosphate deposition, hydroxyapatite deposition, both together, or neither. Calcification appears to be intrinsic to the evolution of many cases of osteoarthritis.

We acknowledge the financial support of the Arthritis and Rheumatism Council, the Wellcome Foundation, the European Biological Research Association, and the Medical College of St Bartholomew's Hospital. We would like to thank Joel (UK) Limited and Perkin-Elmer for help with the analysis.

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(*Accepted 21 September 1977*)

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Details of six patients undergoing biopsy or prosthetic orthopaedic surgery for arthritis

Case No	Age	Sex	Affected joints	Operated joints	*X*-ray findings
1	80	F	Hips, knees, shoulders, digital interphalangeal joints, and carpometacarpal joints of thumb	Right shoulder	Advanced osteoarthritis and spotty calcification
2	69	F	Shoulders and knees	Left shoulder	Advanced osteoarthritis and spotty calcification
3	62	M	Ankles, knees, wrists, and distal interphalangeal joints	Right ankle	Advanced osteoarthritis and chondrocalcinosis
4	64	M	Hips and knees	Left hip	Osteoarthritis and chondrocalcinosis
5	72	M	Shoulders, knees, ankles, and distal interphalangeal joints	Left knee	Osteoarthritis, spotty calcification, and chondrocalcinosis
6	62	F	Knees	Right knee	Osteoarthritis, spotty calcification, and chondrocalcinosis