Arthroplasty for ochronotic arthritis

No failure of 11 replacements in 3 patients followed 6–12 years

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Background **Alkaptonuria is a rare single-gene disorder characterized by black pigmentation of cartilage and other connective tissues. Premature degenerative arthritis affects the large joints in many of these of patients. Medical treatment is limited to a protein-restricted diet (phenylalanine and tyrosine) with surgery reserved for end-stage joint disease. As in other metabolic bone diseases, there are concerns about the quality and strength of affected bones and therefore the suitability and longevity of replacement arthroplasty. The histopathology and outcome of joint replacement for alkaptonuric arthritis is unknown and limited to sporadic case reports.**

Patients and results **We describe 11 joint replacements in 3 patients with alkaptonuric polyarthropathy, including shoulder and elbow replacements not previously reported. No prosthetic failures occurred in up to 12 years of follow-up.**

Interpretation **Total joint replacement is an acceptable treatment for degenerative joint disease in alkaptonuric patients, with implant survival comparable to that found in patients with osteoarthritis.**

Alkaptonuria (AKU) is a rare autosomal-recessive metabolic disorder with an incidence of less than 1: 20,000. It is most common in certain areas of eastern Europe (Smith 1996). It results from deficiency of the enzyme homogentisic acid oxidase, which is present mainly in the liver and kidneys. Homogentisic acid oxidase is responsible for the turnover of homogentisic acid (HGA) during the course of phenylalanine and tyrosine catabolism. The acid (a pigmented polymer) accumulates and binds collagen and other tissues, staining them black (ochronosis) (Smith 1996). Classical sites for deposition are the pinnae, sclera, tendons and joint surfaces. Excretion of HGA in the urine and sweat causes staining of clothes. The molecular basis of alkaptonuria was elucidated only in the mid 1990s and the human AKU locus has been mapped to chromosome 3q2 (Janocha et al. 1994).

The high affinity of HGA for proteoglycans of hyaline cartilage is thought to increase the fragility of the tissues, allowing fissuring and early degradation of articular cartilage (Smith 1996). Premature large joint arthritis develops after the third decade and usually affects the hip, knee and shoulder. Spondylitis develops by the fifth decade. The smaller joints are usually spared.

Radiographs of the hip, knee and sacroiliac joints show characteristic signs of osteoarthritis. In the lumbar spine, the intervertebral discs show gross calcification and loss of height, accompanied by a variable degree of fusion of the vertebral bodies (pseudoblock vertebrale) and little osteophyte formation; this is considered almost pathognomonic of alkaptonuria. Radiographically, calcification is found in the menisci, symphysis pubis, pinnae, nasal cartilages, tendons, kidneys, heart valves and great vessels (Justesen and Andersen 1984).

The literature on arthroplasty in this disease is limited to a few case reports describing hip or knee replacement (Table 1). No complications were reported.

Table 1. Summary of published case reports to date

Publication	Joint	A	B	C
Makela and Korkala 1986	Hip	2	57	12
Dom and Pittevils 1997	Hip	1	63	12
Aynaci et al. 2000	Hip	2	53	6
Aydogodu et al. 2000	Hip	1	48	48
Yilmaz and Egilmez 2002	Hip	1	65	15

A Number of joints replaced
B Age at joint replacement in years
C Postoperative follow-up in months

Here we report on 11 staged total joint replacements in both the upper and lower limbs of three patients.

Patients and methods

From the Oxford histopathology registry, we identified the records of 3 patients with alkaptonuric arthritis attending the metabolic bone disease clinic. The ages of the patients, clinical features at presentation, radiographic findings, operative treatment, histopathological examination and surgical outcome were recorded (Table 2).

Table 2. Details of joint replacements in the 3 patients

Case	Joint	A	B	C	D	E
1	hip	57	2	11	A	0
1	hip	60	3	8	A	0
1	shoulder	60	5	8	B	0
1	knee	62	1	7	A	0
1	elbow	63	4	5	D	1
1	elbow	66	4	2.5	A	0
2	hip	75	6	12	C	0
2	hip	76	2	11	A	0
3	hip	71	2	6	A	0
3	hip	73	2	3	A	0

A Age at the time of joint replacement surgery
B Prosthesis used
  1 Biomet AGC total knee replacement
  2 Cemented Charnley total hip replacement
  3 Cemented Hineck total hip replacement
  4 Souter Strathclyde total elbow replacement
  5 Neer shoulder hemiarthroplasty
  6 Cemented Stanmore total hip replacement
C Follow-up (years)
D Outcome
  A Asymptomatic
  B Asymptomatic with a restricted ROM
  C Asymptomatic but dislocated at 12 years post-surgery
  D Developed mild discomfort 5 years post-surgery
E Radiography
  0 No loosening
  1 Lucency of 1 mm on lateral side of humeral component

Case 1

A woman of 53 years with a 15-year history of ochronotic spondyloarthropathy presented with an intertrochanteric fractured neck of femur. This was initially treated with a dynamic hip screw. She was also known to have multiple painful degenerative joints for which she underwent seven sequential joint replacements over a 10-year period. She also had the characteristic ochronotic features of darkly-stained sclera and pinnae. Her cemented hip replacements were secondary to a failure of fixation of the dynamic hip screw 4 years after initial surgery and, 1 year later, after an insufficiency fracture of the contralateral femoral neck.

At review 12 years after her first joint replacement, she was independently mobile with no radiographic or clinical evidence of loosening of her 7 joint replacements (apart form a stable 1-mm lucency around the humeral component of her right total elbow replacement). She died 9 months after last review.

The macroscopic findings at surgery showed that all joints had extensive loss of articular cartilage, with black staining of the remaining degenerative cartilage and the synovial tissues (Figure 1). In the knees the menisci were brittle and darkly stained, and the patellar tendons were stiff and attenuated, making patella dislocation difficult.

Case 2

A 75-year-old woman with a 25-year history of diffuse spondyloarthropathy presented with apparent end-stage hip osteoarthrosis. She was noted to have a gray complexion with dark staining of her pinnae. She underwent bilateral staged hip replacements. At the time of surgery she was noted to have black staining of the joint surfaces and synovium, which on histopathological examination confirmed ochronosis. 12 years after left total hip replacement, she had a dislocation which was treated successfully by closed reduction. Radiographically, there was no evidence of loosening around either the femoral or acetabular components.

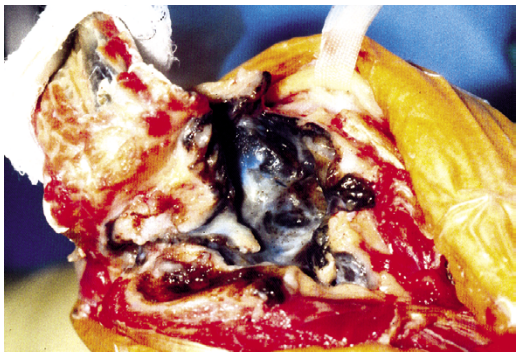

Figure 1. Macroscopic findings at surgery, showing black pigmentation in the synovium and articular surfaces.

Case 3

A 72-year-old woman with spondyloarthropathy and no external clinical features of alkaptonuria (discoloration of sclera or pinnae) underwent staged cemented total hip replacement. Black pigmentation of the articular cartilage was noted and histopathological examination confirmed ochronosis. At the 6-year follow-up, no clinical or radiographic complications were found. She died shortly afterwards of cardiac disease.

Histology

Histology in all cases confirmed ochronotic staining of degenerate hyaline articular cartilage and fragments of articular cartilage deposited in synovial and capsular tissues (Figure 2). The pigmented cartilage showed yellow autofluorescence and stained positively with Schmorl's stain. Other changes of degenerative arthritis were noticed, including fibrous and fibrocartilagenous repair on the articular surface, and pseudocyst and osteophyte formation. Reparative fibrous tissue and a patchy chronic inflammatory cell infiltrate composed of lymphocytes, macrophages and occasional giant cells were seen in response to small and large fragments of ochronotic cartilage deposited in the joint synovium. Localized amyloid deposition was noted in ochronotic cartilage in all cases, and deposition of calcium pyrophosphate crystals was seen in the knee and elbow joints of case 1. Immunohistochemistry confirmed the presence of amyloid P component; there was no reaction against immunoglobulin light chains, pre-albumin, amyloid A protein or beta-2 microglobulin. Undecalcifed sections of subchondral bone showed no signs of marked osteopenia, increase in osteoid or other significant histological abnormality.

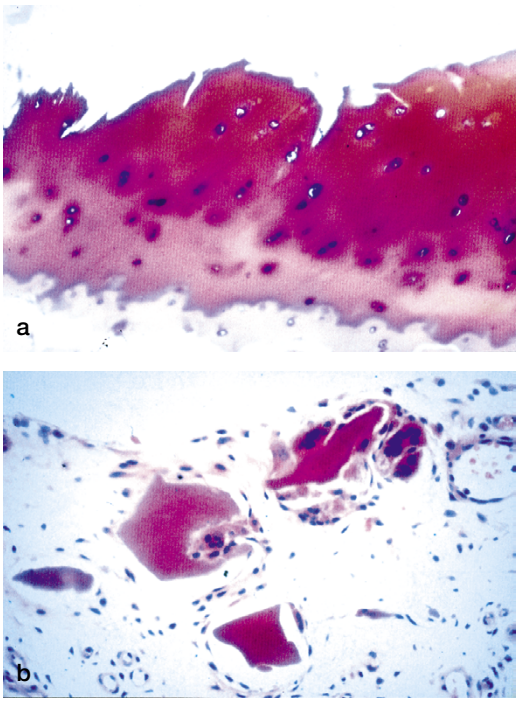

Figure 2. Photomicrograph of histological changes of ochronosis in case 1, showing fissures in pigmented articular cartilage (a) and fragments of pigmented cartilage deposited in the synovial membrane (b). (HE, ×250).

Discussion

There is no medical treatment for alkaptonuria, and the surgical treatment for ochronotic arthritis is limited to a few case reports with short follow-up. Metabolic bone and joint diseases may affect the mechanical properties of connective tissues and decrease the strength of bone, leading to early implant failure. Even though one patient suffered two hip fractures following low-energy falls and later a DHS implant failure, we found no evidence of this in our patients. Histologically, in all 3 of our patients, there was no marked osteopenia, increase in osteoid or other significant histological abnormality in the subchondral bone. The articular surfaces showed typical gross and histological features of ochronosis with degenerate pigmented articular cartilage.

Concomitant ochronosis and deposition of calcium pyrophosphate crystals has been recognized previously, but localized amyloid deposition in articular cartilage has not been reported. This may be age-associated, or may reflect matrix changes occurring as a result of homogentisic acid deposition.

11 arthroplasties in both upper and lower limbs were undertaken in 3 patients with end-stage ochronotic large joint degenerative disease, with good clinical results and no evidence of implant failure or complications. This study demonstrates that joint replacement in alkaptonuric patients with ochronotic arthritis is associated with prosthetic survival comparable to that found in patients with osteoarthritis, thus confirming the results of previous reports.

We are grateful to Mr M K Benson FRCS who performed many of the joint replacements.

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