Rheumatol Int (2006) 26: 561–564
DOI 10.1007/s00296-005-0087-y

ORIGINAL ARTICLE

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Ochronotic arthropathy, an approach to osteoarthritis bone remodelling

Published online: 25 January 2006

Abstract The objective is to use hip ochronotic arthropathy for an indirect approach to osteoarthritis bone remodelling in a human joint via an identified causal chondropathy. The method is via radiology connecting pathology and nosology, based on the study of seven ochronotic femur heads excised in alcaptonuric patients. Due to the brittleness of ochronotic cartilage, bone remodelling similar to that of hip osteoarthritis exists with diffuse narrowing of the interarticular space and (except in one case modified by intermediary surgery) poorly developed osteophytes. Ochronotic arthropathy is only a privileged model of osteoarthritis bone remodelling, the pathology of which might well evidence the stages of the process, with marking by pigmented cartilage remnants Thus it may lead to various reflections in rheumatology, among others concerning the respective radiological hip images of osteoarthritis and rheumatoid arthritis. The use of the pathology–radiology files provided by hip surgery of ochronotic arthropathy might offer a useful reference model for investigating various aspects of osteoarthritis.

Keywords Ochronosis · Osteoarthritis · Hip osteoarthritis · Rheumatoid arthritis · Pathology

> "Ces corps divers sont des expériences toutes prepares par la nature...comme nous pourrions desirer de le faire dans nos laboratoires."
> (These different bodies are nature's ready-made experiments...like those we would like to carry out in our laboratories)
>
> Georges CUVIER
> (Le règne animal distribué d'après son organization, 1836)

Introduction

Alongside numerous studies devoted to the genesis of osteoarthritis (OA) after experimental cartilage deterioration, ochronotic arthropathy is the cause of bone remodelling due to the connection of a genomic disorder with the static and dynamic local conditions of a human joint, thus illustrating in pathology the formula proposed by Cuvier in normal biology to emphasize the role of comparative observations.

The disorder is alcaptonuria which, by producing a tanning of collagen fibres by an irreversible bond with polymerized oxidized homogentisic acid [1], causes hardness and decreased elasticity of the cartilage, hence its brittleness [2–4]. This is reproducible in in vitro incubation [2]. The local mechanical conditions are those of certain joints, not hand and foot joints but mainly the knee, shoulder and hip [5]. The involvement of the latter has led to the study of files associating clinical, radiological and pathological data.

Materials and methods

To identify the key points of bone remodelling in osteoarthritis via ochronotic arthropathy, we used data pooled from previous observations and illustrated by a new selection of figures. The study was based on seven ochronotic femoral heads excised in alcaptonuric patients and investigated by pathology–radiology correlation.

Results

Alongside macroscopic and histological remnants of the original pigmented cartilage, the ochronotic femoral

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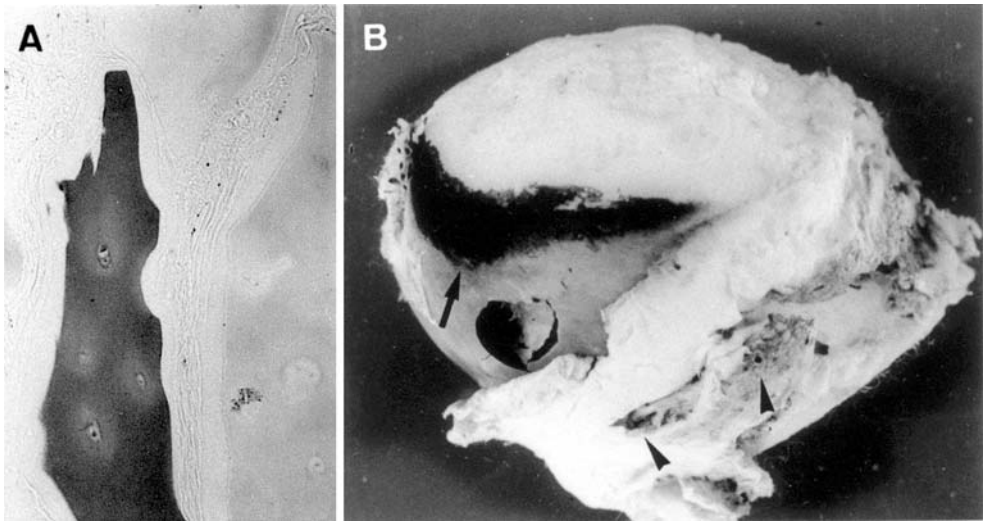

Fig. 1 Overview of hip ochronotic arthropathy. **a** Pigmented hyalin cartilage shards. On the *left*, well pigmented, presumably from the cartilage deep layer. On the *right*, poorly pigmented with pigment phagocytosis and chondrocytic necrosis (unstained slide ×60). **b** Remodelled femoral head, posterior half. Eburnated weight-bearing area separated by an intermediary abraded strip (*arrow*) from the smooth persisting cartilage (round peroperative artefact)—hyperplastic synovial membrane with cartilage debris (*two arrowheads*). For X-rays of femoral head and hip joint, see Refs. [7, 8]

heads presented bone remodelling similar to that of osteoarthritis (Figs. 1, 2). The peculiarity of the causal chondropathy was a brittleness resulting in shards of pigmented hyalin cartilage (Fig. 1a)

In the ''intrinsic'' remodelling the unprotected bone reacted by associating bone erosion and bone formation with, sometimes, necrotic areas [6–8]. This led to surface eburnation with deeper embedding of cartilage debris, similar to that occurring in an associated detritic synovitis (Figs. 1b, 2a). The ''extrinsic'' remodelling was typified by a marginal non-enthesopathic osteophyte covered by a newly formed cartilage (Fig. 2b–d) as was also noted in knee ochronotic arthropathy [9]. This covering cartilage was non-pigmented, underlying the fact that cartilage impregnation by the ochronotic pigment appears to be essentially related to the age as well as the structure of the receptor cartilage. Mainly inferomedial, the osteophytes were discrete [6–8] except in one case where the local mechanical conditions had been modified by intermediary surgery [6, 8].

Discussion

An historical and conceptual overview

The connexion of osteoarthritis with ochronotic arthropathy had already been emphasized by the OA pioneer, Archibald Garrod, about a quarter of century after he had based his concept of Inborn Error of Metabolism on alcaptonuria. Without underestimating the role of ''wear and tear'' in the condition, he added, ''I cannot doubt that there is also some underlying cause at work, which may be congenital or acquired'' and cited in support, ''namely the peculiar liability of persons with alcaptonuria and ochronosis to develop osteoarthritis lesions in later life'' [10]. Today's pathology data fit in with this pioneer's opinion. In order to avoid any semantic ambiguity in the present paper, we distinguished nosology and pathology [11] by considering ochronotic arthropathy and osteoarthritis as two nosological entities, even though their common bone remodelling was evidenced by pathology. Thus, in addition to the study of the ochronotic cartilage itself, a common approach to ochronotic arthropathy and osteoarthritis could be presented: first of all in teaching, as a didactic illustration of OA bone remodelling, thanks to the labelling of the original cartilage; furthermore in showing that in the mechanical conditions of a human joint, a genome-specific chondropathy could lead to the same bone remodelling as that caused by the still mysterious ''degenerative '' chondropathy which often sticks close to the OA concept. However, as in ochronotic spine versus ankylosing spondylitis [12], ochronotic arthropathy does not reproduce OA disease but is only a privileged model providing the opportunity to study similarities as well as differences.

Lessons drawn from the pathology–radiology approach

A combined view gives a morphological approach to ochronotic arthropathy where, thanks to extrapolation from previous comparisons, X-rays translate the pathological data for the rheumatologist. Our observations are on the whole in accordance with the data documented and suggest certain reflections in rheumatology. In addition to the observations concerning osteoarthritis, the bone remodelling of ochronotic arthropathy shows some pathological and radiological similarities

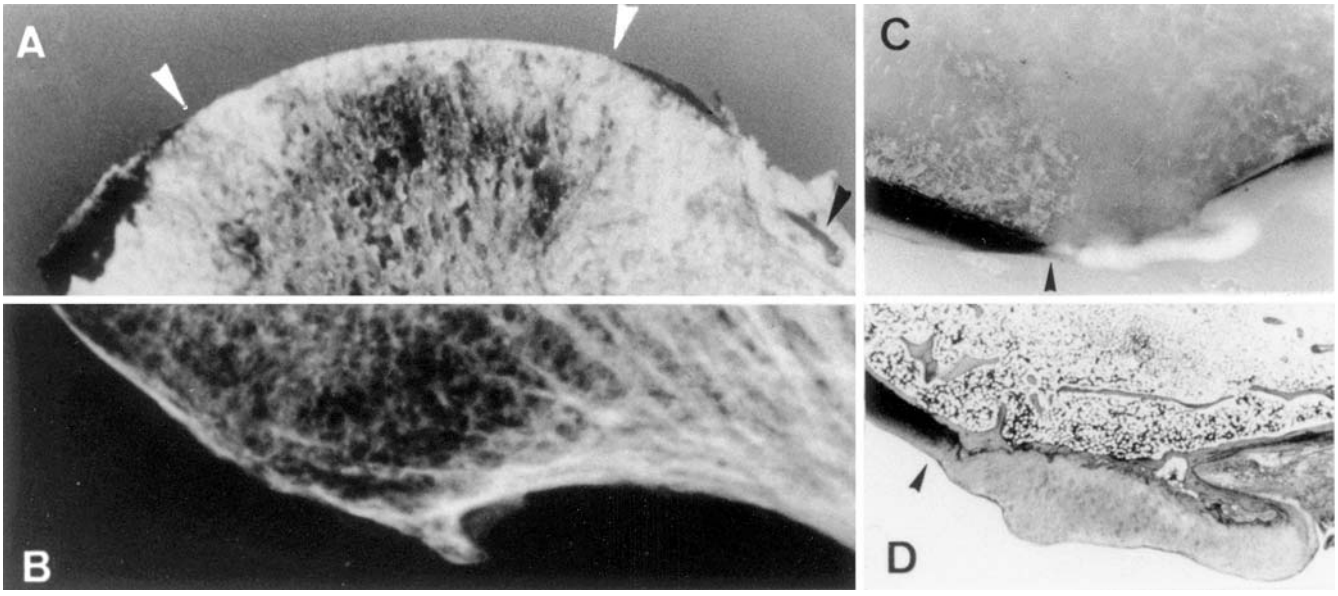

Fig. 2 Two essential territories in an ochronotic femoral head with remodelling of the OA type. On the *left*, medial part. For X-rays of femoral head and hip joint, see Refs. [24, 25]. **a** Between two *white arrowheads*, weight-bearing area with eburnated denuded bone and underlying osteomedullar remodelling in which pigmented cartilage shards are embedded. Medial and lateral remnants of ochronotic cartilage cover. Embedding of a cartilage fragment in hyperplastic synovial membrane (*black arrowhead*); macroscopical slice ×2.5. **b–d** In infrafoveal location, minor form of osteophyte. **b** X-ray showing the bony spur (×4). **c** Junction between the pre-existing pigmented ochronotic cartilage and the non-pigmented newly formed cartilage, indicated by an *arrowhead* corresponding to the one in **d**; macroscopical slice ×5. **d** Histological aspect of the newly formed cartilaginous spur prolonging the ochronotic cartilage and covering the bony spur (stained slide, HE ×10)

with rheumatoid arthritis at an advanced stage [7, 8], i.e. with a nosological entity also due to a chondropathy of extra-articular origin. In both conditions, the intrinsic remodelling in a loaded area has led to the development of an eburnated surface wider than that usually caused by a local mechanical disturbance. Thus the articular interspace is more or less diffusely narrowed, and extrinsic remodelling is seen in discrete osteophytes. In our series, the only one exception was a case where a big inferomedial osteophyte developed after intermediary local surgery [6, 8]. In accordance with other data [13], this leads to the idea that the growth of osteophytes reflects articular imbalance induced by the intrinsic remodelling disorder. Taking the hip as a model, one might say that OA osteophytes appear as epiphenomena which adapt the femur head to the intrinsic remodelling process.

Looking back on osteoarthritis, one thus falls in line with the observations of Salomon et al. [14] according to which there are at least two forms of OA hip: (a) a rather frequent hypertrophic form with obvious osteophytes and localized loss of cartilage, related to malformations or to mechanical local disorders such as in our case, which had been modified by intermediary surgery and (b) an atrophic form with discrete osteophytes and widespread cartilage loss, showing more general joint disturbances. Ochronotic arthropathy might be compared with this latter form.

Alongside the above general approach comparing ochronotic arthropathy with the nosological concept of osteoarthritis, the condition must also be compared with special forms such as ''generalized osteoarthritis'' and ''rapidly destructive osteoarthritis of the hip''. In both conditions, hip arthropathy also presents a more or less diffuse narrowing of the articular interspace in association with discrete osteophytes. They often affect several joints in middle-aged and elderly women, thus appearing related to a special background. In fact, ochronotic arthropathy cannot be a reference model for generalized osteoarthritis since it practically never concerns the hands and feet [5, 15], which (as in rheumatoid arthritis) are classic locations for the condition [16], thus emphasizing the uniqueness of the disease.

On another level, rapidly destructive osteoarthritis of the hip is a condition that has long been reported in European literature and characterized by an evolution which is more rapid than usual in OA. The interspace narrowing is often diffuse and a chondrolytic phase precedes a more or less erosive intrinsic bone remodelling [17–20], as can be detected by MRI at an early stage, with findings similar to those of transient osteoporosis [21]. Pathological examination of the femoral heads emphasizes necrotic areas and intense bone remodelling [22].

A similar process has been reported in ochronotic arthropathy [23]. In our series, a femoral head excised 7 months after the appearance of the initial symptoms showed histologically active bone remodelling with trabecula microfracture and some necrotic areas [24, 25]. We noted that the case had been activated by an acute

mechanical overload and thus also illustrated the presumed role played by superimposed neurovascular dystrophy in certain OA evolutions. However, the bone remodelling appeared less active in a bilateral case [8], the femoral head of which was excised 10 months after the initial symptoms. Ochronotic arthropathy might thus be a reference model in further studies of this form of osteoarthritis in which rapid intrinsic remodelling is preceded by a chondrolytic phase.

In fact the amount of literature devoted to ochronotic arthropathy is obviously unequal to that given to osteoarthritis, and a thorough comparative approach to both diseases requires greater attention to new research into the former. The frequency of hip involvement provides the opportunity for clinical and radiological observations, completed by pathological examination of femur heads (with practically no noticeable financial expenditure or technical extras). Notwithstanding the differences, an analysis of the similarities between both conditions could be of conceptual interest.

Conclusion

Though ochronotic arthropathy is rare, it offers, via similar bone remodelling, a useful conceptual and teaching approach to bone remodelling in osteoarthritis. However, this privileged model cannot be considered a true reproduction of the disease.

References

1. Milch RA (1961) Studies of alcaptonuria: mechanisms of swelling of homogentisic acid–collagen preparations. Arthritis Rheum 4:253–257
2. Eberle P, Mohr W, Claes (1964) Mechanishe Untersuchungen zur Pathegenese ochronotishen Arthropathie. Z Rheumatol 43:249–252
3. O'Brien WM, Banfield WG, Sokoloff L (1967) Studies on the pathogenesis of ochronotic arthropathy. Arthritis Rheum 4:137–152
4. Mohr W, Wessinghage D, Lenschow E (1980) Die Ultrastruktur vo hyalinen Knorpel unf Gelenk-Kapselgewebe bei der alkaptonturschen Ochronose. Z Rheumatol 39:55–73
5. O'Brien WM, La Du BN, Bunim JJ (1963) Biochemical, pathologic and clinical aspects of alcaptonuria, ochronosis and ochronotic arthropathy. Am J Med 34:813–838
6. Lagier R (1980) The concept of osteoarthrotic remodelling as illustrated by ochronotic arthropathy of the hip—An anatomico-radiological approach. Virchows Arch A Pathol Anat Histol 385:293–308
7. Steiger U, Lagier R (1972) Combined anatomical and radiological study of the hip joint in alcaptonuric arthropathy. Ann Rheum Dis 31:369–373
8. Lagier R, Steiger U (1980) Hip arthropathy in ochronosis: anatomical and radiological study. Skeletal Radiol 5:91–98
9. Lagier R, Boussina I, Taillard W, Sasfavian A, Chafitadeh M, Fallet GH (1971) Etude anatomo-radiologique d'une arthropathie ochronotique du genou. Schweiz Med Wochenschr 101:1585–1590
10. Garrod A (1923) Discussion on "the etiology and treatment of osteo-arthritis and rheumatoid arthritis". Proc R Soc Med XVII:1–18
11. Lagier R (2001) Nosology versus pathology, two approaches to rheumatic diseases illustrated by Alfred Baring Garrod and Jean-Martin Charcot. Rheumatology (Oxford) 40:467–471
12. Lagier R, Sitaj S (1974) Vertebral changes in ochronosis. Anatomical and radiological study of one case. Ann Rheum Dis 33:86–92
13. Lagier R (1985) Anatomico-radiological study of an ununited intra-capsular fracture of the femoral head dating back 47 years. Arch Orthop Trauma Surg 104:155–160
14. Salomon L, Schnitzler CM, Browett JP (1982) Osteoarthritis of the hip: the patient behind the disease. Ann Rheum Dis 41:118–125
15. Poulsen V (1910) Uber Ochronose bei Menschen und Tieren. Beitr Pathol Anat 48:346–436
16. Kellgren JM, Moore R (1952) Generalized osteoarthritis and Heberden's nodes. Br Med J 1:181–187
17. Lequesne M, de Sèze, Amouroux J (1970) La coxarthrose destructrice rapide. Presse Med 32:1435–1439
18. Roux JP, Kerboull M, Postel M (1970) Les coxarthroses à évolution rapide. Rev Chir Orthop Reparatrice Appar Mot 58:39–57
19. Rosenberg ZS, Shankman S, Steiner GC, Kastenbaum DK, Norman A, Lazansky MG (1992) Rapid destructive osteoarthritis: clinical, radiographic and pathologic features. Radiology 182:213–216
20. ffFlik K, Vargas JH (2000) Rapidly destructive hip disease: a case report and review of the literature. Am J Orthop 29:549–552
21. Sugano N, Ohzono K, Nishii T, Sakai T, Maragushi K, Yoshikawa H et al (2001) Early MRI findings of rapidly destructive coxopathy. Magn Reson Imaging 19:47
22. Mitrovic DR, Riera H (1992) Synovial, articular cartilage and bone changes in rapidly destructive arthropathy (osteoarthritis) of the hip. Rheumatol Int 12:17–22
23. Corra T, Zaccala M, Galante M (1995) Ochronotic arthropathy: rapid destructive hip osteoarthritis associated with metabolic disease. Clin Rheumatol 14:474–477
24. Cunningham TJ, Roux E, Lagier R, Fallet GH (1989) Rapidly progressive hip osteoarthrosis. A unusual presentation of ochronosis. Clin Exp Rheumatol 7:315–318
25. Lagier R, Baud C-A, Lacotte D, Cunningham TJ (1988) Rapidly progressive osteoarthrosis of ochronotic origin. A pathologic study. Am J Clin Pathol 90:95–102