need for identification of patients with PH where adjunc-
tive therapy with plasmapheresis would be beneficial. A 
recent study has confirmed the benefit of plasmapheresis 
compared with i.v. MPS in AAV patients presenting with 
creatinine >500 μmol/l in renal survival at 3 months 
[9]; such thresholds for patients with PH need to be 
defined.

PH in AAV is a life-threatening entity, often with a fulmi-
nant course if untreated. Speed in making a diagnosis and 
instituting therapy for AAV is essential, especially in the 
face of life-threatening PH or rapidly progressive glomer-
ulonephritis [10]. Our study highlights the importance of 
prompt diagnosis and initiation of immunosuppressive 
therapy with prednisolone and cyclophosphamide. The 
role of plasmapheresis as adjunctive therapy remains to 
be established.

**Rheumatology key message**

- Prompt immunosuppressive therapy is important to 
  improve the outcome of PH in ANCA-associated 
  vasculitis.

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connecting one fibre to other neighbouring fibre(s). These large shards were sometimes seen attached to large granules located in the centre of individual fibres. Fibres with pigment protruding tended to appear swollen when compared with non-pigmented fibres. Pigment protruding from fibres was in some instances observed binding to extra-fibrillar pigment. Many fibres in the region of interest had no notable shards but appeared structurally abnormal, showing a more pentagonal or hexagonal cross-sectional shape (Fig. 1C). The most distinct feature of the ochronotic connective tissue in longitudinal section was the presence of many electron-dense ochronotic shards on the surface of the collagen fibres. Single collagen fibres were frequently associated with more than one pigmented deposit. In some regions, a gradient of pigmentation was noted, from collagen fibres that were free of pigment across to regions of heavy pigmentation (Fig. 1D). A periodic banding pattern of ochronotic shards on individual collagen fibres was observed. Pigmentation was associated with the expected 67-nm periodic banding of the fibrillar collagens (Fig. 1D, inset). This regular periodicity of ochronotic pigment binding was seen on multiple fibres within the tissue. Alongside the regular pattern observed on some fibres, it was possible to identify very early signs of pigment deposition. Small granules appeared in a regular pattern on the longitudinal surface of the fibres (Fig. 1D, inset arrows). AKU is a rare autosomal recessive condition, which has no effective treatment or cure. The clinical manifestations and advanced ochronosis are well documented. Our macroscopic examinations of the ligamentous capsule were consistent with previous examinations of soft joint tissues, with both pigmented and non-pigmented regions observed [2, 4]. Microscopic examination of the ligamentous capsule revealed pigmentation consistent with previous findings of diffuse extracellular pigmentation [2, 5] combined with intracellular pigmentation of fibroblasts [6–8]. We noted two extremes of extracellular pigmentation. Some areas showed only minute granules on the collagen fibres, whereas others showed substantial pigmentation in

Fig. 1 Microstructure and ultrastructure of ochronotic pigment. (A) Photomicrograph showing ochronotic pigment granules in the fibroblasts of ligamentous capsule (H&E). (B) Transmission electron microscopy (TEM) image showing collagen fibres in transverse section. Numerous fibres appear with small electron-dense granules located within the fibre body. Other fibres appear to have been completely replaced by the pigment. Some fibres show no obvious association with pigment. (C) TEM image showing large electron-dense ochronotic shards located within the fibre body, often protruding out into the interfibrillar space and connecting to other fibres. Shards can also be seen originating from large granules located within fibre bodies. Numerous fibres show no notable pigmentation but appear structurally abnormal displaying many variations in shape and diameter. (D) TEM image of ochronotic ligamentous capsule. Collagen fibres in longitudinal section show a distinct electron-dense pigment on their surface. Not all fibres present with pigment deposition. Numerous pigment shards can be seen on single fibres. Gradient of pigmentation can be seen running right (no pigment on fibres) to left (large electron-dense shards replacing fibres). Inset shows a distinct periodic binding pattern associated with pigment granules on a single fibre (arrows).
which fibres were completely encrusted in pigment in a crystalline fashion. It is not clear if these two types of pigmentation are directly related, with the smaller granules representing nucleation points for the process of polymerization that leads to complete encrusting of fibres in ochronotic pigment. Alternatively, two or more independent mechanisms of pigment formation and deposition may overlap in soft or joint tissues. Pigmentation was not uniform at all levels within the tissue and it is not clear why some of the collagen fibres were unaffected. The results confirm that the presence of HGA cannot be the sole factor in pigmentation; other local factors must promote or inhibit nucleation and deposition of ochronotic pigment, such as pH, redox potential or the presence of other currently unidentified factors. The small nucleating pigment appears as a regular pattern and may provide clues to the exact point to which the HGA is attracted in these tissues and could be used in the future to elucidate the binding mechanism as a therapeutic target.

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Rheumatology key message

• Ochronotic pigmentation in AKU deposits intra- and extracellularly and associates with the ultrastructural periodicity of collagen.

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Bone ankylosis of the wrist as a possible indicator of treatment efficacy in rheumatoid arthritis

Sir, Chronic joint inflammation usually causes irreversible bone structural damage. In RA, this is characterized by the occurrence of erosions with very small potential of repair processes [1]. On the contrary, joint fusion can be seen in seronegative spondyloarthritides, in particular in AS. The balance between bone destruction and bone formation is regulated by a number of proteins in equilibrium, including RANK ligand and osteoprotegerin, bone morphogenetic proteins and noggin and wingless proteins and Dickkopf proteins [1]. In spite of these considerations, small joint ankylosis can also occur in RA and its significance has been recently addressed [2]. This very uncommon radiological finding has been interpreted as a consequence of long-lasting disease or of the possible coincidence of RA and seronegative spondyloarthritides.

In addition, the hypothesis that bone ankylosis is likely to disappear due to the increased efficacy of RA treatment has been suggested.

We report the case of an RA patient in whom bone ankylosis occurred after disease activity improvement because of successful treatment. Based on these findings, we suggest that bone ankylosis could represent a reparative process. The patient, a 38-year-old lady, had a 5-year history of seropositive, anti-cyclic citrullinated peptide antibody-positive RA. Due to the absence of psoriasis, family history of psoriasis, low back pain or enthesitis, we believe that this patient had a classic RA, although RA and seronegative spondyloarthritides could theoretically co-exist. She had been treated with MTX, 20 mg weekly, followed by adalimumab and etanercept. Response to anti-TNF-α agents was partial and short-lived. For this reason, rituximab was started in November 2007 with good control of the signs and symptoms of RA. Disease activity score (DAS)-28 decreased from 6.6 to 4.8 and the