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Case report

Coexistence of Ochronosis and B 27 Positive Ankylosing Spondylitis

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A B S T R A C T

We describe a 49-year-old man with coexistence of ochronosiss and B 27 positive ankylosing spondylitis. This is the first report documenting the simultaneous occurrence of ochronosis and B27 positive ankylosing spondylitis, with no positive familiar history for seronegative spondylarthropathies. The relations of these rheumatic diseases are discussed.

Key words: *ochronosis, ankylosing spondylitis, HLA B 27 antigen*

Introduction

Alkaptonuria is a rare, hereditary, metabolic disease in which homogentisic acid, an intermediary product in the metabolism of phenylalanin and tyrosin, cannot be further metabolized. The metabolic defect causes characteristic triad of homogentisic aciduria, ochronosis and arthritis. Ochronosis is characterized by the presence of homogentisic acid in the urine, on standing and when oxidized, turns typically black[1,2]. Ochronosis is the late developing complication of alkaptonuria in patiens living to the 4th decade. The deposition of the characteristic, brownish-black pigment in the interverebral disc and articular cartilage is the cause of the ochronotic spondylosis and arthropathy, which are, in some cases, very similar that of ankylosing spondylitis (AS). These 2 diseases can be distuingished easily by typical radiological features in the spine and the sacroiliac (SI) joints. Whereas the coexistence of these 2 conditions in the same patient has rarely been reported[3–6], the occurrence of ankylosing spondylitis with positive HLA B 27 antigen in patients with classical clinical and radiological picture of ochronosis, has not previously been reported. We describe a 49-year-old man with ochronosis and AS, who showed the concomitant presence of both diseases, as well as the presence of B 27 antigen.

Case Report

In January 1999, a 49-year-old Caucasian man, complaining of pain in his right knee, lumbar spine, groins and left heel, came to our rheumatic disease unit.

His medical history revealed that he had suffered from numerous attacks of low back pain and morning stiffness in the last 20 years. Low back pain and stiffness, characteristically improved by exercises, had become permanent, and in the last few years had been followed by arthritis of the knees, shoulders, together with entesopathy of the knees and Achilles tendon.

He denied a family history of ankylosing spondylitis or ochronosis or any other seronegative spondylarthopathies, especially associated with HLA B 27 antigen. He also denied having had inflammatory bowel diseases, uveitis, conjuctivitis, psoriasis or urethritis.

During the examination, we found the typical ochronotic (black-brownish) pigmentation of the ear and nose cartilage, of the sclera, and in the axillar and groin region with the presence of black sweat (Figure 1 and 2).

The examination of the locomotor system demonstrated accentuated dorsal kyphosis, forward prominence of the head and cervical spine (with occiput-wall distance 9 cm), and severe reductions of the spine movements in

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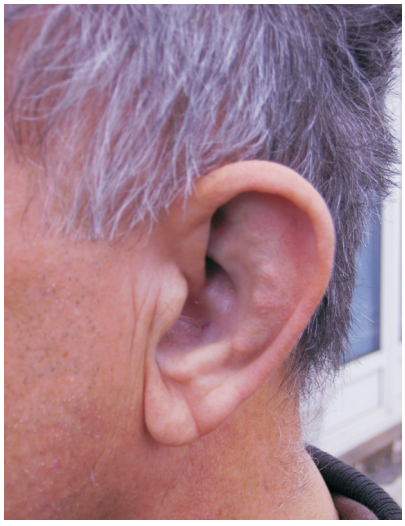

Fig. 1. Typical ochronotic (black-brownish) pigmentation of the ear cartilage.

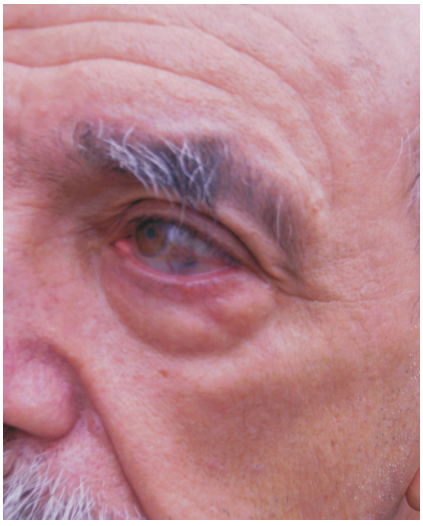

Fig. 2. Typical ochronotic pigmentation of the sclera.

all directions (Schober 0 cm, chest expansion 1 cm). Peripheral joint examination showed a limited painful mobility of both shoulders and hips, arthritis of the knees and left ankle and tendinitis of left Achilles tendon. Pain was induced by pressure at the insertion of the tendon of the adductor muscles of both tighs, both greater trochanters, and at the insertion of the right patellar tendon into the tibial tuberosity and at insertion of left Achilles tendon into the calcaneum.

Westergren erytrocyte sedimentation rate (ESR) was 10 mm/h. C-reactive protein (CRP) 8 mg /L (normal < 6), beta globulin 12.5% (total proteins 75.0 g/l), other laboratory tests were within normal limits. Urine concentration of homogentisic acid, using quantitative method was highly positive: 24000 mmol/creatinin mol. Classical patologic values are: 1000–5000 mmol/creatinin mol. On standing, urine darkened and turned black when alkanilized. HLA typing was positive for B 27 antigen (A 1, X B 27, 35). DR was no typed. Ophthalmologist's examination demonstrated brownish-black hyperpigmentation of both conjuctivas. Urologist: right nephrolithiasis.

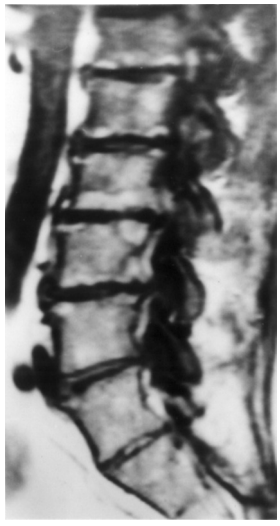

Fig. 3. Computed tomography of the lumbar spine showing Romanus lesion at the upper corner of L1 and lower corner of D12, together with numerous wafer-like calcification and intervertebral disc narrowing, with vaccum phenomenon in the almost all intervertebral discs.

Radiographic imaging of his thoracic and lumbar spine showed thoracolumbal vertebral body squaring, marginal syndesmophytes from Th 10 – L 1, intervertebral disc narrowing. Thoracic kyphosis was accentuated and lumbal lordosis reduced. Numerous wafer-like calcifications and positive vacuum phenomenon in the discs were seen in the dorsal and lumbar spine (Figure 3). Cervical spine radiographs showed reduction of intervertebral space between C5–6 and C6–7, with subchondral sclerosis and narrowing of almost all cervical apophyseal joints.

Radiographs of the pelvis revealed bilateral erosive inflammatory changes of both SI joints (gradus II), together with erosions and osteitis at the symphysis pubis. Severe calcificed aposition of both iliac crests and ischial rami were seen.

Both hips showed joint space narrowing with subchondral sclerosis without signs of coxitis, together with entesopathy of both greater trochanters.

Evaluation of the peripheral joint system revealed: joint space narrowing of the femorotibial and femoropatelar joints of both knees, calcifications of the popliteal fossae. Small, snake-like calcifications around left Achilles tendon was visualized both on radiographs and ultrasonographic assessment of Achilles tendons.

Radiographs of the hands and feet didn't show any inflammatory changes. In order to confirm inflammatory changes both SI joints due to AS, a CT imaging of both SI joints was made. The imaging revealed clearly evidence of erosions, irregularity of joint margins, presence of subchondral cysts and sclerosis of both SI joints.

Discussion

Ochronotic spondylosis and arthropathy are regular manifestation of longstanding alkaptonuria. From the case reports in the literature it appears that alkaptonuric spondylosis occurs at an earlier age and is more severe in males than in females, even though the sex incidence is pretty equal[7]. The deposition of characteristic brownish pigment in the cartilage and intervertebral discs leads to ochronotic spondylopathy and arthropathy, affecting especially the knees, shoulders and hips. The clinical picture is very often similar to that of AS, although the radiological signs are very distinguishing.

X-rays may reveal changes considered almost patognomonic of ochronotic spondylosis[8]. The vertebral bodies of the lumbar and thoracic spine show degeneration of the intervertebral disks with narrowing of the intervertebral space and dense calcification of the remaining disk material. This is accompanied to a variable degree by fusion of the vertebral bodies. In the contrast to degenerative vertebral changes little osteophyte formation and minimal calcification of the intervertebral ligaments are present.

The large peripheral joints involved also differ from osteoarthritis in that the degenerative joint changes in ochronotic artropathy are most common in the shoulders and hips, whereas such joints as the sacroiliac may be narrowed and spared. Calcified deposits are most common in the muscle tendons around the large joints.

Our patient has ochronosis with typical clinical and radiological features of the disease, with highly positive excretion of homogentisic acid in the urine. At the same time he fullfiled all the New York criteria for AS and radiological changes of spine and pelvis, together with B 27 positive antigen undoubtedly suggests diagnosis of AS. The presence of syndesmophytes, fusion of apophyseal joints, bilateral erosive inflammatory changes of SI joint, pubic erosions and symphysitis, vertebral body squaring and affection of Achilles tendon, patellar tendon, and the adductor muscles tendon are all tipical signs of AS.

Gaucher et al.[9] suggested that ochronosis may have been associated with B 27 antigen in a family with 21 members with ochronosis; but no other reports have confirmed this suggestion.

Zanetakis et al.[3] described a 77-year-old man with alkaptonuria and ochronotic arthopathy, showing some of the radiological features of AS together with posttraumatic spinal pseudoarthrosis. They hypothesized that »perhaps the presence of the B 27 antigen in an alkaptonuric patient predisposes that such a patient may have chronic ochronotic arthropathy or affects the severity or clinical manifestation of the disease. It is possible that B 27 positive patients with ochronosis may get more severe and clinically more recognizable axial arthropathy, perhaps resembling AS, than those who lack B27«. The authors categorically excluded the coexistence of ochronosis and AS. Their patients had B 27 positive antigen in the presence of only, some radiological features of AS. Our patient, however, fulfilled all New York criteria of AS, together with positive HLA B 27 antigen.

Gemignani et al.[4] described a 65-year-old female patient with coincidence of ochronosis and AS but their patient was HLA B 27 negative.

The other report by De Keyser et al.[5], described a 50-year-old women with ochronotic arthropathy and B27 positive AS, together with rectocolitis haemorrhagica and recurrent episodes of iridocyclitis, whose family history was positive for seronegative enteropatic spondylarthropathy. Family history for such spondylarthropathy was negative in our patient.

Weinberger[6] described a 70-year-old woman with coexisting ochronosis and AS. His patient was negative for HLA B 27 antigen and presents fusion of sacroiliac joints together with degenerative lesions in the spine from ochronosis.

Turkish authors described a 58-year-old woman with ochronosis and positive family history for alkaptonuria[10]. She was HLA-B 27 positive. Recently, a woman with typical clinical features of the ochronosis was described to have bilateral hip involvement, which was improved by cementless total hip prosthesis[11]. Some authors suggest that the proof of sacroiliac involvement or bamboo spine appearance is not sufficient either for diagnosis of ankylosing spondylitis or exclusion of ochronosis[12]. We don't agree with their opinion, because two illnesses have been already described in few above mentioned reports, in our case too.

In conclusion, we have reported the case of a patient with ochronosis, who also meets all criteria for AS. Radiographs show the features of both diseases. In addition, coexistence of 2 diseases was followed by HLA B 27 positive antigen in our patient, with no previous family history of the seronegative spondilarthropathy, which was not described in the previous reports of same coexistence of those 2 diseases.

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KOEGZISTENCIJA OHRONOZE I B 27 POZITIVNOG ANKILOZANTNOG SPONDILITISA

S A Ž E T A K

U radu je prikazan 49 godišnji bolesnik s istodobnom pojavom ohronoze i ankilozantnog spondilitisa. Ovo je prvi takav prikaz ohronoze i B 27 pozitivnog ankilozantnog spondilitisa s negativnom obiteljskom anamnezom za seronegativne spondiloartritise. Raspravljeni su odnosi između navedenih bolesti.