Case Reports

Ochronosis with Ruptured Lumbar Disc

Case Report

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Alcaptonuria is an hereditary, congenital defect in metabolism characterized biochemically by inability of the organism to reduce homogentisic acid in the urine (alcaptonuria), pigmentation of the tissues (alcaptonuric ochronosis), and degenerative arthritis (alcaptonuric arthritis). The frequency of pain in the back as an initial complaint associated with a characteristic radiological appearance of calcified intervertebral discs should make alcaptonuria a matter of interest to neurosurgeons, although it is an uncommon disease with somewhat less than 250 cases reported. An interesting historical review may be found in these references.1,2,3,5,17,18,23,25,27,28,30-32

Alcaptonuria usually is inherited as a mendelian recessive; however, there have been some cases reported that follow a dominant pattern. The ancestral history of these patients frequently is confused by intermarriage. The current concept of this inheritance is discussed well elsewhere.19-21

The biochemical abnormality is shown in Table 1. In alcaptonuria homogentisic acid cannot be metabolized further, collects in the blood, and is excreted in the urine. The oxidized polymer of the metabolite is deposited in the tissue, resulting in ochronosis. The relationship between pigmentation of the cartilage and arthritis is not clear.13

Ochronotic pigments are widespread throughout the body. Areas such as the cornea, sclera, conjunctiva, cartilage of the ears, nose, larynx, trachea, bronchi, ribs, intervertebral discs, cardiac valves, endocardium, chordae tendineae, blood vessels, arteriosclerotic plaques, meninges, pineal body, pituitary gland, splenic capsule, apical pulmonary scars, islets of the pancreas, tendons, prostatic calculi, kidneys, periarticular ligaments, beds of fingernails, corumen, skin, and elsewhere all may show discoloration.4,8,16,19,28,30 The changes in color depend upon the amount of pigment present and may vary from yellowish-brown to gray or black. Microscopically the pigment usually is deposited as granules in connective tissue but may occur in macrophages situated perivascularly and in parenchymal cells.4 Pigmentation is fine and diffuse in the sparsely involved areas and in the densely pigmented areas it is more particulate and often contained in macrophages.29 In addition to the areas of pigmentation, other findings which may be present are osteoporosis, deformed vertebrae, kyphosis, and arthritic fusion.16,20

There are many excellent discussions which bring out the various clinical facets of the disease.2,4,5,7,10,11,13,15,19,22,23-25,20 The disease usually progresses from simple alcaptonuria to alcaptonuric ochronosis, and finally to alcaptonuric degenerative arthritis.

Simple alcaptonuria frequently is recognized at birth, but may escape detection for a number of years until routine physical examination turns up a reducing substance in the urine which is homogentisic acid rather than sugar.19 Usually the infant is noted to have a black stain on the diapers. There may be a family history of ochronosis, but not necessarily.15,20 The color of freshly voided urine is unusual only if the urine is alkaline.

The second part of the syndrome is alcaptonuric ochronosis which usually is recognized in the fourth decade. The incidence of ochronosis increases with age, the peak being in the fifth decade.4 This phase is characterized by deposition of dense pigment in the ground substance of mesodermal tissue, especially in the skeletal and cardiovascular systems, and by degenerative changes which occur either concomitantly or as a result of such deposition.20 Ocular pigmentation occurs in about 70 per cent of ochronotics and probably is the earliest manifestation.4,28

Smith,40 describing the ocular findings, believed that the slit-lamp appearance of the pigmentation in the cornea is characteristic and that of the sclera nearly so. Pigmentation of the cartilage of the ear frequently occurs simultaneously with ocular findings.4,19 The skin of the axilla and the butterfly area of the face may be pigmented.19 The fingernails are attenuated and pigmented, and perspiration may be discolored.4,19 Pigment is light and patchy in the first decades, but becomes progressively darker and more diffuse. Disturbances may arise from the heart, genitourinary tract, respiratory tract and gall bladder.4,5,15,16,19,22,29

The third phase of the disease is arthritis which occurs with advancing age, involving both the

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TABLE I

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<thead>
<tr>
<th>Phenylalanine (Blocked in phenylketonuria)</th>
<th>Tyrosine</th>
<th>→ 3,4 dihydroxyphenylalanine</th>
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<tbody>
<tr>
<td>Phenylpyruvic acid</td>
<td>p-hydroxyphenylpyruvic acid (Blocked in tyrosinosis)</td>
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<tr>
<td></td>
<td>Homogentisic acid</td>
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<tr>
<td></td>
<td>Maleylacetoacetic acid</td>
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<tr>
<td></td>
<td>Fumarylacetoacetic acid</td>
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<td>Fumaric acid and acetoacetic acid</td>
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axial and appendicular skeleton in varying degrees. In about 30 per cent of alkaptonurics ochronosis develops with degenerative disease of the joints.\(^4\) The age at onset of arthritis averages about 34 years, but may be as late as 50 years.\(^4\)

Pigmentation is deposited in the cartilage which becomes black and brittle, and loses elasticity and cracks easily. Small, detached fragments later become irritants to the joints and synovial effusions may occur. Absorption of lacunar bone occurs under devitalized, destroyed cartilage and minor injury produces fractures. The ultimate process is ankylosis with proliferation of marginal osteophytes. The osteoporosis present is thought to be a phenomenon secondary to disuse. As the disease progresses, pain is not as prominent as might be expected from the pathology observed.

**Case Report**

V.P.W. (411365). A 37-year-old salesman was seen in June 1961, at which time he recalled that in his college years he was found to have a test questionably positive for glycosuria. No evidence of diabetes was determined on further testing. He gave a background history of repeated episodes of low-back pain with or without radicular pain in the left lower extremity, usually lasting 1 or 2 weeks. However, most of his attacks of pain had been within the past 4 or 5 years.

The present episode began 2 months prior to admission when he was awakened in the morning and had difficulty getting out of bed because of stiffness in the back. Within a few days a pain developed in the left lower extremity with radiation to the foot and some pain in the left groin. At times the sensation of pain was described as numbness. The pain in the back was more marked than in the leg and both were incompletely relieved by rest in bed.

**Examination.** The patient was a well-developed, well-nourished, tall white male with early sceral pigmentation temporally in each eye. Pigmentation was present in the cartilages of the ears.

Positive neurologic findings were: a moderate loss of motion of the spine in all directions, straightening of the spine, and moderate spasm of the lumbar paraspinal muscles. Naffziger's sign was positive. Lasègue's sign was mildly positive with reference of pain to the muscles of the left calf and low part of the back. There was questionable weakness of the left great toe, with hypalgesia of the left S1 and L5 dermatomes. The left ankle jerk was diminished moderately and the left knee jerk was weakened slightly.

Results of urinalysis were unremarkable except for a ++ test for sugar. Further testing of the urine revealed the + + test for sugar to be negative for glucose. The fasting blood sugar was found to be 101 mg. per cent, and a 3-hour postprandial blood sugar was 149 mg. per cent. Spinal fluid contained 46 mg. per cent protein and 3 lymphocytes and V.D.R.L. was negative. All tests for homogentisic acid were positive.

Roentgenograms of the lumbar spine are shown in Fig. 1.

**Course.** The patient was treated conservatively and responded.

**Discussion**

The first symptoms related to the joints are of the spine, occurring as a sensation of stiffness in the low part of the back with tenderness and some pain in the spinal area. Sciatica as the initial complaint occurred in 17 per cent of one series, and backache as the initial complaint occurred in about 60 per cent of another series of ochronotics.\(^5\) Early signs are flattening of the physiologic curves of the spine. In 3 to 5 years a fixed, sharp kyphosis in the low thoracic-high lumbar region occurs, reducing spinal mobility. Eventually the lumbar and thoracic spines are ankylosed with short segments of kyphosis, lordosis, and scoliosis.\(^5\) The initial roentgen-ray findings of the spine are narrowing of the discs in the lumbar and thoracic regions, doubling of outlines of the discs and a seeming elongation of the vertebral bodies. Pomeranz et al.\(^6\) described the characteristic radiographic findings as universal calcification of
intervertebral discs appearing as elliptical opaque wafers in intervertebral joints, most clearly visualized in the lumbar areas (Fig. 1). There also may be universal calcification of cartilages. Osteoporosis followed by secondary reactive hyperplasia, deformities of bone and destruction of bone occur. In more advanced cases massive exostosis of vertebral margins develops and the discal spaces may disappear and fusion follow. Radiological evidence of changes in the cervical spine are late.

Peripheral joints are affected with the following frequency: those of the knee in 64 per cent, of the shoulder in about 42 per cent, and of the hip in about 32 per cent. The smaller joints usually are spared.

The laboratory diagnosis of alcaptonuria is made with certainty only by identification of homogentisic acid by isolation of the melting point. Perhaps the most rapid and accurate method of diagnosis is that described by Fishberg wherein a drop of alkalized urine is placed on sensitized photographic paper and a coal-black color develops instantly. (Such a reaction occurs because the chemical structure of homogentisic acid is closely related to the photographic developer hydroquinone.)

There is no satisfactory therapy for alcaptonuria. Symptomatic support is used as needed. Numerous medications and diets have been used to no avail, although there were 2 cases wherein thiouracil apparently afforded some relief. In summary, a case of ochronosis has been reported, noting the various clinical features, the frequency of initial vertebral complaints and the diagnostic appearance of the calcified intervertebral disc. Although there is no effective treatment, awareness of the condition by neurosurgeons may lead to an accurate diagnosis.

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