CASE REPORT

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Winchester syndrome

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Abstract Winchester syndrome was first described in 1969 and since then nine patients have been reported in the literature. The syndrome is characterized by short stature, coarse face, corneal opacities, generalized osteolysis and progressive painful arthropathy with joint stiffness and contractures of distal phalanges in combination with skin changes. The etiology is unknown. Parental consanguinity supports autosomal inheritance. The diagnosis is based on clinical and radiological manifestations. We describe a case in a 7-year-old Pakistani boy.

Résumé Le syndrome Winchester a été décrit pour la première fois en 1969 et seulement 9 cas ont été rapportés dans la littérature. Le syndrome est caractérisé par une petite taille, un visage grossier, des opacités cornéennes, une ostéolyse généralisée et des arthropathies douloureuses progressives avec raideur et contractures des phalanges distales en association avec des troubles cutanés. L'étiologie du syndrome est inconnue. La consanguinité parentale est un facteur favorisant. Le diagnostic est basé sur les manifestations cliniques et radiologiques. Nous décrivons un cas chez un garçon pakistanais de 7 ans.

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Introduction

Winchester syndrome (WS) is a rare disease of unknown etiology characterized by a combination of rheumatic and cutaneous manifestations. We here describe a boy with WS who developed severe functional disability of the hands despite low-dose methotrexate (MTX) treatment.

Case report

A 16-month-old boy presented in 1994 with bilateral arthritis of the third and fourth metacarpal phalangeal (MCP)-joint. The following year he developed a 15×10 mm skin tumor located at the plantar base of the first metatarsal bone. Histological examination of the extirpated tumor showed fibrosis and increased occurrence of fibroblasts in the deep layer of dermis. Immunohistochemical re-evaluation reacted positively for smooth muscle cell actin and calretinin in some of the mesenchyme in the fibroblastic tissue. Collagen IV was also demonstrated. The actin content indicates muscle cell differentiation. The positive reaction for calretinin was surprising. It is a calcium binding protein usually present in neurons in the peripheral and central nerve system and also in mesothelial cells.

At the age of 3.5 years the patient was seen by hand surgeons because of a new skin tumor in the left palm close to the base of the fifth MCP-joint. They found bilateral radial deviation of the four ulnar fingers; dorsal dislocation of the fifth left MCP-joint and bilaterally reduced motion in the third and fourth MCP-joint. The parents of the patient are cousins.

Except for elevated platelet count of 660 billion per liter, there were no abnormal laboratory findings. Examinations for Ig-M rheumatoid factor, antinuclear antibodies and anti-double-stranded DNA were negative. Dental eruption was delayed.

Despite intensive occupational therapy including splints on his hands, his hand function deteriorated. At 4 years of age, a symmetrical linear and nodular pigmented and hypertrichotic thickening 8×1 cm on both sides of the elbows and knees was found.

During the following years cutaneous nodules developed on his face, right elbow, palmar side of all MCP joints of the right hand close to the base, anterior side of left wrist and the base of fourth MCP joint. The hands are now claw-like with immobility of the proximal interphalangeal joints (Fig. 1). The mobility in the joints of the hips, knees and ankles is free. Urinary excretion of oligosaccharides was tested twice and found to be normal.

Fig. 1 Nodules and flexion contractures of the fingers

Fig. 2 Radiograph of the hands showing osteopenia and vesiculation of the metaphyses

Initial radiographs of the axial and appendicular skeleton showed diffuse osteopenia peripheral in the extremities, there was no erosive arthritis (Fig. 2). Total skeleton X-rays at the age of 7.4 years showed progressive arthritis-like changes in the hands and feet with erosions of the caput of the proximal phalanges of both hands and the great toe of each foot, generalized halisteresis most pronounced peripherally, soft tissue swelling matching the erosive finger joints.

From the age of 4.8 years the diagnosis WS was suspected and 1 year later the patient was treated with oral MTX. Changes in the skin and joint mobility improved. However, due to compliance problems, the treatment was changed to hydroxychloroquine with naproxen being added. No improvement was seen within the following year. Since the age of 7 years the patient has been treated with MTX.

Surgical intervention was performed when the patient was 5.3 years old. Dorsal squares in the capsules of the second to the fifth MCP-joints on the left hand were removed and the collateral ligaments were loosened. Furthermore, the fifth MCP-joint was reduced. Thereby a flexion of 70–90° was obtained in the second to the fourth MCP-joints but hardly any in the fifth MCP-joint. Reoperation 9 months later did not improve the range of motion of the fingers.

Discussion

Winchester et al. [8] were the first to describe WS in 1969. Since then nine other cases of WS have been reported in the west [2, 3, 4, 5, 6, 7, 8, 9]. Onset of the disease is usually within the first year of life. The female-to-male incidence is 6:4. In all but one instances there is parental consanguinity (one child is adopted and parental status unknown). Two sets of affected siblings [4, 8] strongly supports autosomal recessive inheritance.

Symptoms at onset include pain, swelling, deformity and limitation of movement of particularly the small joints of the hands and feet. Joint stiffness and flexion contractures progressively lead to claw hands and difficulty with walking. Gingival and lip hypertrophy and a large, fleshy nose with a depressed bridge are reported in the majority of cases. Both weight and height progressively fall below the third centile. Intelligence is normal.

Patches of thickened, hyper-pigmented, leathery skin may appear on the face, trunk and extremities. Cutaneous nodules are seen over the thoracic spine, in the face, extremities, and dorsal or palmar surface of the hands adjacent to joints and on the plantar surface of the feet. Generalized hirsutism or patches of hair on the extremities or trunk may also be a feature.

Skin biopsies reveal fibroblastic hyperplasia, abnormal collagen bundles in the deep dermis, excessive collagen turnover and chronic perivascular infiltrate [1, 4]. Basic laboratory tests are usually within normal limits. In three patients [3, 6] IgM was slightly raised. The excretion of urinary oligosaccharide was increased in two patients [2].

Skeletal radiographs reveal bony resorption with cystic degeneration, especially in the carpal and tarsal regions, and generalized osteoporosis with thinning of the long bones. Other abnormalities include compression fractures of the vertebrae, destruction of the femoral heads, misshapen pelvis, thickening of the metacarpal and phalangeal bones and ankylosis involving the small joints of the feet.

Drug treatment has only been described in one case [7]. This female was treated with sulindac (non-steroidal anti-inflammatory) and orphenadrine citrate (skeletal muscle relaxant, antihistamine). No surgical or physical therapy has been described up until the present case.

The differential diagnosis of WS includes rheumatoid arthritis, thalassemia and nodular systemic sclerosis. During childhood attention should be drawn to generalized congenital fibromatosis, digital fibromatosis, juvenile hyaline fibromatosis and fibroblastic rheumatism. The coarse facial features and severe joint disease are also found in Farber disease and Scheie syndrome. The specific clinical features together with the normal laboratory findings makes it possible to distinguish this disease from other fibrotic, rheumatic and lysosomal diseases.

The etiology of WS is unknown. Winchester et al. [8] found increased metachromatic staining and elevated levels of intracellular uronic acid in skin fibroblasts. On this basis they believed that the disorder should be clas-

sified as an acid mucopolysaccharidosis. Hollister et al. [3] failed to demonstrate lysosomal storage defects in the three patients they studied and therefore suggested reclassification of the disorder as a non-lysosomal storage disease. Dunger et al. [2] revealed in two new cases an abnormal urinary mucopolysaccharide excretion. The oligosaccharide was a trisaccharide containing one fructose and two galactose residues.

We here report of a patient with clinical and radiological WS. MTX treatment resulted in clinical improvement but has not yet induced resolution of the cutaneous fibrosis, nodules and digital contractures. The boy is still troubled by severe contractures despite surgical intervention.

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