Osteoporosis in Stickler syndrome. A new family case with bone histology study

Ostéoporose et syndrome de Stickler. Étude avec analyse histologique osseuse

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KEYWORDS
Stickler syndrome; Bone histology; Osteoporosis; Early osteoarthritis; Collagen mutations

Summary The Stickler syndrome (SS) has been described as a "hereditary progressive arthro-ophtalmopathy" by Stickler in 1965, due to mutations on the collagen genes. Currently about 40 different genes have been identified which encode for at least 27 different collagens. The majority of mutations occur in the COL2A1 gene on chromosome 12q13 (SS type I). Mutations in COL11A1 are less frequent (SS type II). More recently, mutations in COL11A2 and in the COL9A1 gene have been reported with particular phenotypes. The main features of this autosomal inherited disease are ocular, auditory with orofacial abnormalities and early-onset osteoarthritis. We report the clinical presentation of an adult and his son, with a particular focus on the bone status of the father, radiography, bone densitometry and transiliac bone biopsy showing that he was suffering from osteoporosis. The lumbar bone mineral density was low with a Z-score at −2.9. Transiliac bone biopsy showed a dramatic decrease of trabecular bone volume (8.6%; NI: 19.5±4.9%), thin trabeculae and a disorganized trabecular network. A slight increase of osteoid parameters was observed. Bone resorption was markedly increased with an excessive number of active (TRACP+) osteoclasts. The cortical width was normal, but a slight increase of cortical porosity was found. Osteoporosis has been rarely described in the SS. It might be useful to systematically perform a bone densitometry in all patients with SS and to discuss the indication of a transiliac bone biopsy in severe cases.

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MOTS CLÉS
Syndrome de Stickler ;

Résumé Le syndrome de Stickler syndrome (SS) décrit comme une « arthro-ophtalmoplégie héréditaire progressive » par Stickler en 1965, est due à des mutations de gènes du collagène selon un mode autosomique dominant : le plus souvent mutations du gène COL2A1 (12q13.11-q13.2) pour le type I, du gène COL11A1 (SS type II). Des mutations de COL11A2 et COL9A1 ont

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http://dx.doi.org/10.1016/j.morpho.2016.10.001
1286-0115/© 2016 Published by Elsevier Masson SAS.
Histologie osseuse ;
Ostéoporose ;
Arthrose précoce ;
Mutations du collagène

Introduction

Stickler syndrome (SS) was described in 1965 by Dr. Gunner Stickler et al. who studied in the Mayo Clinic a large five-generational kindred with degenerative ophthalmologic and joint problems. They incidentally discovered in hospital records that the institution had been caring for patients suffering from this disorder since 1897! [1—3]. Described as a "hereditary progressive arthro-ophtalmopathy", this syndrome is a chondrodysplasia whose main features are ocular manifestations (severe myopia, cataract, vitreo-retinal degeneration), sensorineural hearing loss, orofacial abnormalities (with the most severe presentation is the Pierre-Robin sequence), variable skeletal and joint disorders (early-onset osteoarthritis of large joints) [1—8]. The Stickler syndrome is an autosomal dominant inheritance disease with a prevalence of 1/7500 [6], that may be underdiagnosed due to the variable expressivity of symptoms [2].

Clinical cases

We report the presentation of an adult and of his son, with a particular focus on bone densitometric results and histological bone status of the father. This 37-year-old man presented to our department with intense dorsal pain. He had a 20-year history of musculoskeletal pain. At the age of 10, an osteotomy had been performed on the left tibia to treat a severe genu valgum. In the third decade, he was diagnosed with early-onset osteoarthritis and underwent bilateral hip arthroplasties (right hip at the age of 27, left hip at the age of 34) (Fig. 1). He also described very severe ocular manifestations: total loss of vision of the left eye in early childhood, secondary to extensive retinal detachment, followed by removal of the eye and ocular prosthesis; surgical treatment of a cataract on the right eye at the age of 7, with current high myopia (~16 diopters). Hearing loss was diagnosed at the age of 6 and the patient received at this time an amplification device. There was no history of previous steroid medication.

X-ray of the spine showed many abnormal features: vertebral end plates abnormalities, intervertebral space narrowing due to severe disk degeneration, unfused epiphysial remnants (limbus bone) (Fig. 2). Radiographs of the knees showed severe osteoarthritis associated with osteochondromatosis of the left joint; cortices appeared very thin with a marked accentuation of the vertical trabeculae (Fig. 3). Osteoarthritis was also observed on the shoulders (Fig. 4A–B), both wrists (Fig. 4C–D) and ankles.

Due to the high number of genes involved in this syndrome, a diagnostic flowchart of criteria for type I Stickler syndrome has been proposed; the score reached by this patient was 8 when 5 points are required for the clinical diagnosis [9].

Figure 1  A. Radiograph of the pelvis. Bilateral osteoarthritis of the hip: protrusio acetabuli deformity of the left joint with global narrowing of the joint space and features of destructive hip osteoarthritis of the right joint. B. Surgical treatment by total hip replacement surgery.
A. Radiographie du bassin. Coxarthrose bilatérale, de type engainante à gauche avec protrusion acétabulaire, évoluée et destructrice à droite. B. Traitement chirurgical avec pose bilatérale de prothèses totales de hanche.