Case reports

Spinal involvement in Camptodactyly Arthropathy Coxa-vara Pericarditis (CACP) syndrome in two Yemeni sisters

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A I M O F T H E W O R K: The objective of this clinical report is to describe the detailed magnetic resonance imaging (MRI) findings of the spine, knee and hip joints in two young sisters with Camptodactyly Arthropathy Coxa-vara Pericarditis (CACP) syndrome.

C a s e s r e p o r t: In two young sisters, both had normal levels of inflammatory markers and typical features of the CACP syndrome with camptodactyly, symmetric joint swelling of both hand joints, knees, ankles and both feet. The affected joints were not tender on palpation with no overlying redness or hotness. Coxa vara on plain X-ray and all cases have evidence of pericarditis. The MRI studies showed the typical rim pattern enhancement of the synovial membrane in the knee and hip joints in both, with no evidence of pannus formation, yet a sizable amount of joint effusion. Both had protrusio acetabuli and one had a unilateral synovial cyst of the hip. MRI studies of the lumbar spine showed evidence of facet joint arthropathy and facet joint effusion, a synovial cyst in both cases and synovial enhancement in post-contrast images with no associated facet joint ankylosis.

C o n c l u s i o n: The findings of the two cases confirm the possible axial affection in the CACP syndrome in the form of facet joint disease as a new finding in this rare syndrome. Spinal involvement should be screened in all cases, as it may have consequences for diagnosis and treatment.

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1. Introduction

The Camptodactyly Arthropathy Coxa-vara Pericarditis (CACP) syndrome is an autosomal recessive condition characterized by the association of congenital or early-onset camptodactyly and noninflammatory poly-arthritis. The disease gene has been assigned to human chromosome region 1q25-q31, and truncating mutations have been identified in the megakaryocyte stimulating factor gene [1]. This gene encodes for “proteoglycan-4” (PRG-4), which is a surface lubricant for joints and tendons [2]. Previous molecular studies described the identification of 15 mutations associated with CACP syndrome and the majority of them were found in Arabian families [3–5], in one Pakistani family segregating CACP syndrome [6] and more recently a European cohort that comprised 13 patients, and identified 5 novel mutations [7].

In all previous reports, non-inflammatory pattern of arthropathy involving the peripheral joints with typical coxa vara deformity was described [8–10].

CACP syndrome has distinctive radiological and histological features, which are important to recognize since it may clinically mimic juvenile idiopathic arthritis (JIA) at first presentation [2]. We recently described the first case in the literature with CACP syndrome and spinal involvement [11]. The magnetic resonance imaging (MRI) and computed tomography (CT) showed evidence of bilateral facet joint arthropathy at L5/S1 level and bony ankylosis together with bony ankylosis and enhancement pattern of the
facet synovial lining in post gadolinium enhanced MRI. The aims of the current report is to present the pattern of axial spinal affection as well as enhanced MRI features of hips and knees in two new cases with this rare syndrome and to review the literature regarding MRI findings in CACP syndrome.

2. Case reports

Two female cases in one Yemeni family with CACP syndrome were included. They were 3 and 5 years of age and shared the same typical features of the syndrome with non inflammatory polyarthropathy that involved wrist, elbow, knee and ankle joints in bilateral and symmetrical patterns with associated sizable synovial effusion to variable degrees. Both have coxa vara of both hips causing a waddling gait pattern, congenital camptodactyly and pericarditis. Routine laboratory investigations were carried out including the erythrocyte sedimentation rate (ESR) 1st hour, C-reactive protein (CRP) levels and autoimmune profile in the form of rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP) antibodies and anti-nuclear antibody (ANA). Echocardiography was performed to investigate the pattern and the degree of associated pericarditis. In both contrast enhanced MRI studies were performed for lumbar spine, hip- and knee joints. All MRI studies were analyzed by two experienced musculoskeletal radiologist (YR) and (OI). The study was approved by the local ethics committee of Dr. Erfan and Bagedo General Hospital and the patients’ guardians gave their consent to be included in the case report.

Laboratory findings showed typically normal ESR 1st hour, negative CRP levels, negative RF, negative anti-CCP antibodies and ANA. Echocardiography showed evidence of pericarditis in both, with minimal pericardial effusion in one case and moderate pericardial effusion in the other with associated thickened pericardium (Fig. 1).

MRI of the lumbar spine showed facet joint (axial) involvement. The MRI of the lumbar spine featured evidence of facet joint effusion and synovial enhancement of facet joints in post contrast images in both cases and synovial cysts (Figs. 2c, d & 3e, respectively) with no associated facet joint bony ankylosis.

Contrast enhanced MRI in knee and hip joints showed evidence of synovial enhancement in both with no evidence of hypertrophy of the synovial membrane lining or pannus formation, yet sizable knee and hip effusion was observed in both cases (Figs. 2a, b, f-h and 3a–d respectively). In both cases no evidence of cartilaginous or bone erosions were seen and joint space was maintained. In one case a synovial cyst in the hip joint was observed (Fig. 2g) and both cases have bilateral protrusio acetabuli.

3. Discussion

In our first report [11] we assumed that the facet joint involvement in the CACP syndrome is disease related for many reasons: the most important being that it can be expected that facet joints are synovial lined joints and will also be involved in CACP syndrome as it primarily affects synovial lined joints. In post contrast MR images we found enhancement of the synovial lining of the involved facet joints reflecting chronic synovial pathology that eventually may lead to bony ankylosis in the facet joints [11]. The facet joints were bilaterally affected suggesting a disease related process, together with intact disco-vertebral junction, there was no other argument to suggest other pathology that can lead to facet joint arthropathy (e.g. spondyloepiphyseal dysplasia, septic arthritis of the facet joints and spondylodiscitis) and there were no paravertebral masses or other destructive and/or lytic lesions [11].

In the new two cases that belong to one family, enhanced MRI showed facet joint effusion and enhancement of the synovial lining which again document and support our early findings regarding a possible spinal affection in this syndrome. These new findings should be taken into consideration while evaluating newly diagnosed cases with CACP syndrome.

Regarding the knee joint our MRI findings are consistent with those previously reported by El-Garf et al. [10] who investigated 10 Egyptian patients with CACP syndrome, the authors observed a rim pattern of synovial enhancement. Likewise in our two studied cases we did not observe any evidence of bone or cartilaginous erosions and joint spaces were perfectly preserved. Additionally sizable knee effusion was a prominent MRI sign with no tendency for synovial hypertrophy or any tendency for synovial proliferation.
Figure 2. (a) Sagittal T2WI showing sizable knee effusion (white arrow); (b) Sagittal T1WI Fat Sat showing synovial enhancement (rim pattern) without synovial membrane thickening or proliferation (white arrow); (c, d, e) Sagittal T1 post contrast Fat Sat of the lumbar spine showing synovial cysts (white arrows) and enhancement related to L4/L5 and L5/S1 facet joints; (f, g, h) Coronal T1WI Fat Sat post contrast of both hips showing bilateral sizable joint effusion without synovial proliferation and intraosseous synovial cyst (white arrow), also bilateral coxa-vara and protrusio acetabuli.

Figure 3. (a, b) Coronal T2WI for hip and knee joints showing bilateral large joint effusion without evidence of synovial proliferations (white arrow); (c, d) T1WI post contrast Fat Sat for hip and knee joints showing synovial enhancement without thickening (white arrows) with no evidence of cartilaginous or bone erosions and maintained joint space; (e, f) Sagittal T2WI Fat Sat of lumbar spine showing synovial cysts related to L4/L5 and L5/S1 facet joints (white arrows).
on post contrast MR images. Especially protrusio acetabuli was a prominent MRI feature and synovial cysts were also observed in both cases. These MRI features match well with the symmetric non inflammatory pattern of joint arthropathy observed in CACP syndrome bases on clinical findings of affected joints which are not tender on palpation and with no overlying redness or hotness. The normal ESR and CRP levels again document the non inflammatory nature of the disease.

A synovial biopsy was not performed for these two sisters. In the study of El-Garf et al. [10] synovial histopathology revealed noninflammatory synovial hyperplasia in the six obtained out of 10 cases and described the presence of multinucleated giant cells in four of them. In another study [12], synovial biopsy in 3 cases reported the presence of macrophage.

Lubricin, a glycoprotein specifically synthesized by chondrocytes located at the surface of articular cartilage, has been shown to provide boundary lubrication of congruent articular surfaces under conditions of high contact pressure and near zero sliding speed. Given the fact that mutations in the gene proteoglycan 4 (PRG4), affecting lubricin production, which is an essential protein for joint function and lubrication of these surfaces is critical to normal joint function. Moreover, mutations or lacking of lubricin gene have been shown to link to the joint disease such as CACP syndrome, synovial hyperplasia and failure of joint function, suggesting an important role of lubricin in the pathogenesis of these joint disease [13].

In conclusion, in this report we documented our early findings and explained possible facet joint disease in CACP syndrome. Axial affection in CACP syndrome in the form of facet joint disease is a new finding in this rare syndrome and should be taken into consideration in further studies to delineate the exact prevalence and its association with this rare syndrome.

Conflicts of interest

None.

References