Utility of Ultrasonography in Children with Camptodactyly-Arthropathy-Coxa Vara-Pericarditis Syndrome

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Abstract

Background: Early recognition of Camptodactyly-arthropathy-coxa vara-pericarditis (CACP) syndrome is very important for counseling and avoiding unnecessary treatment with anti-rheumatic drugs including biologic agents.

Objective: to evaluate utility of ultrasonography in CACP syndrome patients and to compare the findings of the wrist and metacarpophalangeal joints with those in JIA patients.

Materials and Methods: The study cohort consisted of children with CACP syndrome and JIA with a poly-articular course. Each patient completed the same assessment: clinical examination of six joints (wrist, 2nd and 3rd metacarpophalangeal joints bilaterally), laboratory assessment, conventional radiography, and ultrasonography of the above-mentioned six joints. Ultrasonography assessment was performed in the same day as clinical and laboratory assessment.

Results: A total of 24 patients have completed the evaluation: 19 JIA and 5 CACP syndrome patients with a total of 144 assessed joints, with each patient having completed the same assessment. Most patients had synovial membrane thickening. However, synovial proliferation was more prominent in CACP syndrome (26/30) compared to JIA patients (56/114) (P 0.0002). Interestingly, all CACP syndrome patients showed normal vascularity of the synovium as by color Doppler, while 25% of the assessed joints in JIA patients had increased synovial vascularity (P 0.0025). Joint effusion and bone erosion were more frequent in JIA patients compared to CACP syndrome. However, the difference was not statistically significant.

Conclusion: Our findings suggest that ultrasonography is probably beneficial in differentiating inflammatory arthritis from non-inflammatory arthropathy.

Key words: Ultrasound, camptodactyly-arthropathy-coxa vara-pericarditis, juvenile idiopathic arthritis

Introduction

Camptodactyly-arthropathy-coxa vara-pericarditis (CACP) syndrome is an autosomal recessive disorder, which is characterized by non-inflammatory arthropathy affecting mostly hips, wrists and small joints of the hands in the form of joint swelling with effusion associated with thickened synovium and limitation of movement. These
manifestations are easily confused with the most common childhood chronic arthritis, namely juvenile idiopathic arthritis (JIA) [1-3].

Careful clinical assessment and proper investigations should help in differentiation of inflammatory from non-inflammatory articular disorders, and early recognition of non-inflammatory arthropathies such as CACP syndrome will help in appropriate management and to avoid unnecessary treatment with anti-rheumatic drugs [3].

The Erythrocyte sedimentation rate (ESR) is an essential part of the assessment in children with JIA and considered a good tool for changes in disease activity. However, it can be influenced by a number of unrelated factors such as concurrent infection. Additionally, normal ESR does not rule out inflammation.

No single modality meets every imaging need at this time; nonetheless, methods for detecting radiographic changes of JIA are dramatically improving. Conventional radiography remains the primary imaging assessment for evaluation of children with JIA. Though there are few radiographic changes suggestive of arthritis, these changes are non-specific; moreover, conventional radiography does not allow direct assessment of the early articular cartilage and synovial changes [4,5].

Currently, ultrasonography is increasingly used for evaluation of joint disease [6,7].

It has several advantages over other imaging modalities, including non-invasiveness, rapidity of performance, relatively low cost, ability to scan multiple joints at one time, repeatability, safety, and high acceptability among patients. However, it is operator-dependent and related to the quality of the equipment used [8].

Inflamed synovium looked as an area of mixed echogenicity lining the articular cartilage, again these are non-specific findings. However, Power Doppler ultrasonography can assess the vascularity of the synovium and might be considered beneficial criteria for evaluating active inflammatory synovitis; several reports proved its usefulness in disease activity assessment of JIA patients [7,9].

The purpose of this study is to evaluate utility of ultrasonography in CACP syndrome patients and to compare the findings of the wrist and metacarpophalangeal joints with those in JIA patients.

Patients and methods

The study cohort consisted of children with CACP syndrome and JIA with a poly-articular course who were followed at the pediatric rheumatology clinic at the King Faisal Specialist Hospital and Research Center (KFSH-RC), Riyadh. All patients were reviewed for demographic characteristics, disease duration and underwent a similar clinical assessment and laboratory and imaging work-up. Each patient completed the same assessment: clinical examination of six joints (wrist, 2nd and 3rd metacarpophalangeal joints bilaterally); laboratory assessment included ESR, C-reactive protein (CRP), rheumatoid factor (RF), and anti-cyclic citrullinated peptide antibody (anti-CCP); conventional radiography (standard posterior-anterior view) and ultrasonography of the above-mentioned six joints.

Ultrasonography assessment was performed in the same day as clinical and laboratory assessment by a well-trained specialist using a LOGIQ e General Electric machine, while the conventional radiography was reported by an expert musculoskeletal radiologist; both assessments were completed independently.

The following variables were studied: soft tissue swelling, synovial membrane thickening, effusion, osteopenia, joint space narrowing, erosion as well as vascularity of the synovium using color and power Doppler.

All collected clinical and laboratory findings (other than ultrasonography) are the result of routine medical practice. All extracted data was saved, and confidentiality of the patients ascertained.

Informed consent was obtained from all patients or parents, as appropriate.

The Research Affairs Council at KFSH-RC approved this study.

The variables were compared using a t-test for significant differences for nominal variables, while a chi-square test or Fisher exact test was used when appropriate to compare the proportions. The results are expressed as mean + standard deviation (SD) for continuous variables and percentages for categorical variables. The P value of <0.05 was considered significant.
Results

A total of 24 patients have completed the evaluation: 19 JIA and 5 CACP syndrome patients. The mean age of the patients in our study was 10.4 years (range 5–16), while the mean disease duration was 10.2 years (range 5.2–12). The total number of assessed joints was 144, and each patient completed the same assessment: clinical and ultrasonography examination of six joints (wrist, 2nd and 3rd metacarpophalangeal joints bilaterally); 114 joints of JIA patients and 30 joints of CACP syndrome patients. All included CACP syndrome patients had the typical musculoskeletal features in the form of camptodactyly and large joint (wrist, elbow, knee, and hip) arthropathy. The initial findings were noticed through the 1st year of life. On the other hand, all JIA patients had a poly-articular course.

All CACP syndrome patients had normal inflammatory markers and negative RF and anti-CCP, while six JIA patients had raised inflammatory marker levels and RF and four patients had positive anti-CCP.

All JIA patients were on treatment including non-steroidal anti-inflammatory drugs (NSAIDs), methotrexate and biologic agents, while CACP syndrome patients were on NSAIDs as symptomatic treatment and vitamin D and calcium supplements. Most patients had clinical findings affecting wrist and metacarpophalangeal joints in the form of swelling, contracture and tenderness. Table I summarized the demographic, clinical and laboratory features and treatment of both groups.

All CACP syndrome and JIA patients completed the same ultrasonography assessment that comprised evaluation of synovial proliferation, joint effusion, color Doppler, and bone erosion. Table II summarized the ultrasonography findings.

Most patients had synovial membrane thickening. However, synovial proliferation was more prominent in CACP syndrome (26/30) compared to JIA patients (56/114) (P 0.0002). Interestingly, all CACP syndrome patients showed normal vascularity of the synovium as by color Doppler, while

### Table 1.

<table>
<thead>
<tr>
<th></th>
<th>CACP</th>
<th>JIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients No.</td>
<td>5</td>
<td>19</td>
</tr>
<tr>
<td>Gender F: M</td>
<td>2:3</td>
<td>15:4</td>
</tr>
<tr>
<td>Age; year</td>
<td>10.6 (5-16)</td>
<td>9.7 (6-15)</td>
</tr>
<tr>
<td>Age at onset</td>
<td>4 months</td>
<td>4.4 (1-10)</td>
</tr>
<tr>
<td>Disease duration; years</td>
<td>10.2 (3-16)</td>
<td>5.2 (1-12)</td>
</tr>
<tr>
<td>Limited range of motion</td>
<td>7/30</td>
<td>19/114</td>
</tr>
<tr>
<td>Effusion</td>
<td>9/30</td>
<td>33/114</td>
</tr>
<tr>
<td>Tenderness</td>
<td>10/30</td>
<td>12/114</td>
</tr>
<tr>
<td>ESR (high)</td>
<td>0/5</td>
<td>6/19</td>
</tr>
<tr>
<td>CRP (high)</td>
<td>0/5</td>
<td>5/19</td>
</tr>
<tr>
<td>RF (high)</td>
<td>0/5</td>
<td>5/19</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>5</td>
<td>9/19</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>0</td>
<td>6/19</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>0</td>
<td>15/19</td>
</tr>
<tr>
<td>Biologic agent</td>
<td>0</td>
<td>15/19</td>
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</tbody>
</table>
Table 2. Showed ultrasonography features of both groups.

<table>
<thead>
<tr>
<th></th>
<th>CACP</th>
<th>JIA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients No.</td>
<td>5</td>
<td>19</td>
<td>-</td>
</tr>
<tr>
<td>Joints No.</td>
<td>30</td>
<td>114</td>
<td>-</td>
</tr>
<tr>
<td><strong>Ultrasonography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synovial proliferation</td>
<td>26/30</td>
<td>56/114</td>
<td>0.0002</td>
</tr>
<tr>
<td>Effusion</td>
<td>12/30</td>
<td>51/114</td>
<td>0.6417</td>
</tr>
<tr>
<td>Doppler</td>
<td>0/30</td>
<td>28/114</td>
<td>0.0025</td>
</tr>
<tr>
<td>Erosion</td>
<td>3/30</td>
<td>6/114</td>
<td>0.3403</td>
</tr>
</tbody>
</table>

25% of the assessed joints in JIA patients had increased synovial vascularity (P 0.0025). Joint effusion and bone erosion were more frequent in JIA patients compared to CACP syndrome. However, the difference was not statistically significant.

Conventional radiography of both hands in CACP syndrome and JIA patients revealed soft tissue swelling, peri-articular osteopenia. On the other hand, bone sclerosis and erosion and joint space narrowing were more frequent in JIA patients but were not statistically significant. It is worth mentioning that conventional radiography in CACP syndrome patients did not show bone erosions.

**Discussion**

CACP syndrome is a non-inflammatory arthropathy disorder with contracture of hips and small joints of hands; it is characterized by coxa vara and normal inflammatory markers. It is commonly confused with JIA, particularly if the patient had small joint tenderness and the conventional hip X-ray did not show the typical radiographic changes [3].

Several reports proved that ultrasonography is a useful tool in assessing inflammatory synovitis of metacarpophalangeal and wrist joints in adults as well as children [10-13]. It can show early destructive and inflammatory changes in metacarpophalangeal joints with adequate agreement with MRI findings [14].

Ultrasoundography is superior to conventional radiography in the detection of bone lesions and probably visualizing early erosions in metacarpophalangeal joints of rheumatoid arthritis [12,15].

Absence of bone erosions in conventional radiography is suggestive of non-inflammatory arthropathy such as CACP syndrome, but it is crucial to remember that conventional radiography does not allow direct assessment of the articular cartilage and synovium, so subtle bone erosions that are not shown in conventional radiography are probably visualized by another imaging modality such as ultrasonography or MRI [16-18].

Furthermore, color Doppler expedites detection of hyperemia and vascular abnormalities which are highly suggestive of inflammatory synovitis [15].

We studied 144 joints (metacarpophalangeal and wrist joints) of CACP syndrome [30] and JIA (114) patients using ultrasonography for soft tissue swelling, synovial proliferation, effusion, erosion as well as vascularity of the synovium using color and power Doppler.

All CACP syndrome patients had the typical muscular-skeletal features. Interestingly, 1/3 of the examined joints were tender, but featured no associated morning stiffness. Those joints were significantly swollen with synovial thickening; we speculate that the tenderness was due to mechanical causes.

As expected, all CACP syndrome patients had normal inflammatory markers and negative RF and anti-CCP. In contrast, 26% of JIA patients had raised RF and anti-CCP antibodies.

Hip conventional radiography is probably a valuable finding in the diagnosis of CACP syndrome; typical coxa vara should raise suspicion of CACP syndrome. However, some patients might show atypical findings — such patients are perhaps misdiagnosed.
Ultrasonography proved its utility in visualizing early synovial and bone changes in inflammatory arthritis [12,15]. A recent report showed that physical abnormalities were significantly associated with ultrasonographic synovitis, but agreement was low between ultrasonographic and physical findings, which probably signifies the subclinical joint findings [9].

Our findings showed a statistically significant difference between CACP syndrome and JIA patients, namely in synovial proliferation and color Doppler findings, while joint effusion and bone erosions were not significantly different between the two groups. In fact, color and power Doppler were essential in detecting hyperemia and increased synovial hyper-vascularity, which show active synovitis.

These findings probably suggest that ultrasonography is a beneficial tool in differentiating CACP syndrome from JIA patients and is worth considering in evaluating CACP syndrome patients.

Obviously, ultrasonography has its own limitations: it is operator-dependent and related to the quality of the equipment used.

Despite our work having limitations, particularly the small sample, we believe that our study showed that ultrasonography is a valuable measure in CACP syndrome patients' assessment.

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References


