Camptodactyly arthropathy coxa vara pericarditis syndrome in two siblings

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ABSTRACT

Camptodactyly-Arthropathy-Coxa vara-Pericarditis (CACP) syndrome is a rare autosomal recessive disorder caused by mutations in PRG4 gene that encodes for proteoglycan 4, a mucin-like glycoprotein that is the major lubricant for joints and tendon surfaces. Till date only 15 disease causing mutation in PRG4 gene has been listed in the human genome mutation database. This disease causing mutation has been predicted to prematurely truncate the protein produced. We report here 2 children of the same family getting affected by multiple effusions of the large joints with deformities.

Keywords: Camptodactyly arthropathy coxa vara-pericarditis,Congenital familial hypertrophic synovitis, siblings

INTRODUCTION

CACP syndrome is a rare inherited disorder characterized by autosomal recessive inheritance. CACP patients have normal joints at birth, but with aging they experience a noninflammatory hyperplasia of the synoviocytes, which is responsible for the development of camptodactyly and arthropathy that lead to premature joint contracture. Clinical manifestations of CACP include congenital or early-onset camptodactyly, noninflammatory arthropathy with synovial hyperplasia, progressive coxa vara deformity, and noninflammatory pericardial effusion. Sometimes camptodactyly will be not present. It should be differentiated from the common juvenile rheumatoid arthritis, which is more common on the basis of absence of any inflammation or granulomas. Other differential diagnoses include familial arthritis and Blau syndrome, both of which are inflammatory conditions.

CASE REPORT

We report 2 children of the same family, the elder one 11 year's male child, and a 5 years female child, presenting to the outpatient department with complaints of swellings of the knee joints and unable to squat properly. The symptoms in the girl appeared much earlier and showed moderate pericardial effusion as compared to a male child on USG, so the father of the children brought her to the hospital along with other kids. The male child had more severe involvement of joint than the girl child. He had complaints of difficulty in squatting and sitting. On examination there was painless effusion of the both knee joints, and unable to flex the knees more than 90 degrees, he had no other joint involvement, there was no history of fever with rash, throat infection, on examination on the couch the child had exaggerated lumbar lordosis and both knees were swollen, no erythema or wasting was noted, thickened synovium is palpable medially, no local rise of temperature or tenderness, no joint line tenderness and squeaky nature of joints can be noted on flexion and extension. There was flexion deformities in both hips of about 30 degrees. Girl child having bilateral knee swelling with flexion deformity at proximal interphalangeal (PIP) joint 2nd and 5th, she also had exaggerated lumber lordosis. On auscultation mild friction rub was heard over lower left sternal border. [Figure 1]. Radiographs showed increased joint space and increased soft tissue shadow [Figure 2]. USG for girl child was done which confirms little pleural collection [Figure 3]. Hematologic investigations like ESR, CRP were normal; ASO titer, RA factor and Antinuclear Antibody (ANA) antibodies were negative. Synovial fluid analysis showed yellowish liquid and increased cell count. Radiographs revealed increased joint space.

DISCUSSION

CACP is caused by mutations in PRG4 gene that encodes for proteoglycan 4, a mucin-like glycoprotein that is the major lubricant for joints and tendon surfaces[1]. The causative gene is located on chromosome band 1q25-31[2]. CACP is characterized by congenital or early-onset camptodactyly, childhood-onset noninflammatory arthropathy associated with synovial hyperplasia, progressive coxa vara deformity and noninflammatory pericardial or pleural effusion.The definition of camptodactyly is a congenital or acquired nontraumatic flexion deformity of the PIP joint of one or several fingers.

Camptodactyly in CACP is usually bilateral and congenital, but in some cases, it develops in early childhood. The degree of contracture need not be equal in both and the deformity may progress or not improve.

Arthropathy principally involves large joint, such as elbows, hips, knees, and ankles. Synovial fluid analysis reveals non-inflammatory findings. Histopathologic analysis of synovial tissue reveals pronounced hyperplasia of synovium without evidence of inflammatory cell infiltration or vasculitis, while synovial hyperplasia in rheumatoid arthritis is associated with chronic inflammation. It was first described by Jacobs. He described immaturity, learning difficulties, arthritis, camptodactly, swollen joints, and joint stiffness pericardial effusion as its symptoms

Homemade described flexion deformities of one or more fingers and a symmetrical polyarticular large joint involvement in a 14 year old male and his 2 month old brother without systemic involvement and in his first degree relative[3]. Lucila Stange Rezende et al described similar findings in a seven year old boy and his cousin. There is a painless limitation of the hip and knees in children, they are unable to completely squat, more in the middle child. Biochemical investigations showed no inflammatory activity of joints and synovial fluid analysis was normal in all the three. Colchicines may be helpful for therapy[4,5]. Athreya et al described the pathologic features in synovium that demonstrated synovial hyperplasia, necrotic villi, deposition of eosinophilic and PAS-positive material, and large numbers of multinucleated giant cells. The synovium shows a distinct histology that differentiates it from others[6]. Byung-Ryul Choi described pericardial effusion, coxa vara, noninflammatory arthropathy with early onset camptodactyly in a 10 year old child with no family involvement[7].CACP syndrome Radiography showed, coxa vara, short broad femoral necks and intraosseous cysts. Abnormal modeling of the acetabulum, increased joint space. Effusion and thick cartilage were seen in the knees. Other large joints showed increased joint space. Flexion deformities of the fingers were seen[8].

Though CACP is a rare entity, it should be considered in the differential for childhood arthritis. The occurrence in families and joint swellings without inflammatory signs should make us think about this entity and should be differentiated from juvenile idiopathic arthritis which is much more common. The differentiation is important as aggressive anti inflammatory drugs show no response in this condition. Correct identification of the disease helps to prevent unnecessary aggressive anti inflammatory drugs and timely use of therapy and rehabilitation.

CONCLUSION

CACP syndrome should be considered in all patients who present with a noninflammatory arthropathy or with "atypical juvenile idiopathic arthritis," particularly if radiographs reveal an absence of erosions[9]. In the correct clinical setting, large acetabular cysts on pelvic radiographs may be considered pathognomonic of CACP syndrome

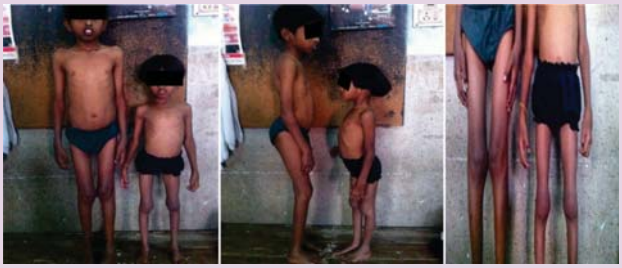
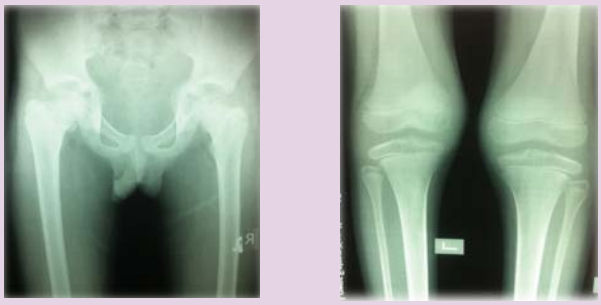


Figure 1: Clinical picture of both siblings showing knee swelling with exaggerated lumbar lordosis and flexion deformity at proximal interphalangeal joint



a b

Figure 2: Anteroposterior radiographs of the pelvis show a smooth flattening of femoral heads and acetabulae are irregular(a).Anteroposterior radiographs of bilateral knee show an increase of joint space(b).

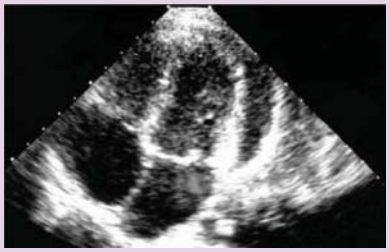


Figure 3: Showing pleural effusion.

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