THE CINCA SYNDROME : A RARE CAUSE OF CHRONIC ARTHRITIS AND MULTISYSTEM INFLAMMATORY DISORDERS

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Chronic infantile neurological cutaneous articular (CINCA) syndrome is a rare disorder with neonatal onset characterised by a chronic progressive inflammatory process with skin rash, articular and central nervous system involvement. This primary systemic inflammatory disorder should be distinguished from juvenile rheumatoid arthritis (JRA). Although the articular findings are characteristic features of CINCA syndrome, there is a certain degree of variability in the articular involvements which are not always symmetrical nor is the degree of severity uniform. The etiology of CINCA syndrome remains unknown. No single treatment has been found to be effective. This syndrome is known in the American medical literature as infantile onset multisystem inflammatory disease (IOMID).

Key words : chronic infantile arthritis ; CINCA syndrome ; IOMID.
Mots-clés : arthrite chronique infantile ; syndrome CINCA ; IOMID.

INTRODUCTION

CINCA syndrome is a rare disorder of unknown etiology characterised by a chronic multi-organ inflammatory process with skin rash, severe arthritis and central nervous system involvement. There are frequently additional generalised lymphadenopathy, hepatosplenomegaly, recurrent episodes of fever, hydrocephalus and persistent open fontanelles, eye lesions, hearing loss and mental retardation. Although descriptions of patients with physical findings consistent with CINCA syndrome have been published earlier (1, 10, 12), Prieur and Griscelli (16) recognised it as a new clinical entity distinct from juvenile rheumatoid arthritis (JRA). Hassink and Goldsmith (7) named this condition "neonatal onset multisystem inflammatory disease" (NOMID), while Kaufman and Lovell in 1986 designated it as "infantile onset multisystem inflammatory disease" (9). This syndrome is now termed IOMID in the American medical literature (6). In 1987 Prieur *et al.* described the syndrome in a study of 30 patients and suggested the name : "chronic infantile neurological cutaneous and articular syndrome" (17). Since then the term CINCA syndrome has gained currency in Europe (14, 15). Because of the articular involvements in children with this disease, the pediatric orthopaedic surgeon may be involved in the management of these patients and therefore we thought it appropriate to present the case of a boy with this rare condition.

CASE REPORT

The boy was born after an uneventful pregnancy to non-consanguineous parents at 40 weeks of gestation. No abnormalities were noted at birth. He weighed 2320 grams, his height was 46 cm and his head circumference was 34.5 cm. Apgar scores

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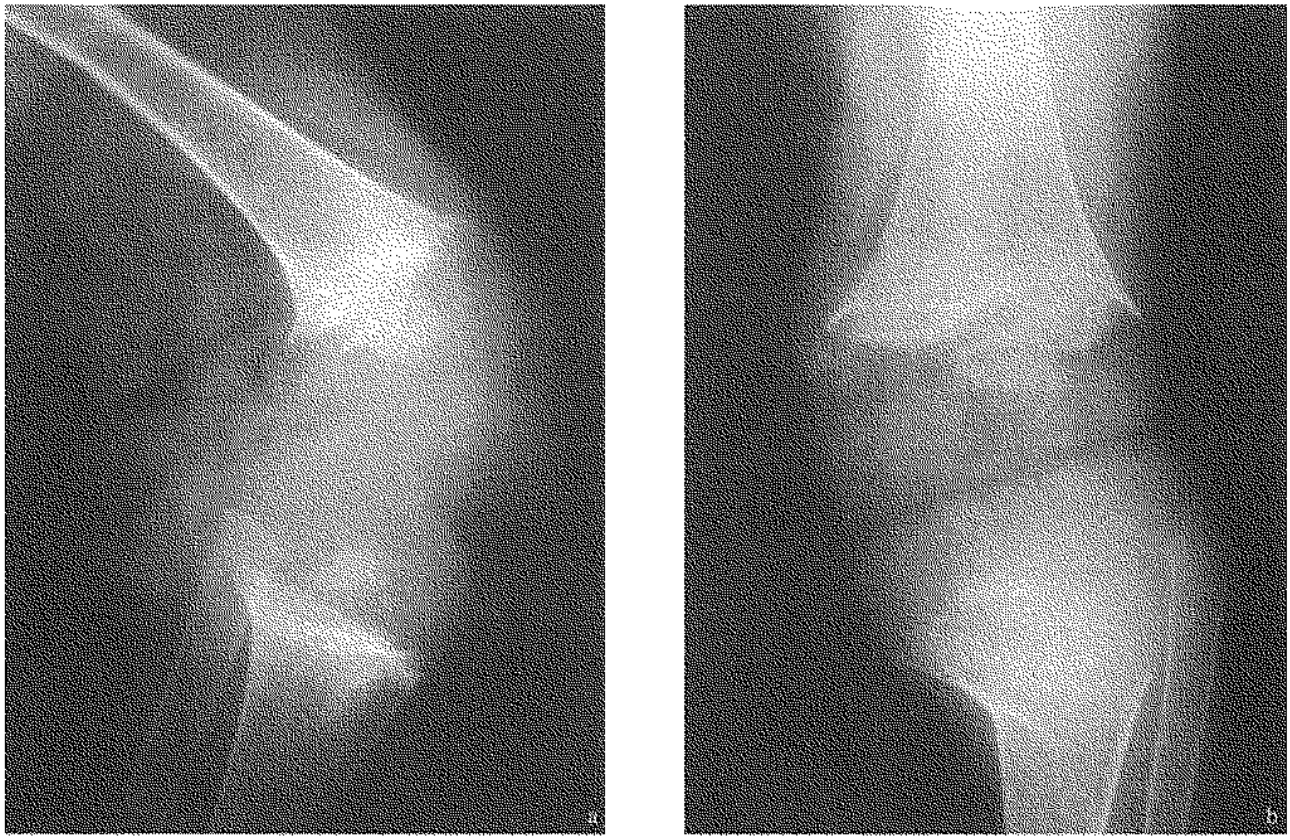

Fig. 1. — Anteroposterior and lateral radiographs of the left knee at age 6 months show abnormal development of the femoral and tibial epiphyses. Varus angulation of the tibia becomes evident.

were 2 (1 min), 6 (5 min) and 10 (10 min). There was a family history of psoriasis. Two weeks after birth, swelling of the right hand was noticed and two days later swelling of the fingers of the same hand which recovered spontaneously the following day.

Three weeks after birth a generalised maculopapular erythema appeared, visible only during a few hours followed by a relapse the next day. The boy was thought to have an infection and was treated with antibiotics. Five days later the symptoms had improved but not completely resolved. The boy was admitted to our hospital when one month old with suspicion of sepsis. He suffered from fever, a generalised skin rash and enlarged lymph nodes at the axillary and inguinal areas. Further physical examination demonstrated signs of meningitis. The liver was palpable 4 cm below the costal margin. At the time of admission in our hospital no joint involvements were noted.

Results of antibody screening for toxoplasmosis, rubella, cytomegalovirus, HIV, mycoplasmosis, histoplasmosis and herpes virus were negative. Serologic test for syphilis was negative. Immunologic assessment showed normal concentration of immunoglobulines and normal circulated complement levels.

Although there was no proof of infection, he was further treated by antibiotics. At the age of 6 months, the infant was readmitted to the pediatric department because of severe swelling and flexion contractures of both knees and with persistent generalised skin rash and lymphadenopathies. Radiographs of both knees showed irregular metaphyses of both distal femora and both proximal tibiae (fig. 1).

Skin biopsy demonstrated vasculitis. Eye examination was normal.

The boy was thought to have some form of JRA and was treated by local and systemic corticosteroids however without any improvement. Based on the unusual evolution, the clinical presentation and the severe and progressive articular derangements, the diagnosis of CINCA syndrome was made at the age of 8 months. The following months there was more and more swelling of the knee joints and he also developed limitation of motion of the hip joints. Swelling and tenderness progressively worsened and were followed by severe flexion contractures, marked limitation of motion and severe pain of both knees. Flexion contractures and pain at the hip joints became also more and more prominent in the further course of the disease. Radiographs of the knees showed the typical evolution at the knees as described by Kaufman and Lovell (9) with enlarged and fragmented epiphyses, flaring and cupping of the metaphyses, bowing of the tibiae, premature fusion of the physes (fig. 2).

There were also deformities of the hips with enlarged epiphyses.

Currently at the age of 5 years, the child is irritable and uncomfortable. He is unable to stand or to walk. Growth and mental retardation are evident. He is unable to talk. He continued to have a maculopapular rash and intermittent fever.

Nonsteroidal anti-inflammatory drugs and local or systemic corticosteroid therapy have been ineffective.

Physiotherapy had no sense for this patient. Analgesics are required to relieve pain.

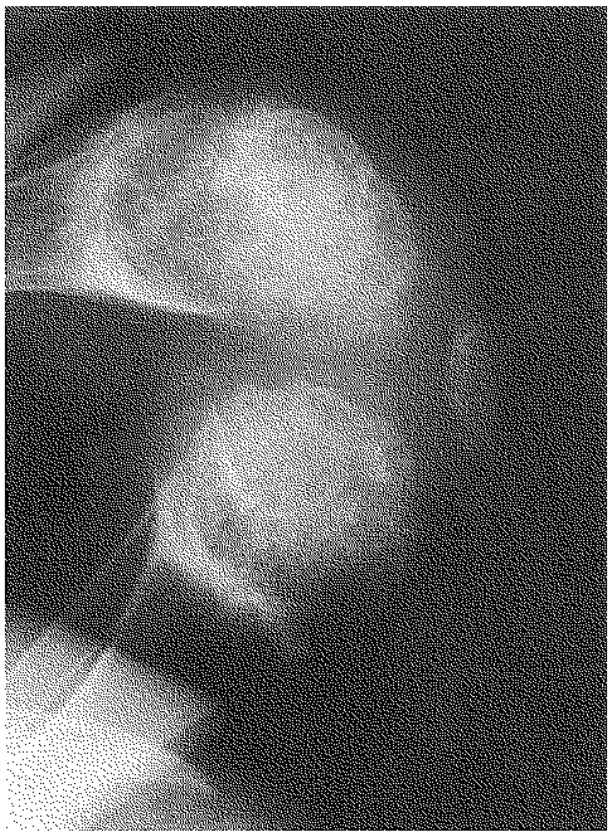

Fig. 2. — Lateral radiograph of the left knee at age 5 years. There is severe flexion contracture. Note grotesque enlarged epiphyses. The epiphyses look like incorporated in the metaphyses. The right knee – not showed – has the same radiological abnormalities.

DISCUSSION

CINCA syndrome must be distinguished from generally known rheumatic disorders in children. Chronic infantile neurological, cutaneous articular syndrome was initially thought to be a subset of JRA but as more patients with the characteristic features were studied, it became apparent that the disorder constitutes a distinct condition (3, 5, 7, 11, 19). The first signs and symptoms occur in early infancy while JRA is rarely observed in the first year of life (4). The clinical presentation of CINCA syndrome is variable however there are some common features. Most cases of CINCA syndrome are first seen with maculopapular erythema being apparent at birth or shortly thereafter. Skin involvement with maculopapular rash was part of the first manifestation of all 30 patients studied in 1987 by Prieur *et al.* (17) and in all other cases published since that time. Chronic meningitis with progressive neurological signs is another feature of CINCA syndrome. Developmental retardation, hydrocephalus, cerebral atrophy, persistent open fontanelles, ocular involvement and hearing loss are all described.

Generalised lymphadenopathy, fever, hepato- and splenomegaly seem to be constant findings in nearly all patients. The joint involvements are the most striking and characteristic features of CINCA

syndrome (2, 18, 19). Radiographs of the affected joints have a unique appearance which differs significantly from those manifested in JRA (9, 18). Kaufman and Lovell gave a detailed description of the radiological findings (9). Bowing and shortening of the long bones, irregular metaphyses and large irregular and fragmented epiphyses and absence of cartilage erosions are diagnostic for CINCA syndrome. It is a chronic disease with great variability in its clinical presentation. Death in early childhood has been noted in 7 children (and in one adult) of the 30 cases studied by Prieur *et al.* (17). The cause of death was known in 4 children : one fatal myeloblastic leukemia (16), one infant died following *Haemophilus Influenzae* meningitis (3), one child died of necrotizing leukencephalopathy related to a head injury (11) and one child died of secondary amyloidosis (17) (one adult died of gangrene of the feet). The cause was unknown in three cases.

The most common joint complaints are severe swelling, joint contracture and pain at motion.

Typical is the evolution with rapid progression leading to significant disability although the syndrome may have a less severe course. Joint involvements may vary from minimal swelling without osseous changes to severe swelling with destructive arthropathy. Hashkes and Lovell even believe that mild and incomplete forms of CINCA syndrome may be more common than is generally thought (6). The time of onset of the articular involvement seems to have a prognostic value. Children with joint involvement appearing during the first year of life generally have a bad prognosis while those children with joint affection that begun after two years of age have a better prognosis with less joint destruction and less disability (6, 17).

Our patient had severe joint anomalies which appeared in the first year of his life. Apart from swelling and contractures of the knees he had involvement of both hips ; the latter is rare in CINCA syndrome (17). At the age of five years he is unable to stand. How many patient with CINCA syndrome reported in the literature up to now, are ambulant is unclear from the data available. The prognosis for our patient is poor and there is no hope that he ever will stand or walk.

The etiology of CINCA syndrome is unknown. It has been suggested that it originates during foetal development as a result of intra-uterine infection but it has never been proved (7, 13, 19). As suggested by De Cunto *et al.* (2) immunogenetic predisposition and environmental insults must also be considered as possible causes but to date these etiologic hypotheses await final proof. As the etiology and pathophysiology remain unclear, treatment is difficult and largely ineffective. Non steroid anti-inflammatory drugs and anti-rheumatic drugs have been used with variable results. Although some authors (8, 16, 18) reported good results with systemic corticosteroids it is generally believed that no medication is really effective. Treatment is mainly supportive and symptomatic. Traction to overcome knee contractures seems of no benefit (18). Physiotherapy may be helpful in mild cases, but in our patient it was ineffective. Several studies, principally in pediatric and rheumatological journals, described the clinical and radiological findings of CINCA syndrome (or IOMID). We only found one paper dealing with this rare condition in the orthopaedic literature (13). Pediatric orthopaedic surgeons however may be confronted with a child with CINCA syndrome because of the articular involvements. The purpose of this paper is to draw attention to this rare condition. The unique characteristics of this syndrome with its neonatal onset and typical radiological findings should lead to an early diagnosis.

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SAMENVATTING

H. DE BOECK, T. SCHEERLINCK, J. OTTEN. Cinca syndroom. Een zeldzame vorm van chronische artritis en multisystemische, inflammatoire aandoeningen.

Het Cinca (chronic, infantile, neurological, cutaneous, articular) syndroom is een zeldzame vorm van chronische artritis bij het kind. Dit syndroom wordt gekenmerkt door een chronisch, progressief inflammatoir proces met huiduitslag, gewrichtsaandoeningen en aantasting van het centraal zenuwstelsel. Het Cinca syndroom heeft kenmerkende gewrichtsaandoeningen en moet onderscheiden worden van chronische juveniele artritis. De oorzaak van het Cinca syndroom is niet gekend. Dit syndroom wordt in de Amerikaanse medische literatuur beschreven als „infantile onset multisystem inflammatory disease (IOMID)".

RÉSUMÉ

H. DE BOECK, T. SCHEERLINCK, J. OTTEN. Le syndrome CINCA : une cause rare d'arthrite chronique et d'atteinte inflammatoire multisystémique.

Le syndrome CINCA (chronic infantile neurological cutaneous articular syndrome) est une maladie rare qui débute dès la naissance. Elle est caractérisée par un processus inflammatoire chronique progressif accompagné d'une éruption cutanée ainsi qu'une atteinte des articulations et du système nerveux central. Cette affection systémique inflammatoire primaire doit être distinguée de l'arthrite rhumatoïde juvénile. Bien que l'atteinte articulaire soit typique dans le syndrome CINCA, il existe une certaine variabilité en ce qui concerne le degré et le type d'articulation affectée. De plus l'atteinte articulaire n'est pas toujours symétrique.
L'étiologie du syndrome CINCA reste inconnue et il n'existe aucun traitement efficace. Ce syndrome est connu dans la littérature américaine sous le nom de IOMID (infantile onset multisystem inflammatory disease).