

# Recurrent monoarthritis in an 11-year-old boy with occult coeliac disease. Successful and stable remission after gluten-free diet

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## Key words:

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## ABSTRACT

*A case of occult coeliac disease (CD) presenting with recurrent monoarthritis in a boy aged 11 years is reported. The case is unique due to the association of occult untreated CD and arthritis in childhood. Peripheral or axial arthritis as a first manifestation of occult CD has been described in adult patients, with an interval between the arthritis and CD of up to 15 years. In our case the interval between the appearance of arthritis and the diagnosis of CD was 2 years. The boy was asymptomatic for bowel disease and his nutritional status was normal. The diagnosis of CD was established using anti-gliadin (AGA) and anti-endomysium (EMA) antibody tests and was confirmed by small bowel biopsy. The introduction of a gluten-free diet resulted in the persistent remission of arthritis. As the treatment of CD-associated arthritis is based on dietary therapy, physicians should be alert to the possibility of occult CD in any child with arthritis of unclear origin.*

## Introduction

The association of arthritis and coeliac disease (CD) is a rare condition that was first described in 1982, with only a few cases observed over the following decade (1, 2). More recently, the availability of sensitive tests such as those based on anti-gliadin (AGA) and anti-endomysium (EMA) antibodies, allow the diagnosis of CD even in patients who exhibit no intestinal manifestations. In a high percentage of occult CD patients, arthritis is the presenting symptom of the gut disease, the diagnosis being subsequently confirmed by small bowel biopsy. Both arthritis and mucosal alterations have been reported to improve with a gluten-free diet (3-7).

On the other hand, arthritis has rarely been reported in CD patients treated with such a diet, confirming the hypothesis that gluten may trigger joint inflammation. We report the case of an 11-year-old boy who developed recurrent episodes of monoarthritis before the diagnosis of CD. A persistent remission of arthritis was observed after the dietary therapy.

## Case report

An 11-year-old boy suffering from a painful, swollen left knee with limited motion was referred to our Paediatric Department. His medical history was unremarkable except for recurrent upper respiratory tract infections since the age of 3. His family history was negative for rheumatic diseases, psoriasis and inflammatory bowel disease (IBD). He had no history of trauma or local infection.

Physical examination showed a boy with a normal nutritional status, who was not in acute distress. Upon admission, his weight was 32.5 kg (> 25<sup>th</sup> percentile), his height 146 cm (> 50<sup>th</sup> percentile), and his arterial pressure 120/70 mm Hg. His puberty stage was 2 according to Tanner.

Knee X-rays excluded bone abnormalities, while ultrasound evaluation revealed a marked synovial effusion at the level of the left knee. <sup>99m</sup>Tc bone scintigraphy was normal. Lung X-rays, electrocardiogram and echocardiogram were all normal. Laboratory test results were also within the normal range, including a complete blood count, erythrocyte sedimentation rate, C-reactive protein, alanine and aspartate aminotransferases, antistreptolysin titre, immunoglobulin and complement levels, rheumatoid factor, and clotting evaluation. A Mantoux test was negative. Serological tests for known viral and bacterial infections were all negative. No antinuclear antibodies were detected. Slit lamp control did not reveal ocular inflammation.

Non-steroidal anti-inflammatory therapy (NSAID), Flurbiprofen (5 mg/Kg/day), and local ice packs were prescribed. The inflamed knee progressively improved, normalising within 1 month, and NSAID therapy was withdrawn. After discharge the boy remained well for 7 months, but then the arthritis flared up again. All blood tests and an eye evaluation were normal. An ultrasound exam showed synovial effusion at the left knee. Late-onset juvenile chronic arthritis (JCA) was suspected and Flurbiprofen was resumed. An arthrocentesis was not performed since the joint normalised within a few days with anti-inflammatory treatment and local ice packs.

HLA tissue typing was performed to

check for the presence of the B27 haplotype which is usually associated with late-onset JCA. The boy was found to be B27-negative, while carrying HLA, A1, A33, B8, B14, Bw6, DR1, DR3, DR52, DQ1, and DQ2. Despite the continuation of NSAID therapy, two similar flares were observed over the next two months. At the fourth flare of arthritis, an MRI was performed which confirmed the presence of increased synovial fluid but excluded any alterations of the meniscus, ligaments and synovia. On this occasion AGA and EMA were again tested. AGA IgA were within the normal range while AGA IgG were raised; EMA were also positive. A diagnosis of CD was made, and confirmed by small bowel biopsy which revealed the presence of villous atrophy, crypt hyperplasia, and lymphocyte infiltration of the intraepithelial and lamina propria. The heterodimer DQA\*501 DQB\*0201, which is strongly associated with CD due to the linkage disequilibrium of this allele with the HLA-DR3 haplotype (8), was then tested for and found to be positive.

A gluten-free diet was introduced and since then the patient's arthritis has been in stable remission for a follow-up period (to the present time) of 5 years. Compliance with the gluten-free diet has been regularly checked by AGA and EMA testing. After 6 months and to the present time, the results of both tests have been consistently negative, confirming adherence to the diet. One year after the introduction of the diet the boy's weight reached the 40<sup>th</sup> percentile.

## Discussion

Our patient represents a paediatric case of occult CD whose presenting manifestation was a recurrent monoarthritis that was successfully treated with a gluten-free diet. The patient never developed bowel symptoms and his nutritional status was not predictive of any underlying intestinal damage. The diagnosis of CD was established by AGA and EMA testing and then confirmed by intestinal biopsy. In a previous study from our group, we reported a seven-fold increase in the incidence of CD in children affected with JCA (9).

Joint involvement has rarely been observed in CD patients treated with diet-

ary therapy, while in untreated patients arthritis has frequently been observed (3-7) and a swollen joint may be the first manifestation of the underlying coeliac intestinal lesions (2-7). The first report of peripheral arthritis in an adult patient with CD was published in 1982 (1) and over the following ten years this association has been sporadically observed (2, 3). In the last decade, when the diagnosis of CD was facilitated by the development of the AGA and EMA tests, arthritis has been reported with increasing frequency in occult CD patients (4-6). In 1985 six adult CD patients, 3 of them asymptomatic for bowel disease, were reported; arthritis commonly involving the knees preceded the diagnosis of CD by up to 15 years, and went into remission after dietary therapy (3). CD-associated arthritis usually affects multiple joints, although monoarthritis has been reported in several patients. In particular, oligoarthritis as the presenting manifestation of occult CD was observed in one adult with little evidence of malabsorption, who was subsequently diagnosed to have CD by intestinal biopsy. Joint inflammation was controlled by a gluten-free diet and never relapsed (2).

In 1993, another case of silent CD presenting with monoarthritis was reported in an adult patient who eventually developed severe and erosive bone damage in the talo-navicular joint, although his inflammation was brought under control with a gluten-free diet (4).

The overall prevalence of arthritis in CD has recently been evaluated in a large study involving 200 adults. Arthritis was detected in 26% of untreated patients, with the peripheral and axial joints frequently involved, while the incidence in patients on dietary therapy was lower (6). The onset of CD-associated arthritis in adults may be acute or insidious, and in most cases the outcome is favourable. The arthritis is characterised by swelling, limited motion, pain and morning stiffness and is comparable to the IBD-associated arthritides.

A different degree of demineralisation may be detected by conventional X-rays and blood tests may be normal except for a reduction in the values for nutrition parameters.

To the best of our knowledge, few studies have been carried out on the incidence of arthropathy in paediatric patients with occult CD (10). CD is known to be associated with JCA (7), although the reported data on its incidence are conflicting (9-11). Moreover, it remains unclear whether JCA and CD are coincidental diseases or if there is a relationship between these two immune-mediated conditions (12, 13). Gut-derived lymphocytes could mediate the immune response and promote the development of arthritis. The introduction of a gluten-free diet helps to repair the flattened villous mucosa and usually induces remission of the arthritis. CD shares HLA haplotypes with other autoimmune disorders, such as thyroiditis and connective tissue diseases. The occurrence of systemic lupus erythematosus has been reported in a 12-year-old child whose CD was diagnosed during the first year of life (14). Recently we observed in a very young girl the co-existence of dermatomyositis and CD, diseases which share a common genetic background (15).

The introduction of gluten-free therapy in our case induced a sustained remission of arthritis, suggesting the possible role of gut damage as a trigger of joint inflammation. Serological tests for CD should be performed in all children with arthritis of unclear etiology since joint involvement could be the presenting manifestation of gluten intolerance.

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