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Case report

A suspected genetic form of bilateral osteochondritis dissecans of the knee in a Dutch family

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ABSTRACT

Osteochondritis dissecans (OCD) mostly has an idiopathic origin, but syndromic and familial forms have been reported. Mutations of the aggrecan (ACAN) and COL9A2 genes are associated with familial OCD, but these patients present with syndromic features. This article describes a mother and a daughter who both have bilateral OCD of the medial femoral condyles, and the monozygotic twin sister of the mother who has confirmed unilateral OCD (and possible bilateral OCD) of the medial femoral condyle. No short stature or any other syndromic features were present. None of the syndromic features associated with ACAN or COL9A2 mutations or any other known syndromes were present in this case. This case suggests a possible unknown genetic anomaly.
Level of evidence: IV case report.

1. Introduction

Osteochondritis dissecans (OCD) is a disease characterised by the necrosis of the subchondral bone with secondary cartilage damage. The incidence of symptomatic OCD in the knee is estimated to be 9.5/100,000 among children aged between six and 19 years, most of whom are male [1,2]. OCD occurs mostly in the medial femoral condyle. Bilateral disease occurs in 5.7 to 7.3% of the cases [1,2]. OCD is classified as a juvenile or an adult form, depending on whether the physes are open or closed [3]. Theories about the aetiology of OCD have been put forward over the years since its discovery by König in 1888, such as inflammatory causes [4], ischaemic or embolic causes [5], traumatic causes [6], repetitive micro-trauma [7], accessory ossification centres [8] and genetic factors [9] (all described in Mei-Dan et al. [10]). Apart from repetitive micro-trauma and accessory ossification centres most of them have been more or less abandoned [10]. Treatment options include both conservative and surgical options. The consensus is to treat symptomatic and unstable lesions surgically, although solid evidence is lacking [11].

Bernstein (1925) was the first to publish about a possible genetic aspect of OCD. He reported a case of bilateral OCD of the knee, occurring in three siblings [9]. Throughout the years, several reports have been made of similar, in some cases bilateral, OCD lesions of the knee in multiple family members and monozygotic twins [10,12–15]. Nevertheless, Petrie et al. found only one affected first-degree relative of 34 OCD patients, and they concluded that in most cases OCD is sporadic and that familial occurrence is uncommon [16].

OCD of the knee has been linked to several syndromes, sometimes involving other joints such as the elbows, hips and ankles, suggesting a genetic cause or a contributing genetic factor [17–23]. Short stature and dwarfism have been linked to OCD of the knee [17,21–25]. Recently, two mutations linked to familial OCD were discovered. Mutations in both the aggrecan (ACAN) and COL9A2 genes code for proteins with an important functional and structural role in the cartilage and the subchondral bone, resulting in OCD and short stature [24,26]. Sporadic studies on monozygotic male twins with identical OCD lesions of the knee in the absence of syndromic features have been reported [10,12–14].

We present a mother and a daughter with similar bilateral OCD lesions of the medial femoral condyle, and the monozygotic twin sister of the mother with a unilateral OCD (also possible bilateral OCD) lesion of the medial femoral condyle. The unique presentation of familial (bilateral) OCD affecting female monozygotic twins and family members in the absence of syndromic features has not been reported before, to the authors' knowledge. The authors have obtained written informed consent from all three patients for printed and electronic publication.

1.1. Case 1

In 2012, a 12 year old girl presented with pain in both knees, predominantly felt in her left knee. The onset of the pain was several years prior, without a history of trauma. A radiograph of the right knee was performed in 2009 with no abnormal features present at the time (Fig. 1A). Recently, she developed a sensation of locking in the left knee, and she felt a loose body on the lateral or medial side of the knee. The patient used to play soccer three times a week, but stopped due to increasing pain. The patient measured 164 cm in height (approximately +1 standard deviation (SD) above the Dutch national

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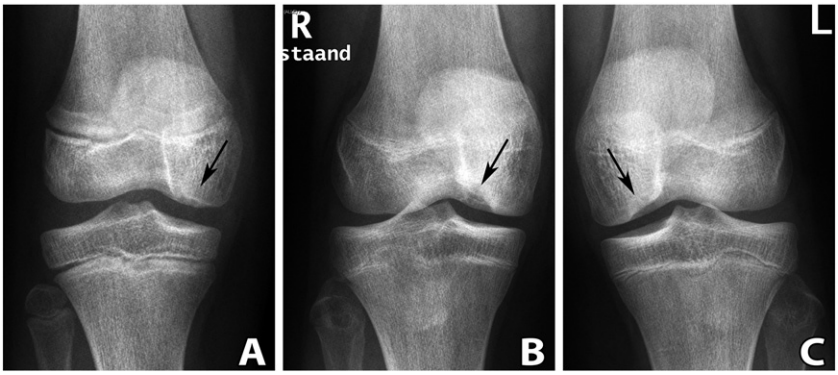

Fig. 1. Patient 1: Anterior–posterior (AP) radiographs of the right knee (A) performed in 2009 and initially described as 'normal' by a radiologist. In retrospect, some small anomalies, possibly representing the first signs of an OCD lesion, are visible on the medial femoral condyle (black arrow). (B) Right knee: an OCD lesion is visible in the medial femoral condyle (black arrow), and the right knee (C): an OCD lesion is visible in the medial femoral condyle (black arrow).

average), with a body mass index (BMI) of 22. On physical examination, normal alignment of the leg, no swelling of the knee, no instability of the collateral and cruciate ligaments and a full and symmetrical range of motion (flexion/extension: 140°–0°–0°) were seen. There was focal tenderness on the medial side and lateral side of the patella. Radiographs of the left knee showed OCD of the medial femur condyle (Fig. 1C). Magnetic resonance imaging (MRI) of the left knee confirmed a lesion of 1 cm, extending from the cartilage to the subchondral bone, with local oedema. The OCD fragment was located craniodorsally to the patella (Fig. 2A–C).

The fragment measuring 1.5 × 1 cm was removed in 2013 with arthroscopic surgery. The local defect in the medial femoral condyle was overgrown with fibrous tissue, which was scraped off. The underlying subchondral bone was treated with a micro-fracture technique.

After five months of rehabilitation, the pain in the right knee increased. No swelling, giving-way or locking sensations were reported. Physical examination showed a stable right knee without swelling. Radiographs of the right knee subsequently showed an OCD lesion of the medial femur condyle (Fig. 1B). Retrospectively, some minor abnormalities of the medial femoral condyle can be seen on the radiograph performed in 2009, which possibly show the first signs of a developing OCD lesion (Fig. 1A). MRI of the right knee showed an OCD lesion of 2.2 cm in diameter, bone marrow oedema and the absence of cartilage on the weight-bearing part of the medial femur condyle (Fig. 3A,B). A large fragment of the bone and cartilage measuring 2 × 2.5 cm was removed during arthroscopy of the right knee in 2013. The non-vital layer of the sclerous bone was removed, and micro-fractures were made. After several months of uneventful rehabilitation with crutches and physical therapy, almost no pain was reported. Activities were resumed without problems.

1.2. Case 2 (mother of case 1)

In 1981, an 11 year old patient presented with pain in both knees present for two years, predominantly felt in the right knee. No significant history of trauma was reported. An OCD lesion of the left knee was diagnosed earlier. Pain increased after exercise and after having sat with a flexed knee for a long time. No trauma, swelling, locking sensations or instability were reported. The patient used to swim, cycle and perform ballet. The patient measured 159 cm in height (approximately +1 SD above the Dutch national average), with a BMI of 15.8. Physical examination of both knees showed no swelling or instability, a sensitive medial joint line, normal leg alignment, normal gait, slight lateralisation of the patella and a symmetrical range of motion (flexion/extension 150°–0°–0°). Radiographs of both knees showed bilateral OCD lesions in the medial femoral condyle, with signs of dissection.

Resting and withdrawing from all sporting activities were advised as conservative treatment, aiming for the stabilisation of the fragments by consolidation. Asymptomatic dissection of the fragments (L ≥ R) was seen on radiographs in 1982. An arthrotomy was performed, and the fragment of the left medial femoral condyle was fixated. The cartilage appeared undamaged. A non-ossifying fibroma (NOF) of the right femur was discovered in 1987 during a routine check-up. No symptoms were reported at a check-up in 1991, and radiographs of the left knee showed only an old OCD lesion (Fig. 4C). In 1992, the patient reported new-onset pain of the right knee with locking sensations and the feeling of a loose body. Radiographs confirmed loose bodies in the right knee (Fig. 4A,B). Three loose bodies were removed subsequently with arthroscopic surgery, and a drilling of the subchondral bone was performed. Recent imaging shows clear signs of old OCD lesions in both knees (Fig. 5).

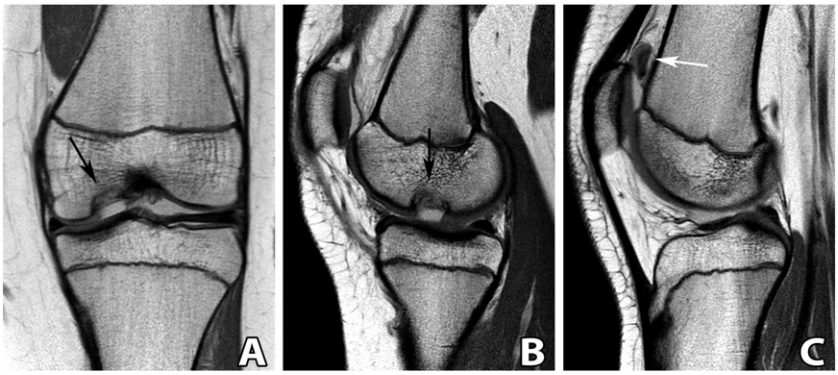

Fig. 2. Patient 1: MRI, T1 PD TSE-weighted signal of the left knee. (A) Coronal view: an OCD lesion involving the cartilage and subchondral bone of the medial femoral condyle, approximately one centimetre in diameter, is visible (black arrow). (B) Sagittal view: an OCD lesion involving the cartilage and subchondral bone of the medial femoral condyle is visible (black arrow). (C) Sagittal view: a loose body is visible dorsal/cranial to the patella (white arrow).