Bilateral Osteochondritis Dissecans of the Knees in Monozygotic Twins: The Genetic Factor and Review of the Etiology

Omer Mei-Dan, MD, Gideon Mann, MD, Gilbert Steinbacher, MD, Ramon B. Cugat, MD, and Pedro D. Alvarez, MD

Osteochondritis dissecans (OCD) is an idiopathic lesion of subchondral bone that results in delamination and sequestration, which can occur with or without articular cartilage involvement and instability.[1] The incidence of this condition, which has juvenile and adult forms, has increased recently because of the growing participation in competitive sports by children of both sexes at younger ages.[2] The majority of cases of adult OCD are thought to result from persistence of an unresolved juvenile OCD lesion, though the literature includes reports of adult OCD lesions arising de novo.[2]

Sir James Paget[3] first described an OCD lesion in 1870 as a "quiet necrosis." In 1888, König[4] suggested the term *osteochondritis dissecans*. He thought that trauma caused necrosis of part of the articular surface, and he described "dissecting inflammation," which followed the trauma and eventually led to fragment separation.[5]

Although there are several other postulated causes, including inflammation, genetics, ischemia, ossification, and repetitive trauma, there is not enough evidence to conclusively support any of these as the etiologic basis of OCD.[1]

The occurrence of OCD in more than one family member is unusual and lends credence to the suggestion that, in such cases and particularly in polyarticular OCD, there is an underlying constitutional or developmental factor.[6]

Dr. Mei-Dan is Resident, Orthopedic and Sports Division, Meir University Hospital, Kfar-Saba, Israel.

Dr. Mann is Head, Sports Department, Orthopedic and Sports Division, Meir University Hospital, Kfar-Saba, Israel, and Head, Olympic Sports Department, Ribstein Center for Sport Medicine Sciences and Research, Wingate Institute, Netanya, Israel.

Dr. Steinbacher is Orthopedic Surgeon, and Dr. Cugat is Head, Mutualidad de futbolistas Españoles, Delegación Catalana, Barcelona, Spain.

Dr. Alvarez is Orthopedic Surgeon, Mutualidad de futbolistas Españoles, Delegación Catalana, Barcelona, Spain, and Clinica Quirón, Barcelona, Spain.

Address correspondence to: Omer Mei-Dan, MD, Orthopedic Division, Meir University Hospital, Tchernichovsky Street, Kfar-Saba, Israel (tel, 972-9-747-2549; fax, 972-9-747-1293; e-mail, omer@extremegate.com).

We present the case of 11-year-old monozygotic twins with bilateral OCD of the medial femoral condyles and review the literature concerning the genetic factor. We are not aware of any similar cases reported in the literature. The authors have obtained the patients' guardian's written informed consent for print and electronic publication of the case report.

CASE REPORT

Identical (monozygotic) twin brothers (11 years old, Caucasian) presented to our clinic for evaluation of mild right knee pain. They were both playing in a basketball league and had been training intensively for 5 years. Pain had been present for several weeks and was aggravated by sports activity. They reported no pain in daily activities. Symptom onset was simultaneous, consistent, and parallel for the brothers. No swelling, instability, or giving way was reported or evidenced on physical examination. The only positive finding was mild pain on the medial joint line of both knees, but tests on knee ligaments were normal.

The twins demonstrated normal growth and development and had no significant medical history. Despite their young age, they were 170 cm tall. Their mother and father were 180 and 190 cm tall, respectively. The parents had no other children.

Plain radiography raised the suspicion of medial femoral condyle OCD in both patients (Figure). Magnetic resonance imaging (MRI) showed bilateral OCD lesions of the medial femoral condyles in both patients (4 lesions total). For each patient, the lesion on the left medial femoral condyle was asymptomatic.

As the pain occurred only during sports activity, conservative treatment was selected. The patients were advised to avoid all sports and to undergo aggressive physical therapy directed at quadriceps strengthening and stretching. No braces or casts were prescribed.

By 1-year follow-up, the lesions in both knees of both twins had healed. The boys gradually resumed their activities at their preinjury levels and had no recurrence and no complaints.

DISCUSSION

Development of bilateral OCD of both medial femoral condyles in identical twin brothers with simultaneous onset and parallel clinical course implies a genetic component to OCD.
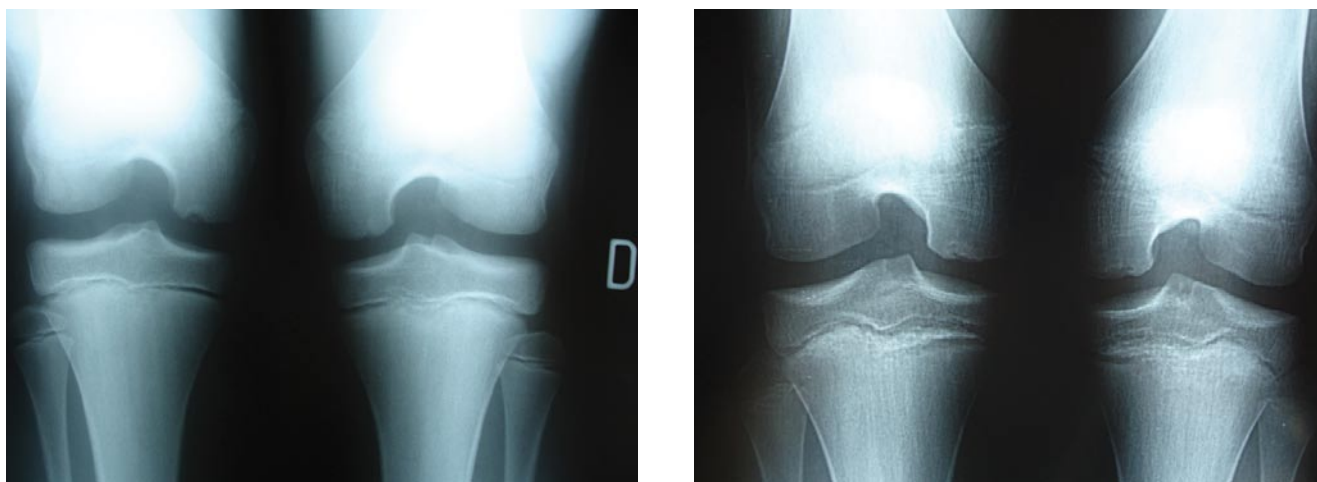
Figure. (A, B) Radiographs show osteochondritis dissecans lesions of both knees in both twins.

Nineteenth-Century Hypotheses. Attempts to explain the pathophysiology of OCD date to the 19th century. In 1870, Paget[3] described a pathologic process ("quiet necrosis") that resulted in the creation of loose, necrotic osteochondral fragments from articular surfaces. König[4] in 1888 described a pathologic condition that led to the formation of loose bodies of femoral origin with no evidence of preexisting trauma. As he thought that a major component of this condition was an inflammatory reaction of both bone and cartilage followed by spontaneous necrosis, he chose the term *dissecting inflammation*. Later, investigators noted the absence of inflammatory cells in histologic sections of excised osteochondral loose bodies, and König's theory was refuted.[7]

The Ischemic (or Embolic) Theory. The ischemic (or embolic) theory was first suggested by Axhausen in 1912.[5] Postulating that an interruption in the blood supply to an area of subchondral bone would eventually lead to sequestration of the bone with the overlying articular cartilage, he proposed that the lesion could be embolic. Reiger in 1920 suggested that fat emboli were the casual mechanism of OCD.[5] Two years later, Rosner and Sommer independently suggested trauma to the blood vessels as a possible etiology.[5] Although Watson-Jones related the condition to red blood corpuscle clumps in 1952,[5] Rogers and Gladstone[8] in 1950 found a rich blood supply to the lower end of the femur and added that ischemic changes in the lower end of the femur, even after a fracture, are unknown.[5,6] Rogers and Gladstone essentially ended the ischemic theory in 1950, and, accordingly, recent histopathologic studies also failed to establish avascular necrosis or ischemia as an etiology for OCD.[1,9]

The Traumatic Theory. According to the traumatic theory, strongly advocated by Fairbanks[10] in 1933, impingement of the tibial spine against the medial femoral condyle, in internal rotation, was a possible mechanical cause. Smillie[11] in 1960 strongly supported this theory and postulated a relation to a demonstrable abnormality, such as genu recurvatum. This theory also was abandoned relatively quickly, as it could not explain the presence of lesions at other joints and sites. Furthermore, though it explained possible rotational-strains impingement, it could not explain impingement on a normal functional stable knee (a common finding).[5] Many investigators, refuting the traumatic theory, indicated that a single trauma would be expected to result in ligamentous damage or acute fracture rather than an OCD condition. Other researchers noted that trauma is an unlikely cause of OCD, as the affected sites are in specific anatomical locations in the knee and are not located randomly, as would be expected with acute trauma.[12]

The Repetitive-Trauma Theory. Another theory, first investigated in the early 1950s and still widely supported, involves repetitive trauma. Rehbein[13] was the first to produce OCD-like lesions, both histologically and radiologically, by subjecting dogs' knees to repeated microtrauma injury. Since then, many histologic, radiographic, biomechanical, and clinical investigations have lent support to the microtrauma theory. Today, repetitive trauma is widely accepted as a cause of OCD, particularly in people who play sports.[2] It is thought that repetitive trauma may induce a stress reaction formation resulting in a stress fracture within the underlying subchondral bone. Eventually, the stress fracture leads to fragment dissection, separation, and nonunion.[1]

The Accessory Ossification Center Theory. The accessory ossification center theory was first proposed in 1941 by Sontag and Pyle,[14] who noted a partial or total loss of epiphyseal regularity. Their theory was supported by the work of Ribbing[15] in 1955 and was later adopted by others.[16] The appearance of hereditary factors, as proposed in the accessory ossification center theory, leads to the main part of our work—the genetic factor in the pathophysiology of OCD.

The Genetic Factor

Bernstein[17] in 1925 was the first to describe OCD lesions in a few members of a family and to suggest a hereditary or constitutional factor. Neilsen[18] in 1933 found the incidence of OCD at the elbow to be 4.1% in 1000 otherwise normal men, but 14.6% of the male relatives of the affected men showed unmistakable evidence of OCD disease. Since then, reports of familial phenomena have been described by many

authors (eg, Wagoner, 1931; Muller, 1933; Novotny, 1952; Gardiner, 1955; Pickering, 1955; Tobin, 1957; Smith, 1960; all of whom are mentioned in Petrie[19]; see also Stougaard, 1964[20]). Associations to different concurrent conditions have also been presented. Quoting earlier work (by Schaefer and colleagues) on endocrine dwarfism, White[21] in 1957 established an association between dwarfism and OCD. He suggested that in such case presentations the underlying constitutional disturbances were endocrine imbalances that began at puberty. The condition was also described by other authors and, recently, in a very large multicenter study by Hefti and colleagues,[22] who found that 2.2% of patients with OCD also had short stature/dwarfism. There was no such relation in the case of our patients.

There have been reports of associations between OCD and other orthopedic conditions, including Perthes disease, discoid meniscus, ligamentous laxity, genu varum, and genu valgum.[2,22] Another condition related to the genetic association is Stickler syndrome; 30% of patients with this syndrome presented with multiple OCD lesions, and 13% were of short stature.[23]

In 1966, in a thorough review, Stillman[24] related OCD to coxa plana and postulated that the basic disturbance in familial cases of OCD could be traced to inheritance of a constitutional predisposition. He proposed that a superimposed trauma initiates the pathologic process of OCD in these patients. Reported cases of OCD in multiple joints support this theory.[20]

The previously reported[2,22] association between OCD and traction-related apophysitis, such as Osgood-Schlatter or Sinding-Larsen-Johansson disease, raised an important point, as both conditions relate to athletic activity. Adolescents are usually more active than adults, and they are more prone to these conditions. This observation alone does not contradict a possible genetic component to OCD.

The genetic predisposition to OCD was strongly advanced in 2 cases in which a significantly high percentage of family members was found to have OCD. Stougaard[20] in 1964 described a 38-member family with 11 members (29%) affected over only 2 generations. In 1979, Mubarak and Carroll[25] reported that 12 family members over 4 generations had OCD. On the other hand, in 1966 Green[5] concluded, "It seems that patients showing a familial tendency are not commonly seen compared with the number of patients presenting with OCD." Petrie[19] in 1977 identified OCD in only 1 of 86 first-degree relatives and concluded that the common form of OCD is not familial—thus contradicting and weakening the previous findings. However, of the 34 patients in Petrie's research, only 2 were younger than 17. This discrepancy between the findings of Mubarak and Carroll[25] and those of Petrie[19] has 2 implications. First, it assumes that the genetic factor of OCD plays an increased role in adolescents compared with adults, as the juvenile form of OCD is self-limited in many cases and heals at maturity. Second, adolescents are usually more active than adults and therefore are more prone to repeated microtrauma, which is believed to play a major role in this multifactorial condition. Petrie called for physical examination and radiography for patients' relatives who report joint pain. Exclusion of asymptomatic relatives who may have had OCD created an immeasurable bias; as in our twins' left knees, many cases of this condition are asymptomatic.

Most of the recent OCD authors have cited the article by Petrie[19] as the basis for eliminating a genetic factor for OCD. In their 2006 review of management of OCD of the knee, Kocher and colleagues[1] wrote, "The common form of OCD is thought not to be familial." In the present article, we suggest the possibility that it is too early to dismiss a genetic component to OCD. We suggest that a larger and more comprehensive study be conducted to try to locate the genes that might play a role in this condition.

Evidence for a genetic predisposition to OCD has been documented in joints other than the knee. In 1995, Woods and Harris[26] reported on unilateral OCD of the medial talar dome in identical twins presenting with ankle pain 2 months apart. The authors concluded that this finding suggests an underlying predisposition to the condition, presumably of an inherited nature and supporting the genetic theory.

Recently published large twin studies confirmed that knee cartilage volume variance and other aspects of cartilage degeneration have an important genetic basis, as has joint space narrowing in most forms of knee osteoarthritis.[27,28] Battié and colleagues[29] reviewed MR images of the lumbar spines of 20 identical twins to assess the degree of similarities of degenerative findings with respect to endplate changes, disc desiccation, disc bulging or herniation, and decrease in disc space height. The similarities between the twins in their study were compatible with a marked genetic influence and might shed light on other aspects of the influence of genetic factors on cartilage and subchondral bone pathologies. Simultaneous occurrence and presentation of some other orthopedic entities during adolescence show that many authors rely on those cases and point to a genetic predisposition. Allen and Calvert[30] reported on simultaneous slipped capital femoral epiphysis in identical twins—supporting a previously mentioned autosomal-dominant pattern of inheritance with variable penetrance. Others have reported on bilateral Kohler disease, Freiberg infarction, and even synchronous lumbar disc herniation, all in identical twins,[31-33] and concluded that an underlying congenital predisposition to these conditions may play more of a role than previously considered.

CONCLUSIONS

In this article, we have presented the case of monozygotic twins with bilateral OCD lesions in their knees. We are not aware of any similar cases reported in the literature. Our twins had identical genetic compositions and, therefore, similar hormonal environments. However, it is unlikely that their environments, in terms of knee trauma, have been identical.

There is reasonable evidence from our case report and review of the literature that genetic factors affect the likelihood of developing OCD. Attempts to identify these genetic factors might reveal significant information regarding the structural integrity and pathophysiology of cartilage disease.

AUTHORS' DISCLOSURE STATEMENT

The authors report no actual or potential conflict of interest in relation to this article.

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