Risk of Osteochondritis Dissecans (OCD) Lesions in Family Members of Patients with OCD: A Pedigree Analysis

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Introduction

The exact etiology of osteochondritis dissecans (OCD) lesions remains undetermined, although repetitive microtrauma, ischemia, and genetics have all been proposed as likely contributors.[1,2] Overall, the incidence of OCD in the general population is 1.2%, although this number appears to be higher in family members of those with OCD. Across the literature there have also been several case reports suggesting familial inheritance of OCD.[2-7] In those reports with sufficient pedigree analysis, an autosomal dominant pattern has been suggested.[8-11] However, as the families in these reports were all selected due to their unique histories that included a significant number of family members with OCD lesions, this may not accurately represent OCD inheritance patterns at large.

Anecdotally, we have observed that immediate relatives of patients with severe OCD lesions, which we defined as either bilateral lesions or those requiring multiple revision surgeries, were more likely to report a family history of OCD. Therefore, the primary objective of this study was to assess the incidence of OCD amongst family members of treated patients. Additionally, we sought to further subcategorize inheritance based upon the type/severity of lesion. Overall, we aimed to describe a broader, more representative pattern of OCD inheritance applicable to all affected patients.

Methods

Institutional Review Board approval was obtained prior to this prospective cohort study with a retrospective chart review component. The Children's Hospital of Philadelphia (CHOP) patient databases, billing lists and surgical logs were queried in order to identify patients treated by the senior author between March 1st, 2004 and March 1st, 2014. Inclusion criteria included all patients aged 0 to 18 years at the time of initial visit and having a diagnosis of OCD. A questionnaire was designed that asked for the number, age, and gender of all immediate family members and the history of OCD lesions in any family member (immediate or extended). For all positive responses, patients were further queried regarding the age at diagnosis and relevant treatment details (e.g. surgical vs. non-surgical treatment, unilateral vs. bilateral lesions). All identified patients were contacted via mailed questionnaires with simultaneous phone calls in a retrograde consecutive fashion. Enrollment proceeded until approximately 100 total questionnaires had been completed. Retrospective chart review was further conducted for all enrolled patients. Patients were stratified into four categories of disease severity: successful conservative treatment, unilateral lesions requiring surgery, bilateral lesions (treated both conservatively and surgically), and those patients requiring multiple procedures for the same lesion. To facilitate uniform comparison, only OCD lesions of the knee were considered, although patient reports of family members with lesions in other locations were included. Differences between the study groups were assessed using Chi-square tests (categorical variables) or *t*-tests/ANOVA (continuous variables). An alpha level of 0.05 was used for all tests.

Results

486 total patients were identified in the initial search. After all questionnaires were returned, 103 patients were included: 20 who were successfully treated conservatively and required no surgical intervention, 50 with unilateral lesions, 21 with bilateral lesions, and 12 who required multiple surgical procedures. There were no significant differences among the treatment groups in terms of baseline demographics. These included gender, lesion laterality, lesion location, number of secondary procedures at the time of the first surgical intervention, or average number of immediate family members (Table 1). Although of unclear clinical significance, patients in the unilateral group were marginally older. Additionally, there were no differences in these baseline characteristics when stratifying patients by family history status (data not shown).

In all, 14 patients (14%) were identified as having an immediate or extended family member with a history of OCD (Table 2). There was not a higher proportion of positive family history in any of the subgroups ($p = 0.619$). Only one patient had a family history notable for more than two successive generations positive for OCD, and no patients noted more than two other combined immediate and extended family members with a history of OCD. The cohort

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Table 1: Baseline Demographics in OCD Patients by Treatment Type

	Conservative+	Unilateral+	Bilateral+	Repeat+	p-value *
Number of Patients (%)	20 (19)	50 (49)	21 (20)	12 (12)	
Gender					
Male (%)	15 (75)	37 (74)	19 (90)	6 (50)	0.641
Female (%)	5 (25)	13 (26)	2 (10)	6 (50)	0.173
Laterality					
Left	11 (55)	26 (52)	n/a	6 (50)	0.980
Right	9 (45)	24 (48)	n/a	6 (50)	0.978
Age, average years (±SD)	12.45 (± 2.33)	14.16 (± 2.06)	12.04 (± 1.66)	13.60 (± 1.72)	0.000
Lesion Location					
Medial femoral condyle (%)	14 (70)	26 (52)	17 (81)	7 (58)	0.522
Lateral femoral condyle (%)	5 (25)	11 (22)	4 (19)	2 (17)	0.958
Trochlea (%)	0	9 (18)	0	2 (17)	0.063
Patella (%)	1 (5)	3 (6)	0	1 (8)	0.693
Unspecified (%)	0	1 (2)	0	0	0.787
Number having secondary procedure❖ (e.g. loose body removal, lat. meniscus repair, etc)	n/a	18 (36)	3 (14)	8 (67)	0.049
Number of immediate family members, average # per patient (± SD)	3.75 (± 1.07)	3.94 (± 1.20)	3.90 (± 0.94)	3.67 (± 1.23)	0.845

n/a = not applicable; SD = standard deviation; ❖ = at time of first procedure

+ Groups correspond to successful conservative treatment, unilateral lesions requiring surgery, bilateral lesions (treated both conservatively and surgically), and those patients requiring multiple procedures for the same lesion.

* p values correspond to inter-group differences calculated via two-tailed Chi-square analyzes (categorical data) based upon the expectation of equal proportions between the groups or by ANOVA (continuous variables)

Table 2: Patients with positive family history for Osteochondritis Dissecans

	Conservative	Unilateral	Bilateral	Repeat	Total	* p-value
Number of Patients (%)	20 (19)	50 (49)	21 (20)	12 (12)	103	
Number with immediate family history (%)	4 (20)	1 (2)	2 (10)	0	7 (7)	
Number with extended family history (%)	0	3 (6)	2 (10)	1 (8)	6 (6)	
Number with immediate & extended family history (%)	0	1 (2)	0	0	1 (1)	
Total:	4 (20)	5 (10)	4 (19)	1 (8)	14 (14)	0.619

Note: Siblings were tabulated as individual patients.

p values correspond to inter-group differences calculated via two-tailed Chi-square analyzes based upon the expectation of equal proportions between the groups

Groups correspond to successful conservative treatment, unilateral lesions requiring surgery, bilateral lesions (treated both conservatively and surgically), and those patients requiring multiple procedures for the same lesion.

included two sets of siblings: one set of monozygotic twins and one brother and sister.

Discussion

Our report is the first to describe inheritance patterns across a broad, heterogenous population of OCD patients. Overall, our results did not support anecdotal evidence that patients with increased phenotypic disease severity are more likely to have a positive family history for disease.

In describing the potential influence of genetics on OCD, Gans et al identified 34 studies across the literature of suggesting a genetic component,[13] including one from our institution describing two sets of monozygotic twins with identical knee lesions (one of which is included above).[3] Multiple reports have also identified potential genetic defects responsible for OCD, with a recent genome wide linkage study by Statin and colleagues identifying a likely candidate gene.[14-16] Furthermore, our 14% rate of positive family history is much greater than the estimated 1.2% incidence rate of OCD in the general population based upon knee arthroscopy,[1] and consistent with the reported rate of 14.6% radiographically affected male relatives amongst men with OCD.[12] All together, these studies suggest a genetic component to OCD, if at least for a subset of affected patients.

Our study has a number of limitations. The data was collected from a single, large urban institution. The chosen methodology using phone and mail surveys is vulnerable to a number of biases, including selection, recall, interviewer and response bias. Further, given the uncommon nature of an OCD diagnosis, not all patients are aware of the exact diagnosis of a given family member. Finally, our sample size may not have been large enough to adequately detect differences between the subsets.

Conclusion

Overall, 14% of treated patients had an immediate or extended family member with a history of OCD. Patients with a more phenotypically severe disease course were not more likely to have a positive family history than those with milder presentations. A large, multi-center and multi-national study may is likely required to adequately delineate differential inheritance patterns in OCD patients.

Disclosures

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