의학석사 학위논문

Osteofibrous Dysplasia of the Tibia

경골의 골섬유성 이형성증

2017년 2월

서울대학교 대학원

의학과 정형외과학 전공

박 종 웅

Abstract

Introduction:

Osteofibrous dysplasia (OFD) is a benign fibro-osseous lesion that occurs in childhood. OFD almost exclusively affects the tibia with or without fibular involvement. Studies to date have shown that the natural history of this tumor is unclear due to its rarity. Several authors have reported that both curettage and localized subperiosteal excision carry the risk of recurrence. However, few published series have provided detailed rationale for when and how surgical intervention must be chosen. Furthermore, pathologic fracture, one of the important factors that troubles patients and leads surgeons to consider surgical intervention, has not been described in previous studies. Our study of a large patient group reports on the behavior and postoperative recurrence of OFD.

Materials and Methods:

We reviewed the medical records of 55 patients who were diagnosed with OFD of the tibia and showed typical features of this tumor. The patients' presentation, disease course, history of pathologic fracture, typical radiographic features, surgical treatment history, and surgical results were investigated.

Results:

The longitudinal OFD lesion size peaks at a mean 13.3 years of age with a mean maximum proportionate size of 0.33. These lesions in 92% of the patients spontaneously presented with a stable disease course, while those in the other 8% continued increasing. There were no significant predictive factors of disease course. Among surgically treated lesions, we noted a higher rate of recurrence after curettage than after excision ($p < 0.001$). Patients who underwent curettage and suffered recurrence were significantly younger than those who did not ($p = 0.01$).

Conclusions:

Our data suggest that observation can be the primary form of treatment for patients with OFD and that the disease would stop advancing with time. If surgery is necessary due to severe morbidity, we recommend wide resection rather than curettage to prevent recurrence, especially for younger patients.

Keywords: Tibia, Osteofibrous dysplasia, Natural course, Recurrence, Pathologic fracture

Student number: 2015-21992

Contents

List of Tables

List of Figures

Introduction

Osteofibrous dysplasia (OFD) is a rare benign fibro-osseous lesion occurring in childhood that almost exclusively affects the tibia with or without fibular involvement. In 1921, Frangenheim reported the first case of OFD, although he termed the condition "congenital osteitis fibrosa" [1]. In 1976, Campanacci named the lesion "osteofibrous dysplasia of the tibia and fibula" in reference to its anatomic location, developmental origin, and histologic resemblance to the fibrous dysplasia [2].

Due to the rarity of OFD, it involves many uncertainties. To clearly define the OFD disease entity and choose its optimal treatment, we must elucidate its typical behavior as well as observation and surgical results. The OFD lesion is primarily detected in the first decade of life and stops expanding after skeletal growth ceases [3-5]. However, the behavioral characteristics of OFD are unclear. Among surgical options, both curettage and localized subperiosteal excision carry the risk of recurrence [3, 6-10], while radical excision and reconstruction may create additional morbidity such as pseudarthrosis [9]. Furthermore, pathologic fracture troubles patients and leads surgeons to consider surgical intervention but has not been described in the literature.

Here we aimed to suggest optimal treatment guidelines for OFD. For this purpose, we describe the natural behavior of OFD, analyze the treatment option results, and investigate postoperative recurrence using long-term observations of a large number of patients with OFD.

Materials and Methods

In our hospital's database, the records of 91 patients who were diagnosed with OFD between January 2000 and December 2015 at our institute were reviewed. Our institute's institutional review board approved this study. As there were no treatments or procedures, informed consent for this research project was waived. For analytic purposes, 10 patients with unusual tumor sites (five of the humerus, four of the femur, and one of the radius and ulna) were excluded, while all of the enrolled patients had lesions on the tibia with or without fibular involvement. Of the remaining 81 patients, those who were observed for <18 months (n = 16), had an uncertain diagnosis of OFD (n = 6), or had insufficient radiographs (n = 4) were also excluded. These exclusions left 55 patients for analysis. The diagnosis of OFD was based on radiography results in 31 (56.4%) cases and histological confirmation in 24 (43.6%) cases. The radiographic features were so characteristic that the diagnosis can often be made with confidence from the radiographs alone before or without histological confirmation [3].

Information extracted from the medical records included age at the initial presentation, history of presentation, disease course, history of surgical treatment, treatment results, history of pathologic fracture, proportionate size of the lesion at the maximum longitudinal length as well as radiographic factors

including anterior cortex pattern, anterior angulation, posterior cortex involvement, and lesion location in the involved bone.

Regarding disease course, we investigated the change in longitudinal lesion size and shape over time. We classified disease course into stable or increasing groups while considering the time to the last visit for patients given conservative treatment or surgical timing for patients given surgical treatment. When the proportionate lesion size did not increase > 1% and the shape did not change grossly on plain films, the disease course was identified as stable. The lesions showing spontaneous regression classified into the stable group. Otherwise, the lesions increasing >1% or forming new osteolytic focus were identified as increasing. For patients with a history of surgical treatment and recurrence, definite surgeries for curative purpose were analyzed and surgeries for incisional biopsy were excluded. For patients with a history of pathologic fracture, we recorded the definite fractures that caused morbidity and excluded the healed microfractures that were incidentally identified.

All radiographic features were obtained from plain radiographs, primarily lateral images. To measure lesion length, we simultaneously measured total lesion length and entire tibia length. We then calculated the proportionate size as the lesion length divided by whole tibia length. Furthermore, we investigated the affected anterior cortex patterns according to involvement shape. In previous

studies, eccentric intracortical osteolysis was one common radiographic feature [3, 11-13]. We defined expansion of the external surface of the cortex as cortical expansion. Cases in which the external surface of the cortex was intact and the osteolytic lesion expanded only intramedullary were identified as intramedullary expansion. In the lesions with an intramedullary expansion pattern, the remaining thickness of the anterior cortex was preserved compared with the cortical expansion pattern (Fig. 1). We evaluated the anterior angulation by comparing it with the contralateral normal bony alignment. Every case in this study showed anterior cortex involvement; therefore, posterior cortex involvement indicated bicortical involvement of the tibia.

Continuous variables were compared using the independent samples t-test, while categorical variables were compared using Pearson's chi-squared test. The statistical analysis was performed using SPSS v.21.0 software (SPSS Statistics for Windows Version 21.0; IBM, Armonk, NY, USA). Null hypotheses without differences were rejected if p values were <0.05.

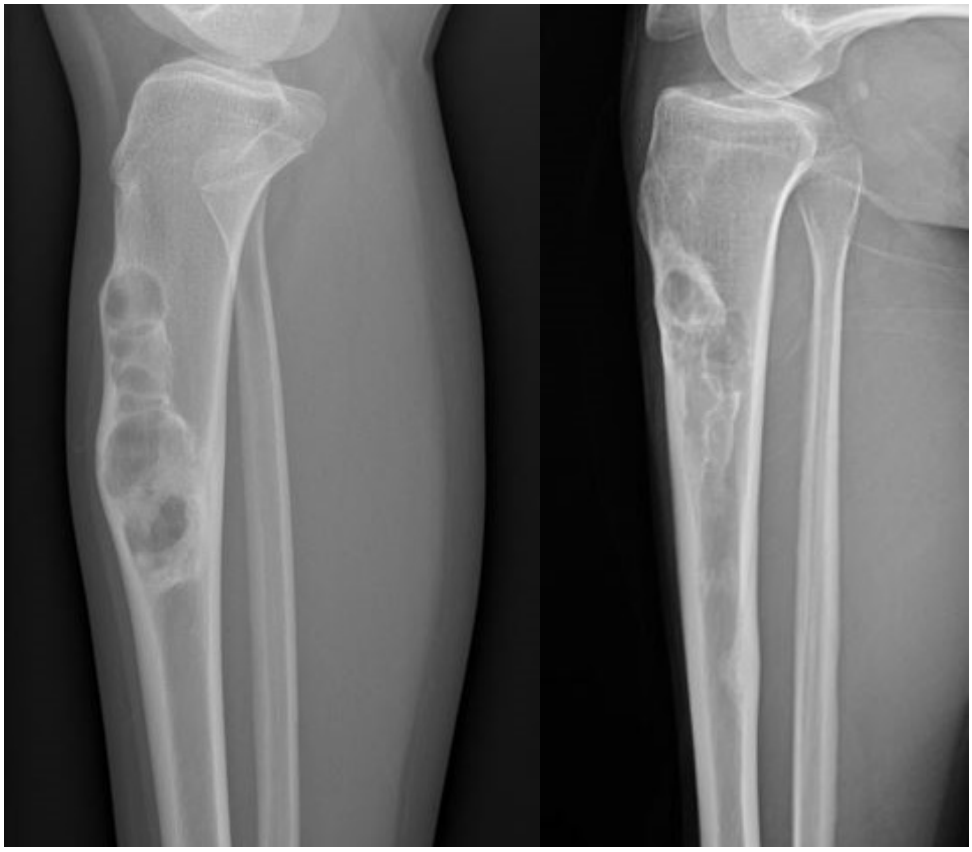

Fig. 1. Plain radiographs of the tibia with cortical expansion (left) and intramedullary expansion (right)

Results

1. Clinical characteristics of OFD

There were 26 (47%) males and 29 (53%) females. The mean age at the initial presentation was 8.7 years (range, 1.7–27.8 years) and the patients were followed-up for a mean 91.4 months (range, 18–233 months). Of the 55 patients, the lesions of 48 (87%) involved the tibia, while those of the other seven (13%) involved the tibia and fibula. The mean maximum proportionate size was 0.33. Six (10%) patients experienced recurrent pathologic fractures, 13 (24%) experienced a pathologic fracture once, and 36 (66%) never experienced a pathologic fracture. The lesion was most commonly an incidental finding (n = 18; 33%), but some patients complained of a palpable bony mass (n = 15; 27%), pain (n = 12; 22%), pathologic fracture (n = 4; 7%), or deformity of the anterior angulation (n = 2; 4%). The OFD lesions were longest at a mean patient age of 13.3 years. The maximal longitudinal proportionate size was 0.33 (range, 0.04–0.64) of the affected bone (Table 1).

Regarding radiographic characteristics, 42 patients (76%) had cortical expansion and 13 patients (24%) had intramedullary expansion into the anterior cortex. Of the 55 cases, 20 (36%) showed anterior angulation and 35 (64%) did not. In 29 (53%) cases, the lesion involved the posterior cortex; in the other 26

(47%) cases, the lesion involved the anterior cortex only. Analysis of the tumor location revealed that 39 (71%) patients were affected at the diaphysis only and 16 (19%) patients had metaphyseal involvement (Table 1).

Table 1. Patient characteristics

Characteristics	
Age at initial presentaion (yrs, SD)*	8.7 (5.0)
Follow up (mos, range)*	91.4 (18 - 233)
Sex (n,%)	
Male	26 (47%)
Female	29 (53%)
Site	
Tibia only	48 (87%)
Tibia and fibula	7 (13%)
Initial presentation (n,%)	
Incidental finding	18 (33%)
Palpable bony mass	15 (27%)
Pain	12 (22%)
Pathologic fracture	4 (7%)
Deformity (anterior angulation)	2 (4%)
Unclear	4 (7%)
Disease course (n,%)	
Stabilized	36 (92%)
Continuously increased	3 (8%)
Increasing during growing period	16 (-)
Maximal proportionate size (mean, SD)*	0.33 (0.16)
Age at the peak (yrs, SD)*	13.3 (5.2)
Anterior cortex pattern (n,%)	
Cortical expansion	42 (76%)
Intramedullary expansion	13 (24%)
Anterior angulation (n,%)	
Yes	20 (36%)
No	35 (64%)
Posterior cortex involvement (n,%)	
Yes	29 (53%)
No	26 (47%)

Location in the bone (n,%)	
Diaphysis only	39 (71%)
Metaphysis involved	16 (29%)
Pathologic fracture (n,%)	
Recurrent	6 (10%)
Once	13 (24%)
Never	36 (66%)
Operation (n,%)	
Done	20 (36%)
Not done	35 (64%)

* Numbers represent mean values.

SD, standard deviation

2. Presentation and disease course

Of the 55 patients, 35 (74%) were observed without surgery and 20 (36%) underwent surgery. Of the 35 patients observed without surgery, 24 had stable lesions and 11 had increasing lesions. Among the 11 increasing lesions, 10 increased during the growing period and one continued to increase after skeletal maturity. Of the 20 patients who underwent surgical treatment, 11 did so before skeletal maturity and nine did so after skeletal maturity. Among the 11 patients who underwent surgery before skeletal maturity, five had stable lesions and six had increasing lesions at the time of surgery. Among the nine patients who underwent surgery after skeletal maturity, seven showed stable lesions and two had continuously increasing lesions.

Overall, the disease course of OFD was revealed in 39 of 55 patients who were observed after skeletal maturity without surgery. Among the 39 patients, 36 (92%) had a stable course and three (8%) had a continuous increasing course. Among the 36 stable lesions, eight showed spontaneous regression (Table 1, Fig. 2). Among the 36 stable lesions, 31 were stable during the growing period and the other five were stable after skeletal maturity. There were no significant predictive factors of disease courses with respect to age at initial presentation, lesion size at initial presentation, maximal lesion size, number of affected bones, any radiographic features, or history of pathologic fracture.

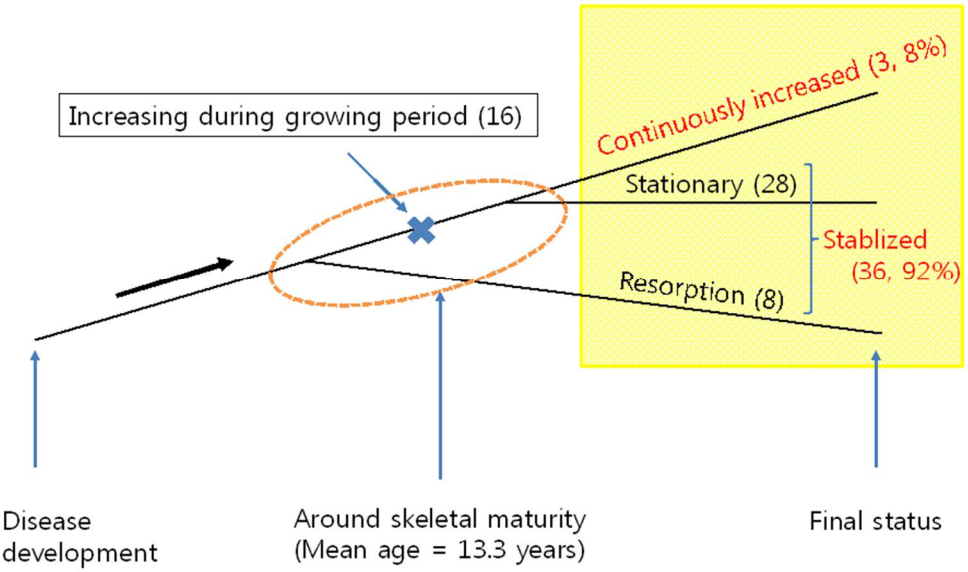

Fig. 2. Schematic diagram of osteofibrous dysplasia disease course. Of the 55 patients, 36 (92%) had stable lesions and 19 had increasing lesions. Among the 36 stable lesions, 28 were stationary and eight had spontaneously regressed. Among the 19 increasing lesions, 16 increased during the growing period and three (8%) increased after the physes had closed.

3. Surgical treatment and recurrence

Of the 55 patients, 20 (36%) underwent surgery. Among them, three underwent surgery twice, so the total number of operations was 23. Indications for surgical treatment were pain (n = 7; 30%), recurrent fracture (n = 4; 17%), deformity (n = 3; 13%), increasing size after skeletal maturity (n = 2; 9%), and large lesion size before skeletal maturity (n = 2; 9%). Another five patients underwent curettage at other hospitals for unknown reasons before visiting our clinic. Among the 23 operations, 12 (52%) were curettage and 11 (48%) were excision and reconstruction. The mean peak longitudinal proportionate size for patients who underwent surgery was 0.38. Four (18%) of the surgical patients experienced recurrent pathologic fractures, six (30%) experienced a pathologic fracture once, and 10 (52%) never had a pathologic fracture (Table 2).

Of the patients treated surgically, eight had recurrent (35%) and 15 had non-recurrent (65%) lesions. Of the 23 operations, all cases of recurrence developed after curettage. The difference in recurrence rate between the two surgery types was statistically significant ($p < 0.001$). In the curettage operation, young age at the time of surgery was significantly associated with postoperative recurrence ($p = 0.04$). The mean age at the time of curettage was 8.0 years with recurrence and 17.8 years without recurrence (Table 3).

Table 2. Patient characteristics for Operation

Characteristics	
Age at operation (yrs) (mean ± SD)	13.8 ± 7.4
Indication of operation (n,%)	
Pain	7 (30%)
Recurrent fracture	4 (17%)
Deformity	3 (13%)
Increasing size after skeletal maturity	2 (9%)
Large size of lesion before skeletal maturity	2 (9%)
Unknown	5 (22%)
Operation type	
Curettage	12 (52%)
Wide resection	11 (48%)
Recurrence (n,%)	
Yes	8 (35%)
No	15 (65%)
Maximal proportionate size (mean ± SD)*	0.38 ± 0.16
Pathologic fracture (n,%)	
Recurrent	4 (18%)
Once	6 (30%)
No	10 (52%)

* Numbers represent mean values.

SD, standard deviation

Table 3. Recurrence of Osteofibrous Dysplasia after Operation

Characteristics	Recurrence	No recurrence	P value
Operation type			0.01*
Curettage	8	3	
Wide resection	0		
Age at curettage (yrs ± SD)	8.0 ± 6.2	17.8 ± 4.5	0.04*

*means statistical significant.

Discussion

OFD is a rare benign bone lesion that occurs in childhood. The most common site of the lesion is the tibial diaphysis, while eccentric intracortical osteolysis with cortical expansion is the typical radiographic feature. OFD usually takes a benign course for which a conservative approach has been recommended [3, 7-9, 14]. The main differential diagnoses are fibrous dysplasia and adamantinoma of the long bone [3]. The distinction between fibrous dysplasia and OFD involves patient age, lesion location, radiographic appearance, and clinical course [2, 3, 11]. Adamantinoma is a rare low-grade malignancy that occurs primarily in the tibia of adolescents and young adults. There is also a histologically intermediate lesion between OFD and adamantinoma called "differentiated adamantinoma" or "OFD-like adamantinoma" [4, 12, 15, 16]. However, there is no consensus on the histologic criteria to distinguish among OFD, OFD-like adamantinoma, and classic adamantinoma [15]. Patient age is one distinguishing factor; OFD occurs mainly in the younger age group compared with adamantinoma, although there is no clear consensus on patient age. No imaging characteristic is pathognomonic of either lesion; in contrast, a significant overlap in the histopathologic features of OFD and adamantinoma has long been noted [15]. Many authors suggest that OFD and adamantinoma are related lesions that

should be considered a continuous spectrum [4, 15, 16].

In the conservative treatment setting, OFD lesions that keep growing after skeletal maturity can be confused with a malignancy such as adamantinoma. In this study, eight patients had growing lesions after skeletal maturity. Of the eight patients, the lesions of five finally stabilized a few years after skeletal maturity, while those of the other three showed a continuously increasing course. Comparison of the eight patients whose lesions continued growing after skeletal maturity with the others (n = 31) revealed that the incidental findings at initial presentation were associated with the growth tendency after skeletal maturity ($p = 0.04$). In the current study, all patients with incidental findings at initial presentation had a stable disease course prior to skeletal maturity. The age at initial presentation, longitudinal lesion size, history of pathologic fracture, and radiographic findings were not associated with disease progression after skeletal maturity. Clinicians should more carefully observe patients with symptomatic OFD at the initial presentation.

Surgical indications included persistent pain, recurrent fractures, deformity, and need for diagnostic confirmation of the diagnosis of OFD because of continuously increasing tumor size after skeletal maturity. The surgical results were acceptable in terms of morbidity resolution and recurrence rate. In patients with significant morbidity, such as pain on physiological loading, recurrent

pathologic fractures, or deformity, surgery is a feasible option to achieve a physically active life despite the patients still being in the growing period.

Our data suggest that curettage was associated significantly with recurrence, particularly in younger patients. Therefore, wide excision seems to be a more appropriate surgical option for OFD and curettage can be considered for adults who need surgical treatment. The reason why the recurrence rate decreases after curettage in older patients is unknown. However, this finding is compatible with behavior of other benign bone tumors such as fibrous dysplasia, non-ossifying fibroma, and simple bone cyst. These benign bone tumors are less aggressive after the growing period [17-19].

The typical radiographic features of OFD analyzed in this study were not associated with disease course but were associated with pathologic fractures. Pathologic fracture causes marked morbidity in patients with OFD, which leads surgeons to consider surgical intervention. The occurrence of pathologic fractures was significantly associated with anterior bowing ($p = 0.03$) and bicortical involvement ($p = 0.02$) (Table 4). There are two possible explanations for this finding. First, when the tibia has an anterior bowing deformity, the apex of the anterior bowing is the point of the stress concentration, while the lesion is usually located in the apex of the anterior bowing. Second, all lesions in this study involved the anterior cortex of the long bone, while the posterior cortex

works as a support beam offering resistance against the fracture. Therefore, bicortical involvement results in a weak support beam to resist fracture.

In summary, our data suggested that observation can be a primary form of treatment for patients with OFD in whom the disease progression is expected to cease over time. If surgery becomes necessary because of significant morbidity, we recommend excision rather than curettage, especially in younger patients, to prevent recurrence.

Table 4. Comparison between patients with and without Pathologic fracture

Characteristics	Pathologic fracture (n=20)	No fracture (n=35)	P value
Maximal proportionate size	0.38	0.31	0.13
Anterior cortex pattern (n,%)			0.47
Expended	15 (40%)	23 (60%)	
Others	5 (29%)	12 (71%)	
Anterior angulation (n,%)			0.03*
Yes	9 (26%)	26 (74%)	
No	11 (55%)	9 (45%)	
Posterior cortex involvement (n,%)			0.01*
Yes	5 (19%)	21 (81%)	
No	15 (52%)	14 (48%)	
Location in the bone (n,%)			0.08
Diaphysis only	17 (44%)	22 (56%)	
Metaphysis involved	3 (19%)	13 (81%)	

*means statistical significant.

References

1. P F. Angeborene Ostitis fibrosa als Ursache einer intrauterinen Unterschenkelfraktur. Arch Kinder Chir. 1921;117:22-9.

2. Campanacci M. Osteofibrous dysplasia of long bones a new clinical entity. Ital J Orthop Traumatol. 1976 Aug;2(2):221-37.

3. Campanacci M, Laus M. Osteofibrous dysplasia of the tibia and fibula. J Bone Joint Surg Am. 1981 Mar;63(3):367-75.

4. Most MJ, Sim FH, Inwards CY. Osteofibrous dysplasia and adamantinoma. J Am Acad Orthop Surg. 2010 Jun;18(6):358-66.

5. WHO classification of tumours of soft tissue and bone / edited by Christopher D.M. Fletcher ... [et al.]. 4th ed.. ed. Fletcher CDM, World Health O, International Agency for Research on C, editors. Lyon: Lyon : IARC Press, 2013.; 2013.

6. Campbell CJ, Hawk T. A variant of fibrous dysplasia (osteofibrous dysplasia). J Bone Joint Surg Am. 1982 Feb;64(2):231-6.

7. Komiya S, Inoue A. Aggressive bone tumorous lesion in infancy: osteofibrous dysplasia of the tibia and fibula. J Pediatr Orthop. 1993 Sep-Oct;13(5):577-81.

8. Ozaki T, Hamada M, Sugihara S, Kunisada T, Mitani S, Inoue H. Treatment outcome of osteofibrous dysplasia. J Pediatr Orthop B. 1998 Jul;7(3):199-202.

9. Wang JW, Shih CH, Chen WJ. Osteofibrous dysplasia (ossifying fibroma of long bones). A report of four cases and review of the literature. Clin Orthop Relat Res. 1992 May(278):235-43.

10. Lee RS, Weitzel S, Eastwood DM, Monsell F, Pringle J, Cannon SR, et al. Osteofibrous dysplasia of the tibia. Is there a need for a radical surgical approach? J Bone Joint Surg Br. 2006 May;88(5):658-64.

11. Park YK, Unni KK, McLeod RA, Pritchard DJ. Osteofibrous dysplasia: clinicopathologic study of 80 cases. Hum Pathol. 1993 Dec;24(12):1339-47.

12. Papagelopoulos PJ, Mavrogenis AF, Galanis EC, Savvidou OD, Inwards CY, Sim FH. Clinicopathological features, diagnosis, and treatment of adamantinoma of the long bones. Orthopedics. 2007 Mar;30(3):211-5; quiz 6-7.

13. Blackwell JB, McCarthy SW, Xipell JM, Vernon-Roberts B, Duhig RE. Osteofibrous dysplasia of the tibia and fibula. Pathology. 1988 Jul;20(3):227-33.

14. Van Delm I, Fabry G. Osteofibrous dysplasia of the tibia: case report and review of the literature. J Pediatr Orthop B. 1999 Jan;8(1):50-3.

15. Gleason BC, Liegl-Atzwanger B, Kozakewich HP, Connolly S, Gebhardt MC, Fletcher JA, et al. Osteofibrous dysplasia and adamantinoma in children and adolescents: a clinicopathologic reappraisal. Am J Surg Pathol. 2008 Mar;32(3):363-76.

16. Kahn LB. Adamantinoma, osteofibrous dysplasia and differentiated adamantinoma. Skeletal Radiol. 2003 May;32(5):245-58.

17. Seligson D. CORR Insights (R): Does fracture affect the healing time or frequency of recurrence in a simple bone cyst of the proximal femur? Clin Orthop Relat Res. 2014 Oct;472(10):3177-8.

18. DiCaprio MR, Enneking WF. Fibrous dysplasia. Pathophysiology, evaluation, and treatment. J Bone Joint Surg Am. 2005 Aug;87(8):1848-64.

19. Arata MA, Peterson HA, Dahlin DC. Pathological fractures through non-ossifying fibromas. Review of the Mayo Clinic experience. J Bone Joint Surg Am. 1981 Jul;63(6):980-8. Epub 1981/07/01.

국문초록

배경: 골섬유성 이형성증은 양성의 섬유성 골화를 특징으로 하는 골종양으로, 소아기에 발병한다. 주로 경골을 침범하는 것으로 알려져 있으며 비골을 동시에 이환하기도 한다. 이 질환은 희귀질환이며, 그 희귀성에 기인하여 질병의 자연 경과에 대해 잘 알려진 바가 없다. 현재까지 알려진 것은 소파술이나 골막하 절제술을 시행한 경우에 재발의 위험성이 있다는 정도에 그치고 있다. 그러나 적절한 치료 방침에 대해 충분한 환자군을 분석하여 근거를 제시한 논문은 없으며, 이 질환과 관련하여 발생할 수 있는 병적 골절에 대해서는 기술된 바가 없다. 본 연구에서는 OFD 의 자연경과를 분석하고, 적절한 치료 방법과 그 결과에 대하여 알아보고자 하였다.

방법: 본 연구에서는 55명의 전형적인 골섬유성 이형성증 환자를 분석하였다. 환자의 증상, 병의 경과, 병적골절의 유무, 단순촬영 영상에서 관찰할 수 있는 특이적인 병의 형태, 시행했던 수술의 종류와 결과, 재발 여부 등에 대해 총체적인 정보를 수집하였다.

결과: 이번 연구에 따르면 병변의 종적 크기는 이환된 골의 전체 길이에 대하여 평균적으로 33% 크기까지 커지는 것으로 나타났으며, 평균나이 13.3세에 병의 경과가 안정화 되는 것으로 나타났다. 환자의 92%에서는 병변의 크기가 저절로 안정화 되는 추세를 보였고, 지속적으로 병변이 진행했던 환자는 전체 환자의 8%에 불과하였다. 그러나 병변의 크기가 지속적으로 증가하는 것을 예측할 수 있는 인자는 없었다.

55명의 환자 중 반복적인 병적 골절, 또는 지속적인 통증을 호소하는 20명에 대하여 수술을 시행하였고, 소파술을 시행한 경우 유의하게 재발이 흔하였다 ($p<0.001$). 소파술을 시행한 환자의 경우, 소파술을 시행한 나이에 따라 결과가 통계적으로 유의한 차이를 보였는데, 더 어린 나이에 소파술을 시행한 환자에서 더욱 흔하게 재발하는 경향이 있었다 ($p=0.01$).

결론: 골섬유성 이형성증은 대부분의 경우 골의 성숙이 진행됨에 따라 저절로 병의 경과가 안정화되는 추세를 보였다. 따라서 환자에서 첫 치료로 보존적인 치료를 시행하는 것은 병의 자연 경과를 고려할 때 적절한 치료라고 사료된다. 그러나 병적골절, 통증 등으로 치료가 필요한 경우에는 성장 중인 환자에도 수술을 시행할 수 있으며 절제술이 소파술보다 적절한 것으로 보인다.

주요어: 경골, 골섬유성 이형성증, 자연경과, 재발, 병적 골절

학 번: 2015-21992