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Nora's disease: a series of six cases

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ABSTRACT

Objectives. Nora's disease is a mesenchymal bone tumor with controversial diagnosis and treatment due to the benign but locally aggressive course and high recurrence rates. *Methods.* A retrospective analysis was made of patients diagnosed with Nora's Disease at Ankara University Orthopedics and Traumatology Clinic. The evaluation was made of the age of the patient, gender, symptoms, lesion location, trauma history, treatment choice and recurrence rates during follow-up. *Results.* Excision was applied to 6 patients diagnosed with Nora's disease, and in 1 patient an additional autograft and internal fixation were required. Recurrence was observed in 3 patients, 2 of whom underwent revision surgery and one who did not as there no patient complaints. *Conclusions.* Nora's disease is problematic for orthopedic surgeons as there are difficulties in diagnosis, there is no absolute treatment algorithm, recurrence potential is high, and there are limited additional treatment choices. Therefore, treatment and follow-up at clinical center's dealing with orthopedic tumor surgery can be considered appropriate.

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Keywords: Nora's disease; excision; recurrence

Introduction

Nora's disease, first described by Nora et al in 1983, is also known as bizarre parosteal osteochondromatous proliferation (BPOP) and is a mesenchymal formation with bone, fibrous tissue and cartilage components, often located in the hands, feet and long bones, which has a benign but locally aggressive course [1]. It is typically observed in the proximal and mid phalanges, the metacarpals and metatarsals. There is no gender dominance and although it can be seen at any age, it is generally observed in young patients [1, 2].

Although the radiological appearance of Nora's disease is confusing, wide-based calcified lesions not continuing with the medulla can be evidently differentiated from the bone cortex and may often be confused with osteochondroma [3, 4]. Histologically, without seeming atypical cellular, they are formed

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from a bone, cartilage and fibrous stroma. The cartilage caps are hyper-cellular and contain large double nucleus chondrocytes. Osteoblastic activity is high in the bone structure and suggests reactive activity.

Due to rapid growth, and radiological and histological difficulties in diagnosis, periosteum rooted malignant and benign lesions can be confused in the differential diagnosis. Absolute diagnosis cannot be made radiologically and clinically and sometimes because of the aggressive course histological confirmation is necessary.

In this paper, we wanted to present our clinical experience related to Nora's disease and review the literature with the challenges for orthopedists due to difficulties in diagnosis and treatment.

Methods

A retrospective analysis was made of 6 patients diagnosed histologically with Nora's Disease between 1990 and 2014 at Ankara University, Orthopedics and Traumatology Clinic Oncology Department. Patients were evaluated by age, gender, symptoms, lesion location, trauma history, treatment and recurrence (Table 1).

Results

The patients comprised 4 females and 2 males with a mean age of 39 years (range, 17- 62 years). The lesions were localized in the metacarpal in 2 cases, in the metatarsal in 2 cases and in the medial distal femur in 2 cases. Physical examination revealed localized swelling in all patients and in 4 patients, the lesion was painful. Apart from 2 patients, there was no history of trauma. The mean follow-up period was 72 months (range, 36-132 months).

Using direct radiographs, CT and MRI, radiological evaluation was made of lesion location,

Table 1. Data of patients with bizarre parosteal osteochondromatous proliferation.

Age / Gender	Location	Size (cm)	Complaint	Treatment	Follow-up / Recurrence
48/F	5th Metacarpal - dorsal	2x3	Painless mass - 2 yrs No Trauma	Excision	11 yrs -No recurrence
58/F	5th Metatarsal - plantar	1x1,5	Painful mass - 1 yrs Trauma +	Excision	6 months-recurrence 5 yrs
17/M	Distal femur - medial	3x2	Painless mass - 1.5 yrs No Trauma	Excision	8 yrs-No recurrence
21/M	5th Metatarsal - lateral	2x1,5	Painful mass - 2.5 yrs No Trauma	Excision Autograft Fixation	4 yrs - No recurrence
28/F	Distal femur - medial	2x2	Painful mass - 1 yr Trauma +	Excision	1 yr -recurrence 5 yrs -No recurrence
62/F	2nd Metacarpal - proximal	1x1	Painful mass - 1 yr No Trauma	Excision	8 months - recurrence 3yrs -No recurrence

periosteal reaction, continuation with the medullar canal, calcifications and soft tissue. Histological examination was made in all cases for an absolute diagnosis.

On direct radiographs, in all lesions, calcified masses adjacent to the bone cortex were seen and damage to the cortex over which they were located. There was no continuation with the medullar canal on CT (Figure 1). On MRI slices, no abnormalities apart from edema were determined in the soft tissue. In the pathological evaluation, the lesion surface was hyper-cellular, fibrous and covered with cartilage tissue, the stroma spindle was of cartilage cells and in the inner part increased osteoblastic activity was observed in the form of bone trabeculae. Following histological confirmation of the diagnosis, the patients were treated surgically.

In 1 patient with metatarsal location, excision, autograft and fixation was applied and in all the other patients only excision was applied (Figure 2 a-d).

Recurrence was observed in a total of 3 patients. In 2 of these patients, revision surgery was applied by extending the excision and recurrence was not observed again in the follow-up. In the other patient with recurrence during follow ups (left foot, proximal 5th metatarsal), as the patient had no complaints, no operation was planned and kept on following for any complaint (Table 1).

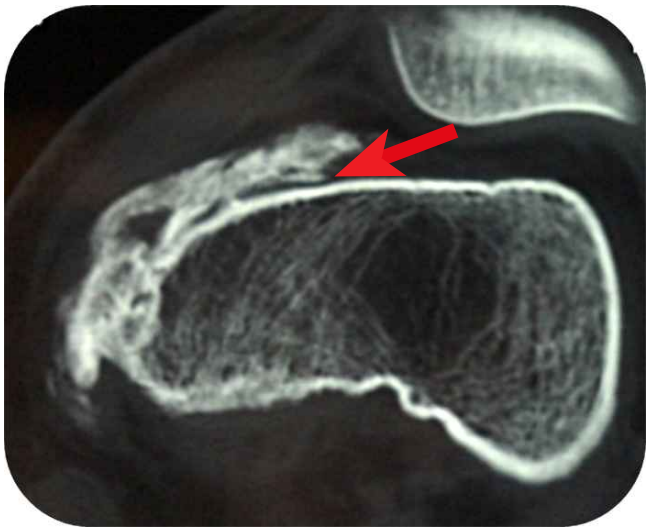

Figure 1. Axial CT image of lesion with distal femur location. There is no continuity of the lesion to the medullar canal.

Discussion

Bizarre parosteal osteochondromatous proliferation is an uncommon reactive mineralizing mesenchymal lesion that typically affects the surfaces of bones in the hands and feet, usually the proximal and middle phalanges, and the metacarpal and metatarsal bones [5]. There are two theories related to the formation of Nora's disease. The first

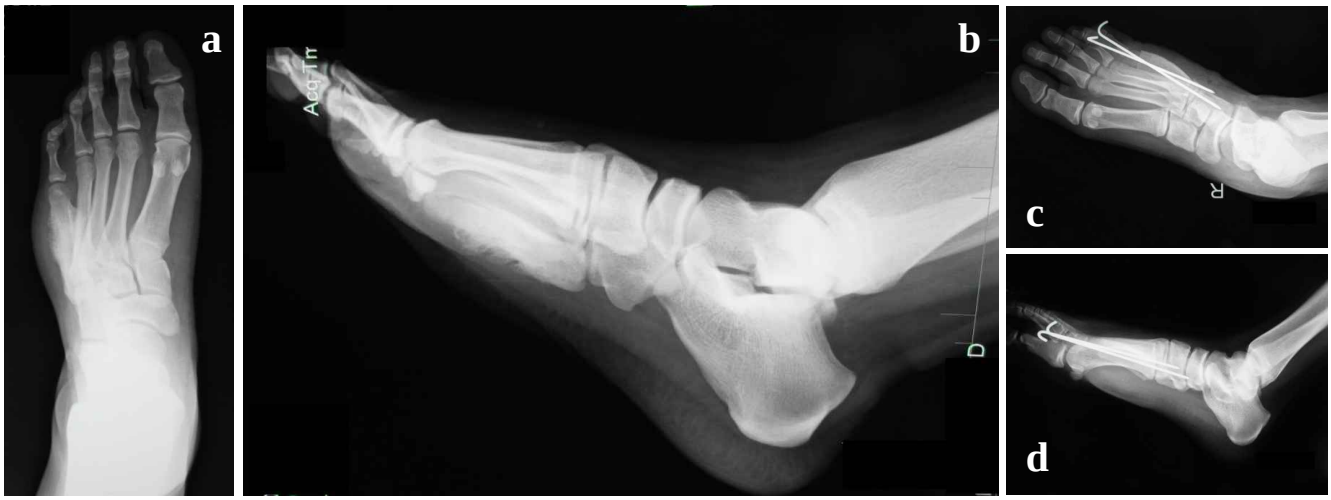

Figure 2. Radiographies of lesion with 5th metatarsal location **(a,b),** image after excision, autograft and fixation **(c,d).**

is that the lesion forms with a periosteal reaction following trauma [6]. According to the second theory, it is a tumoral process characterized by t(1:17) translocation without any trauma [7]. As there was a history of trauma in 2 of the current cases, the trauma could have been a predisposing factor, and when taking the patient history, the etiology should be kept in mind.

Although Nora's disease has a characteristic clinical and histological appearance, it may be confused with other benign and malignant lesions. The parosteal location distinguishes Nora's disease from parosteal osteosarcoma, which is rarely found in the hands and feet. The absence of cellular atypia helps to distinguish this lesion from osteosarcoma [8]. Again due to location, it can be confused with periostitis ossificans, but it often shows location in the hand and other skeletal systems are not involved.

With osteochondromatous composition, osteochondroma, myositis ossificans and subungal exocytosis may be considered in the differential diagnosis [3]. However, although osteochondroma is the most commonly seen benign bone tumor, it rarely shows involvement close to the physis in the long tubular bones, hand and foot location is rare and the lesion forms continuity with the medullar canal [9, 10]. However, in myositis ossificans cartilage caps are not seen. Anatomic locations of subungal exocytosis is typical and they do not contain classic cartilage tissue [11]. However, much heterotrophic ossification may resemble Nora's disease radiologically, there is generally a history of head trauma.

As confusion is created radiologically and clinically in the absolute diagnosis and because there is sometimes an aggressive course, there are reports recommending excision even if the patient has no complaints [12]. Thus, it is possible to make a histological diagnosis of the lesion.

According to some authors, wide excisions made to the depth of the periosteum together with the mass, reduce the frequency of recurrence. However, due to increased surgical morbidity, there are also authors who do not recommend wide excision as the first treatment option. When there is distal extremity location, wide excision may require amputation. If there is no suspicion of malignancy, marginal excision can be selected as the first stage [13, 14]. Although it is predicted that intralesionary excision increases the possibility of recurrence, the rates of recurrence in the en bloc excision with negative surgical limits used in the cases of the current series were seen to be no different to those of other series. The 50% recurrence rate was similar to the 51% rate of Nora *et al.*, thereby showing again how high the actual recurrence rate is in Nora's disease.

Before evaluating the surgical treatment choice for patients with recurrence, observational follow-up may be firstly considered, taking the patient's complaints into account.

As Nora's disease is rarely seen and the diagnosis and treatment algorithm has not been fully defined, this series of 6 cases can be considered to contribute to literature together with the 35-case series of Nora, the 65-case series of Menses *et al.*, the 24-case series of Dhondt *et al.*, and the 13-case series of Jibu *et al.* [1, 3, 15, 16].

As this study was retrospective, there was a reliance on those who had taken the patient records and as the number of patients was low, statistical analysis could not be applied.

Nora's disease is problematic for orthopedic surgeons as there are difficulties in diagnosis, there is no absolute treatment algorithm, having recurrence potential and there are limited additional treatment choices. Therefore, according to our opinion treatment and follow-up at clinical center's dealing with orthopedic tumor surgery can be considered appropriate.

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