

## Foot and Ankle Osteoid Osteomas



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### ARTICLE INFO

Level of Clinical Evidence: 4

#### Keywords:

ankle  
foot  
osteoid  
osteoma  
pain

### ABSTRACT

Foot and ankle osteoid osteomas (OOs) are often cancellous or subperiosteal and rarely present with a periosteal reaction. Additionally, the large number of disorders included in the differential diagnosis and the nonspecific findings on radiographs complicate the diagnosis. We performed a manual search of the senior surgeon's hospitals' operating room records for the terms "benign bone tumor," "foot," "ankle," and "osteoid osteoma" from January 2003 until December 2014. Of 87 surgically treated patients with lower extremity OOs, 9 patients (11%) with foot or ankle OOs were included. The mean age at presentation was 21 (range 6 to 30) years; all 9 (11%) patients were male. The patients were evaluated for swelling, pain, trauma history, night pain, response to pain relievers, duration of complaints, and interval to diagnosis. The mean follow-up period was  $48 \pm 24$  months, and no recurrences had developed. The mean American Orthopaedic Foot and Ankle Society scale score was  $59.04 \pm 11$  before surgery and  $91.56 \pm 6$  after surgery. The difference was statistically significant at  $p \leq .0003$ . Most previous studies have been limited to case reports. The need for findings from a case series was an essential determinant of our decision to report our results. Patients usually have been treated conservatively, often for a long period. However, delays in treatment cause social, economic, and psychological damage. In conclusion, the presence of atypical findings on radiographs has resulted in a preference for magnetic resonance imaging instead of computed tomography; however, the diffuse soft tissue edema observed on MRI can lead to the use of long-term immobilization and a delay in the diagnosis.

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Osteoid osteoma (OO) is a vascularized, osteogenic, benign bone tumor that was first defined by Heine in 1927 (1) and first described by Jaffe in 1935 (2). OOs constitute 10% of all benign bone tumors and 19.4% of all benign bone tumors in the foot and ankle, with a particular predilection for the talus and calcaneus (3,4). OOs can be divided into 3 types according to their location: intracortical, cancellous, and subperiosteal (5). Although long bone OOs cause an aggressive subperiosteal reaction owing to their intracortical location, foot OOs often occur in the cancellous bone or subperiosteally and might not cause a periosteal reaction (5,6). Because of these subtle radiologic findings, the complex anatomy of the ankle and foot with the wide array of disorders included in the differential diagnosis, and the rarity of OOs in this region, a delay can occur in diagnosing foot and ankle OOs. Thus, when a patient presents with foot or ankle pain that is especially longstanding, cannot be diagnosed, and is resistant to medical treatment, the presence of an OO should be considered (7). In the

present study, we retrospectively evaluated the epidemiology, radiologic features, surgical treatment options (including open and percutaneous methods), and functional outcomes of foot and ankle OOs. Most previous studies were limited to case reports; the largest study (8) was a review reported in 2015 and was also based substantially on case reports. The need for the findings from a case series was an essential determinant of our decision to report our series.

### Patients and Methods

The study was performed in accordance with the ethical standards of the Declaration of Helsinki. All patients provided informed consent before inclusion in the study, and a local ethics committee approved the study protocol. The present retrospective study found 87 surgically treated patients with a preoperative diagnosis of a lower extremity OO from January 2003 to December 2014. We performed a manual search of the senior surgeon's (V.G.) operating records for the terms "benign bone tumor," "foot," "ankle," and "osteoid osteoma." Of the 87 patients, 9 patients (11%) had a foot or ankle OO and were included in the present study. The patient data reviewed included sex, age, site of the lesion, clinical and radiologic findings, swelling, pain, response to pain relievers, duration of complaints, interval to diagnosis, biopsy and

**Financial Disclosure:** None reported.

**Conflict of Interest:** None reported.

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**Table**  
Demographic data, diagnostic data, and surgical methods

Pt. No.	Age (y)	Location	Delay in Diagnosis (mo)	Treatment	Imaging Finding				Pathologic Finding
					Radiography	CT	MRI	Scintigraphy	
1	16	Calcaneus	12	RFA	None	Nidus	None	NP	NA
2	20	Talus	12	En bloc resection	None	None	NP	None	Nidus
3	25	Cuboid	12	Burr down	None	Nidus	None	Nidus	Nidus
4	30	Calcaneus	36	Cortical peeling	None	Nidus	None	NP	Nidus
5	6	Metatarsal	12	Burr down	None	Nidus	None	NP	Nidus
6	15	Calcaneus	18	En bloc resection	None	Nidus	None	NP	Nidus
7	11	Talus	18	Cortical peeling	None	Nidus	Nidus	Nidus	Nidus
8	17	Fibula	6	En bloc resection	None	Nidus	None	Nidus	Nidus
9	10	Talus	48	RFA	None	Nidus	Nidus	NP	NA

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; NA, not applicable; NP, not performed; Pt. No., patient number; RFA, radiofrequency ablation.

treatment modality, and functional results. The preoperative and post-operative clinical outcome scores were calculated using the American Orthopaedic Foot and Ankle Society (AOFAS) scale score (9). Patients who had undergone previous percutaneous or open surgical treatment with recurrence were excluded from the study. Preoperative radiographs, computed tomography (CT), magnetic resonance imaging (MRI), and scintigraphy examinations were performed.

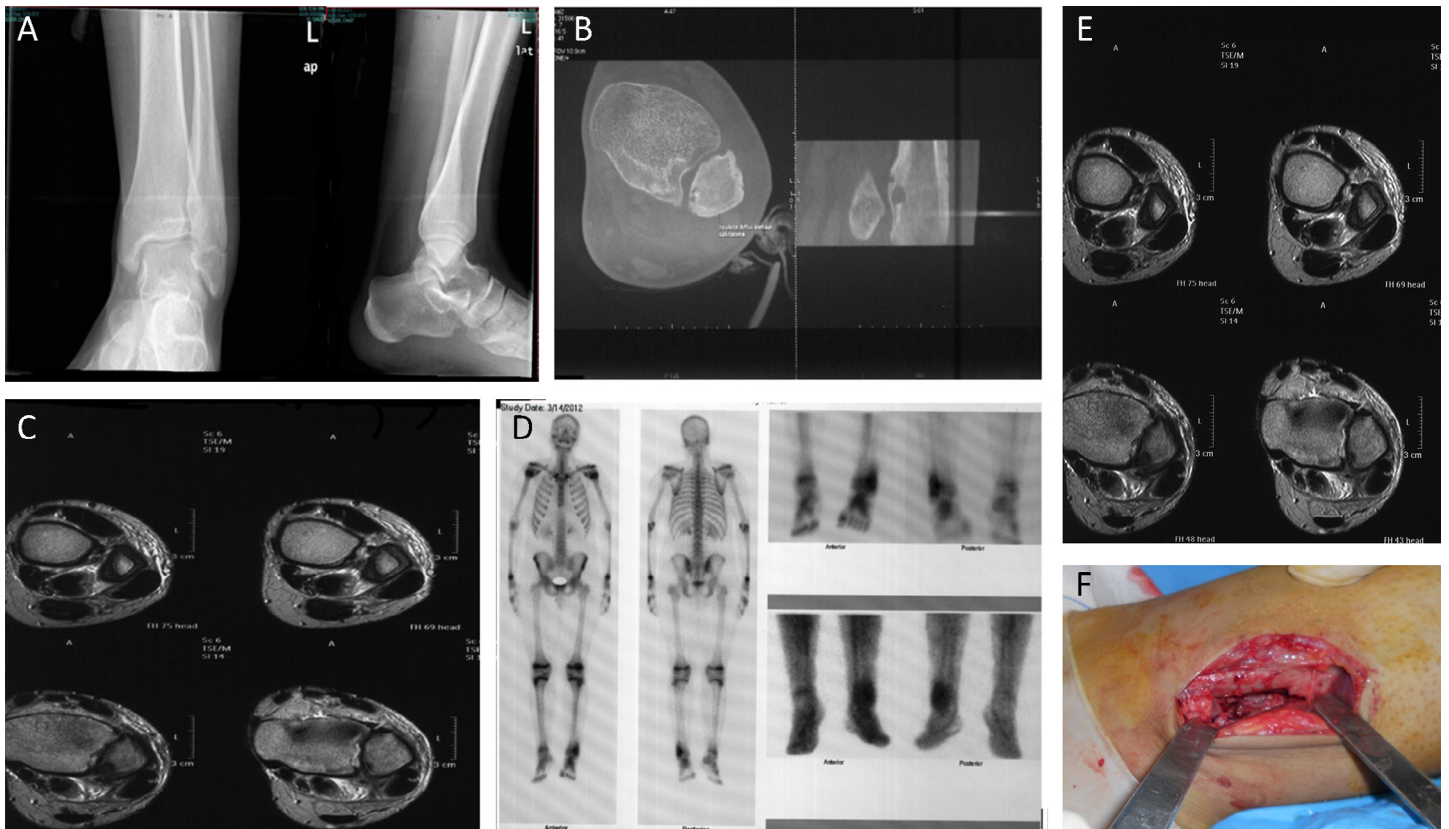
**Statistical Analysis**

Statistical analysis was performed using SPSS software (IBM, Armonk, NY) using an unpaired Student’s *t* test and the Fisher exact test. Statistical significance level was set at  $p \leq .05$ .

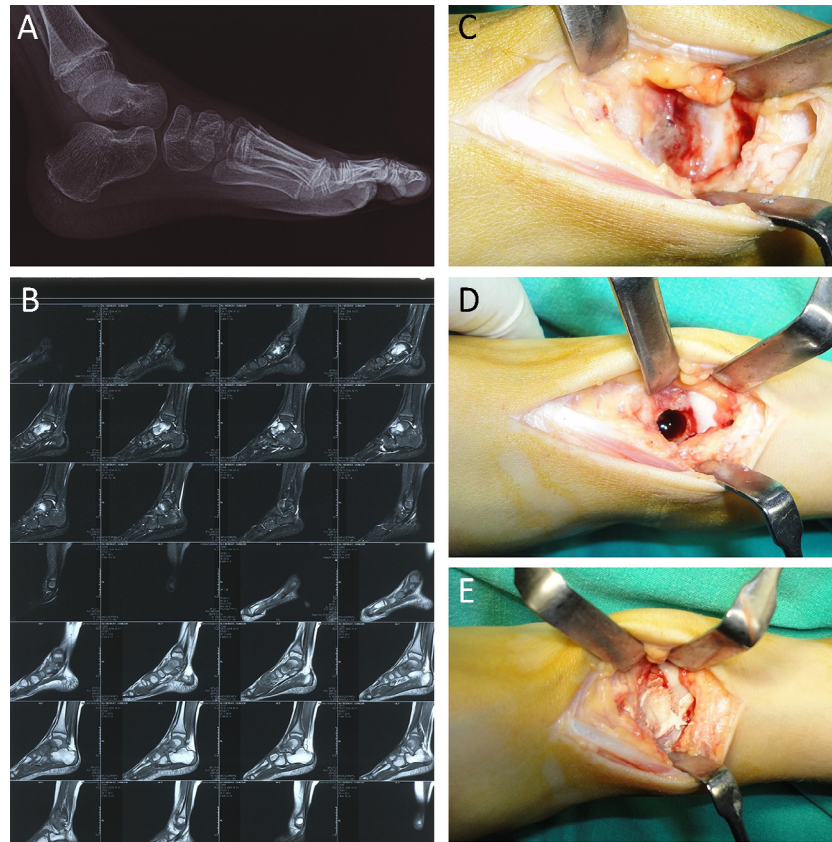
**Results**

The mean age was 21 (range 6 to 30) years, and all the patients were male (Table). Statistical significance was not found for age, similar to the finding for our lower extremity long bone OO patients ( $p \leq .33$ ). The lesion locations were as follows: calcaneus in 4 (44%), talus in 2 (22%), distal fibula in 1 (11%), metatarsal in 1 (11%), and cuboid in 1 (11%; Figs. 1–3).

The mean interval to the diagnosis was 18 (range 12 to 48) months. All patients reported night pain, localized tenderness, a response to pain relievers, pain with weightbearing, local swelling, and an antalgic gait. Slight erythematous changes and a local skin temperature increase were present in 2 patients (22%). The complete blood count,



**Fig. 1.** Images of patient 8, a 17-year-old male. (A) Anteroposterior and lateral ankle radiographs showing a lucent posterolateral lesion in the distal fibula compatible with an osteoid osteoma nidus. (B) Axial computed tomography (CT) scan of the left ankle showing a lytic subcortical lesion with diffuse cortical thickening. (C) Technetium-99m methylene diphosphonate intravenous (20 mCi) contrast-enhanced bone scan showing focal diffuse increased uptake in the distal fibula. (D) Coronal CT scan of the left foot and ankle showing a lytic subcortical lesion with diffuse cortical thickening. (E) Ankle T1-weighted magnetic resonance image showing a low signal, thickened cortex and the nidus. However, the nidus is not as clear as seen on the CT scan because of the soft tissue edema. (F) Perioperative image of the lesion showing a cherry red spot sign and nidus.



**Fig. 2.** Images of patient 7, an 11-year-old male. (A) Lateral ankle radiograph of the patient showing no evidence of a talar osteoid osteoma. (B) Sagittal short tau inversion recovery magnetic resonance imaging sequence of the ankle showing a centrally located low-signal mass and peripheral high-signal diffuse bone marrow edema. (C) Perioperative image of the lesion and red spot. (D) Perioperative image of the lesion after curettage. (E) Perioperative image after curettage and grafting of the lesion.

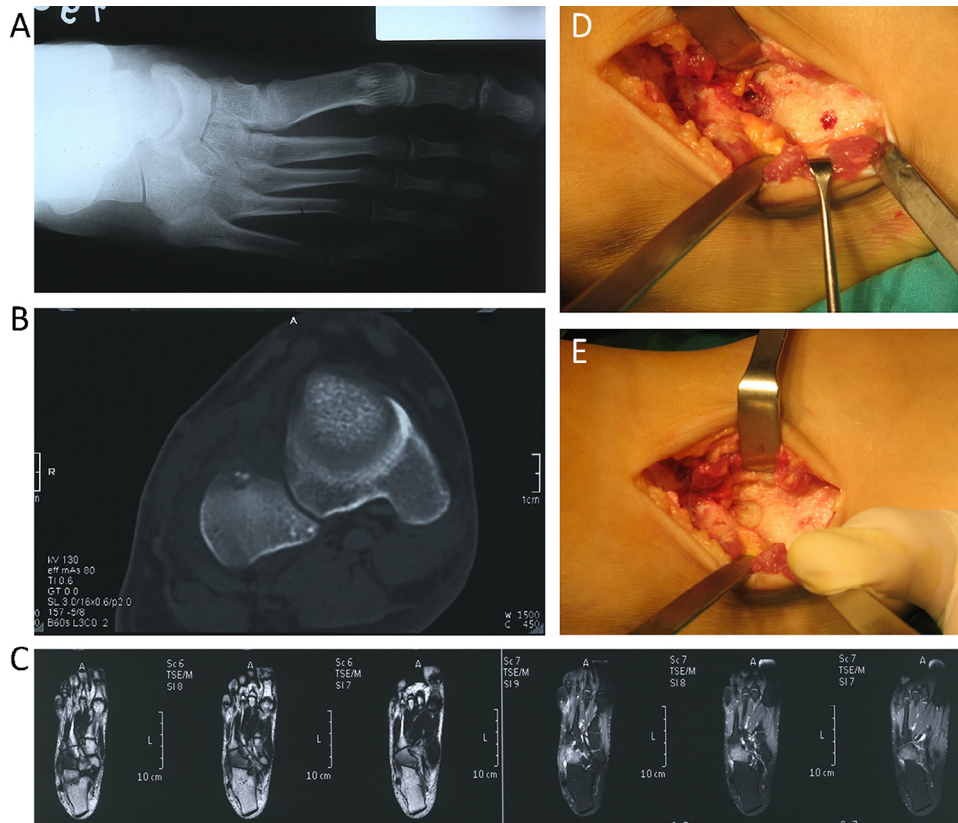
erythrocyte sedimentation rate, and C-reactive protein levels were normal in all 9 patients. All patients had undergone plain x-ray films and CT, 4 (44%) had undergone MRI, and 4 (44%) had undergone scintigraphy using single photon emission CT (SPECT)-CT. Treatment included the following: en bloc resection in 3 (33%), unroofing and curettage with “burr down” in 2 (22%), curettage with cortical peeling in 2 (22%), and radiofrequency ablation (RFA) in 2 (22%). After the team, which included an orthopedic oncology surgeon, a musculoskeletal interventional radiologist, and an anesthesiologist, was formed at the senior author’s (V.G.) institute to perform RFA, 2 patients (22%) with a foot or ankle OO underwent RFA. Another 2 patients (22%), who had been considered for RFA, were found not to be suitable because of the anatomic proximity of the nidus to the neurovascular tissues or articular surfaces. RFA was performed by consultant musculoskeletal radiologists. Before ablation, a CT-guided needle biopsy of the lesion was performed for pathologic diagnosis. The location of the lesions was as follows: subcortically cancellous in 6 (66%), cancellous in 2 (22%), and cortical in 1 (11%). Of the 9 lesions, 8 (89%) were extraarticular and 1 (11%) was intraarticular. The mean nidus diameter was measured using the CT images and was 6.8 (range 5 to 11) mm. Eight patients (89%) reported pain relief after the procedure. One patient (11%) experienced persistent pain for 6 months after surgery despite open curettage. SPECT-CT was repeated and showed a residual nidus with increased uptake. This patient underwent CT-assisted RFA 6 months after the initial procedure. Two patients (22%) who had undergone open surgery developed temporary superficial wound problems, which healed without any surgical intervention. At the final follow-up examination, at a mean of  $48 \pm 24$  months after the initial

procedures, no recurrences had developed. The mean AOFAS scale score was  $59.04 \pm 11$  before surgery and  $91.56 \pm 6$  after surgery, and the difference was statistically significant ( $p \leq .0003$ ; Table).

## Discussion

Few studies of OOs have been reported, and the largest was a systematic review (8) reported in 2015, which was also based substantially on case reports (64 of the 94 included studies were case reports). To the best of our knowledge, most case series were also limited to small numbers of patients. Zouari et al (10) reported on 7 patients (5.2%) with a foot or ankle OO of 133 patients with OOs, and Rehnitz et al (11) reported on 3 patients (4%) with a foot or ankle OO of 72 patients with OOs. Therefore, a large number of prospective randomized trials are still needed to determine the best evidence-based medicine.

OOs are usually seen in patients aged <40 years, and most patients will be <25 years, with males predominating at a ratio of 3:1. The male predominance is valid for foot and ankle OOs; however, to the best of our knowledge, no studies regarding the male predominance have been reported. Our results are consistent with the published data regarding the male predominance and mean age. The most common symptom in OO patients was pain that increased in severity at night and that responded well to prostaglandin inhibition; swelling was the second most common symptom (12,13). It has been thought that the swelling is related to the rich vascular supply of the tumor or the increased soft tissue and vascular permeability that results from the presence of prostaglandins in the mass (12,14). In 2 patients with redness of the skin, the lesion was located close to the skin,



**Fig. 3.** Images of patient 3, a 25-year-old male. (A) Lateral oblique radiograph showing the foot with no evidence of the osteoid osteoma in the cuboid bone. (B) Computed tomography image of the right foot showing the radiolucent lesion and central calcification, which is typical for an OO nidus in the cuboid bone. (C) Fat-suppressed and contrast-enhanced T1-weighted axial magnetic resonance image of the foot showing only diffuse bone marrow edema in the cuboid bone. (D) Perioperative image of the nidus and red spot. (E) Perioperative image after curettage and grafting of the lesion.

and scintigraphy revealed intense activity. It has been thought that the pressure and edema resulting from the lesion cause the pain by stimulating the surrounding nerve fibers. In an immunohistochemical study by O'Connell et al (15), more nerve fibers than were expected were found surrounding the nidus and reactive zone. Consistent with previous studies, all our patients experienced night pain, and in 6 patients (66%), this pain was relieved by nonsteroidal antiinflammatory drugs. This finding is consistent with the review by Jordan et al (8). The reported incidence of OO has ranged from 2% to 10% in the foot (16), followed by the calcaneus (2.7%), phalanx (2%), and metatarsals (1.7%). In contrast to the results reported by Jackson et al (17), we found that the most frequently involved bone was the calcaneus ( $n = 4$ ; 44%). OO has 3 histologic types: cortical, cancellous, and subperiosteal (5). OOs tend to occur intracortically in the long bones and cause an excess subperiosteal reaction. In contrast, they mostly develop in cancellous or subperiosteal locations in the foot, where they cause a minimal periosteal reaction (6). Cancellous OOs were present in 8 of our patients (88%), in agreement with the findings from other studies, and 6 patients (75%) had subcortical OOs. Houdek et al (18) classified the lesions of their patients as intracortical, periosteal, or subcortical (endosteal) according to the relationship of the nidus to the cortex, instead of whether it was subperiosteal or cancellous. Three of their patients' lesions (27%) were intracortical and 8 (73%) were subcortical and were classified as the subcortical type of cortical lesion (18). This is consistent with our results. However, controversy remains regarding whether the localization should be described as cortical or cancellous. Although the clinical presentation is often typical and diagnostic, in some cases, the nidus formation will not be seen on plain

radiographs. This could have resulted from transposition of the small bones (anatomic complexity of the foot), the lack of a periosteal reaction, cortical thickening, a longer time required for nidus formation in the foot and ankle, a lower periosteal response against lesions extending into the joint, and the transposition of OOs that have settled close to the joint with synovial tissue (16,19). Thus, the need to rule out many diseases, including ankle distortions, monoarticular arthritis, anterior impingement syndrome, tarsal spur, osteomyelitis, stress fracture, eosinophilic granuloma, and sarcoma, has led to the preference for using MRI instead of CT. Also, peroneal spasm and foot extensor tenosynovitis have been added to the differential diagnosis (20). However, the diffuse soft tissue edema observed on MRI can lead to the use of long-term immobilization and a delay in the diagnosis (8). The mean interval to the diagnosis was 18 (range 12 to 48) months in our series, similar to that reported by Jordan et al (8) in their systematic review. Also, the mean delay between the initial presentation and the diagnosis was 22 (range 1 to 120) months. The patients had been treated conservatively for long periods, and the delays had caused social, economic, and psychological damage (21). For patients presenting with the typical night pain responsive to pain relievers, who are in the high-risk age group, and in the absence of suggestive findings of OO on radiographs, thin-slice CT should be performed, in addition to MRI, for advanced imaging studies. The bone marrow edema signal commonly seen with OO, which can be intensely visualized using MRI, can mask the typical bony features of the lesion, which are nearly pathognomonic on CT. Also, the diagnosis of OO can be challenging using MRI alone. Failure to diagnose an OO using MRI occurred in 3 of our patients (33%), similar to previous reports (4,22). Therefore, MRI

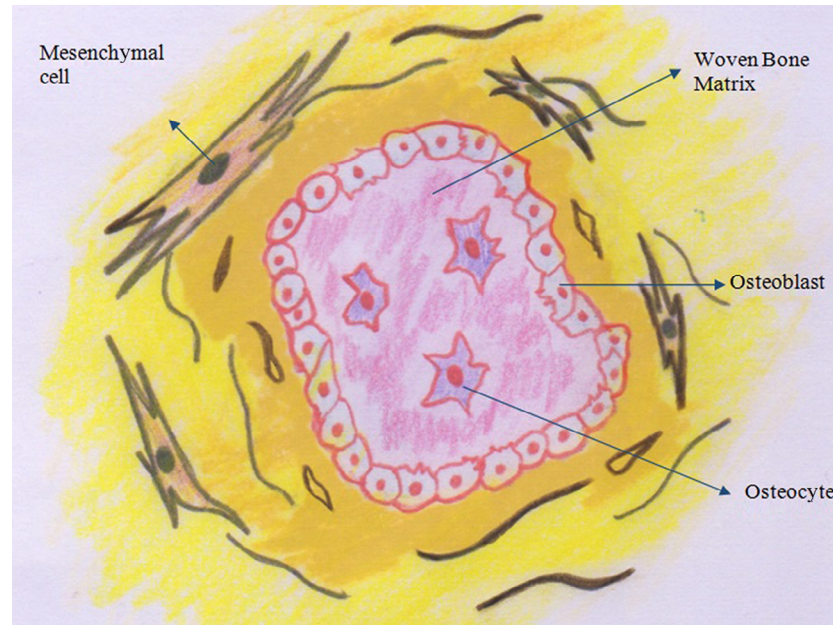


Fig. 4. Drawing showing intramembranous tissue healing process (O.E.).

appears to lack the specificity for diagnosing OO in a significant proportion of patients. Farid et al (23) concluded that compared with bone scanning alone the use of SPECT images with a low-dose CT technique improved anatomic localization and provided more precise morphologic information. A recent study comparing SPECT images with low-dose CT and bone scans to diagnose OOs at all body sites reported that SPECT had greater sensitivity and specificity (both 100%) compared with CT (sensitivity 77.8%; specificity 92.3%) and bone scans (sensitivity 100%; specificity 38.4%) (24). Similarly, in 1 patient, we could not define the lesion although plain radiographs, CT, MRI, and bone scanning were performed. However, SPECT-CT used together with bone scanning, identified the lesion as an OO. Even using advanced imaging studies, a diagnosis will not be made for 11% of the OO lesions (25). These suspected OOs that could be not diagnosed radiologically can be accurately diagnosed using SPECT-CT; however, further investigation is required. The pathophysiology of OOs remains partially unclear. Atypical cellular and trabecular components of the OO nidus can resemble neoplasia, because they are small and have self-limiting characteristics that resemble the inflammatory process (26). Vancamp et al (27) postulated that the nidus is a reactive lesion that occurs in response to trauma or is an unusual healing and vascularization process. more studies are needed regarding the relationship between OO and trauma; however, a history of trauma was present in one third of all cases (11). Also, the similarity to the inflammatory process suggests an association with a history of trauma (22,27). Additionally, pain related to an OO has developed 2 to 8 years after trauma. Kayser et al (28) hypothesized that many OOs will originate in a subperiosteal location and later appear as intracortical or medullary lesions. They termed this inward migration a “shift of nidus.” They also explained that this migration involves bone, which continues with subperiosteal deposition and endosteal erosion (28). We believe this argument also supports the trauma hypothesis. In our series, a history of trauma was present in 4 patients (44%), and the mean time between the trauma and pain presentation was 44 (range 30 to 52) months. OO is generally seen in patients aged <40 years. This trend could also be relevant for bone remodeling. It is known that the balance is in favor of bone formation until the third decade and that bone destruction becomes dominant in the fifth decade and beyond and the bone mass

decreases. The patients in our series had a mean age of 21 (range 6 to 30) years, similar to that reported in other studies. The nidus contains woven bone and a highly vascular stroma of connective tissue centrally, with dilated capillaries. The formation of an OO nidus and the process of intramembranous (IM) healing are histologically similar (Figs. 4 to 6).

IM ossification occurs during flat bone formation and during the healing process of a fracture treated with open reduction and internal fixation. Adil et al (29) hypothesized that invagination of the periosteum during fractures, reduction, or pinning might be a predisposing factor for the development of OO. Thus, the nidus of an OO might be an atopic IM ossification area in the bone. It is unknown why the OO nidus does not become mature. We suggest that the problem is related to either matrix mineralization (transformation of amorphous calcium into hydroxyapatite) or collagen type 1 synthesis and organization. Biochemical and histologic investigations of the nidus using electron microscopy techniques are required to reveal the

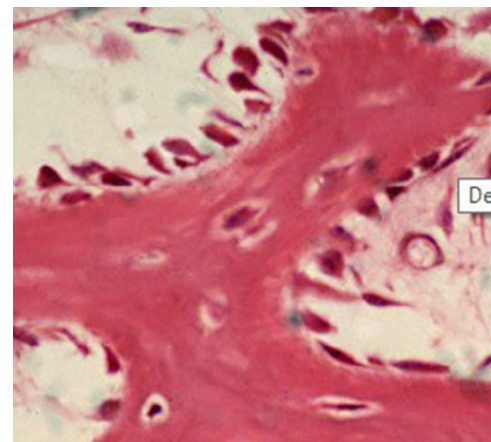
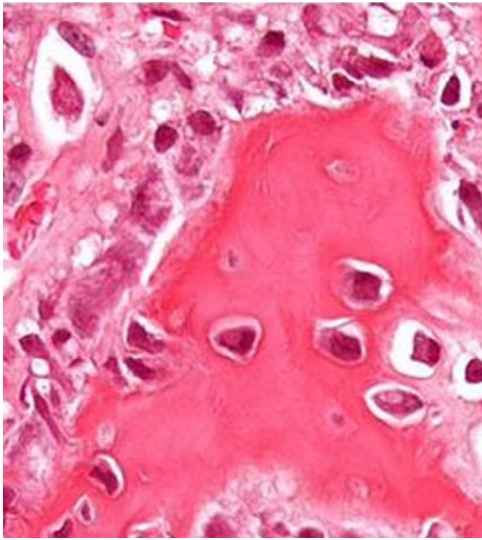


Fig. 5. High-power light microscopy slide showing developing intramembranous bone (magnification  $\times 400$ ; hematoxylin and eosin stain).



**Fig. 6.** Very high power light micrograph of an osteoid osteoma (magnification  $\times 400$ ; hematoxylin and eosin stain).

histologic differences in the collagen array and mineralization between the OO nidus and the fibrous dysplasia, hyperthyroid, and fracture callus. Prostaglandin  $E_2$  is a bone-resorbing cytokine secreted by osteoblasts and causes the typical pain associated with an OO. Thus, an imbalance in prostaglandin  $E_2$  secretion or structure could be present that prevents nidus maturation. We also suggest that insulin-like growth factor 1, which stimulates collagen synthesis, and transforming growth factor- $\beta$ , which promotes osteoid matrix synthesis, should be further investigated in studies of the pathophysiology of OOs. Percutaneous thermal destruction of the vascular-rich nidus is the current treatment of choice and can be performed using a laser or RFA, with a success rate of  $>90\%$  (30). However, in selected cases, the proximity to the chondral surface or neurovascular structures should change the preference to an open technique. The recurrence rates with both open and percutaneous techniques have ranged from 0% to 15%, with similarly successful results. However, with the open technique, the return to work and full weightbearing will require weeks, the risk of fracture is greater, and the severity and incidence of postoperative pain are greater (31). One patient (11%) in our series experienced persistent pain for 6 months after surgery, despite open curettage. He underwent CT-assisted RFA because of a residual nidus. After RFA, the patient was asymptomatic. The success of this procedure depends on an accurate preprocedural diagnosis and the precise anatomic localization with CT. This patient is an example of the importance of CT-guided techniques. In our study, 2 patients (22%) were treated with CT-guided RFA. None of these patients developed recurrence or experienced persistent pain, and the mean AOFAS scale score improved from 58 (range 56 to 60) to 94 (range 92 to 96). The advantages of percutaneous techniques include controlled ablation of the tumor nidus with minimal damage to the adjacent bone tissue and performance as an outpatient procedure, which also allows for immediate weightbearing and return to daily living. In addition, when the average costs of hospitalization and treatment of OO using RFA and surgical excision were compared, RFA was less expensive. RFA-related complications include skin burns, nerve damage, reflex sympathetic dystrophy, cellulitis, and thrombophlebitis. Thus, RFA should not be used for lesions near a neurovascular bundle ( $<1.5$  cm distance) (31). No complications or recurrence had developed within a mean follow-up period of 36 months in our RFA group; however, late recurrence is possible with a longer follow-up duration.

The retrospective study design and small number of cases could be considered a weakness of our study; however, the rarity of foot and ankle OOs makes it difficult to plan a prospective study with a large number of cases. However, wide prospective randomized trials are still required to determine the best evidence-based medicine.

In conclusion, difficulties can be experienced in the diagnosis of OO. The underlying reasons include the large number disorders in the differential diagnosis and the nonspecific findings of periarticular lesions on radiography. MRI has been preferred to CT to determine the cause of foot and ankle pain when performing additional imaging studies. However, the pathognomonic bone findings in OOs that can be visualized using CT will be concealed by the peripheral edema seen on MRI. Thus, for patients presenting with the typical night pain that is responsive to pain relievers and who are in the age group at risk, even in the absence of suggestive findings for OOs on radiographs, advanced imaging studies should include thin-slice CT, in addition to MRI.

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