Alınış / Received: 09.05.2024 Kabul / Accepted: 04.11.2024 Online Yayınlanma / Published Online: 25.04.2025
Araştırma Makalesi / Research Article DOI: 10.22312/sdusbed.1480957

Süleyman Demirel Üniversitesi Sağlık Bilimleri Dergisi
Suleyman Demirel University Journal of Health Sciences

The Role of Histopathology in the Diagnosis of Osteochondroma: Our Experience with Eighty-Eight Cases

Osteokondrom Tanısında Histopatolojinin Yeri: Seksen Sekiz Olgu ile Deneyimlerimiz

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ABSTRACT

Aim: Osteochondromas are the most common benign primary bone tumors with a medullary cavity, covered with hyaline cartilage, arising from the juxtaepiphyseal region of the bone. This study retrospectively evaluates cases diagnosed with osteochondroma presenting with varied localization and clinical findings, along with conventional cases, in light of current literature. Materials and methods: Hematoxylin-eosin and, where available, immunohistochemical stained preparations of samples from 88 patients diagnosed with osteochondroma between January 2010 and December 2023 at the pathology department of the Faculty of Medicine were evaluated. Age, gender, recurrence status, radiological findings, and clinical results were obtained from hospital records. The tumor localization and histopathological characteristics were retrospectively reviewed. Results: Among the 88 cases, 50 (56.8%) were male and 38 (43.2%) female, with ages ranging from 3 to 58 years. The mean age was 22.83, and the median age was 20. Most patients (n=55, 62.5%) presented with pain. Tumors were primarily located in the distal femur (n=33, 37.5%) and around the knee (47 cases, 53.4%). Grade II chondrosarcoma arising from osteochondroma was observed in only 1 case (1.1%). Conclusions: Osteochondroma is a primary benign bone tumor most commonly observed in males and frequently located in the distal femur. Pain is the most common clinical complaint, and surgical resection is the preferred treatment. Although osteochondromas are typically found in long bones, they may present with atypical localization and clinical findings. Malignant transformation, although rare, should be considered in osteochondromas.

Keywords: *Osteochondroma, Bone, Benign, Chondrosarcoma, Localization*

ÖZ

Amaç: Osteokondrom, kemiğin jukstaepifizer bölgesinden ortaya çıkan hyalin kıkırdak ile kaplı, kendi medüller boşluğu bulunan, iyi huylu, en sık primer kemik tümörüdür. Bu çalışmada konvansiyonel olgular ile birlikte farklı yerleşim ve klinik bulgular ile prezente olan osteokondrom tanılı olgularımızın retrospektif olarak değerlendirip, güncel literatür ışığında sunmayı amaçladık. Materyal ve metod: Tıp fakültesi Patoloji anabilim dalında Ocak 2010-Aralık 2023 yılları arasında osteokondrom tanılı 88 hastaya ait hematoksilen&eozin ve varsa immünhistokimyasal boyalı preparatlar retrospektif olarak değerlendirildi. Olguların yaş, cinsiyet, nüks durumları, klinik sonuçları hastane kayıtlarından elde edildi. Tümörün lokalizasyonu, radyolojik görüntüleme bulguları ve histopatolojik özellikleri retrospektif olarak değerlendirildi. Bulgular: Seksen sekiz olgunun, 50'si (%56,8) erkek, 38'i (%43,2) kadın olup olguların yaşlarının 3 ile 58 arasında değiştiği ve ortalama yaşın 22,83, ortanca yaşın ise 20 olduğu saptandı. Olguların en sık ağrı yakınması(n:55, %62,5) ile kliniğe başvurduğu tespit edildi. Tümörlerin en sık yerleşim yeri distal femur (n:33, %37,5) olup olguların büyük çoğunluğunda (47 olgu, %53,4) lezyon diz çevresinde lokalize idi. Yalnızca 1 olguda (%1,1) osteokondrom zemininde grade II kondrosarkomun geliştiği dikkati çekti. Sonuç: Osteokondrom erkek cinsiyette daha sık görülen, en sık distal femurda yerleşen kemiğin primer benign tümörüdür. Kliniğe en sık ağrı yakınmasıyla başvuran olgularda tedavi seçeneği cerrahidir. Osteokondromların çoğunluğu uzun kemiklerde görülmekle birlikte farklı, atipik lokalizasyon ve klinik bulgular ile karşımıza çıkabilirler. Nadir de olsa osteokondrom zemininde malign transformasyon gelişebileceği akılda tutulmalıdır.

Anahtar Kelimeler: *Osteokondrom, Kemik, Benign, Kondrosarkom, Lokalizasyon*

INTRODUCTION

Osteochondromas are the most common benign tumors of bone and are typically detected in the distal femur, proximal humerus, and tibia (1). Although almost all osteochondromas are solitary, an autosomal dominant form of osteochondromatosis, known as hereditary multiple exostoses (HME), can also be observed. Most of these cases are reported to be positive for mutations in the glycosyltransferase (EXT) genes (2,3). Understanding the pathogenesis is useful for increasing knowledge about the disease and can guide treatment. Genetic factors, abnormal embryological development, and growth and developmental disorders are involved in the pathogenesis of HME (4,5,6). Increased BMP signaling and the heightened activity of ranase, an enzyme that breaks down heparan sulfate chains and stimulates chondrogenesis, have also been reported to play a role in the pathogenesis; however, mutations in the EXT-1 and EXT-2 genes are most likely responsible (6, 7). EXT-1, located on chromosome 8q24.11-q24.13, has been detected in 28-65% of affected patients, while EXT-2, located on chromosome 11p11-12, has been detected in 21-61% of affected patients (5). EXT-1 and EXT-2 are genes that encode glycosyltransferases involved in the production of heparan sulfate, which binds to nuclear proteins in the cell membrane and facilitates the production of proteoglycans outside the cell. These mutations have not been detected in 5-34% of HME patients, suggesting that other EXT genes may also be involved in the pathogenesis (8).

Among the primary benign tumors of bone, osteochondromas account for approximately 35% in adults and 20-35% in pediatric patients (9).

Most osteochondromas, which some authors do not classify as true tumors, are asymptomatic (10). In terms of management, cases are typically monitored in the clinic, as they are benign tumors that usually do not cause symptoms. Complete surgical excision is indicated in cases of cosmetic concerns, bursal inflammation, secondary fracture formation, nerve paralysis, vascular compromise, pain, and, rarely, malignant transformation (11). The probability of recurrence after complete excision is less than 2% (2).

The rate of surgical intervention is higher in the osteochondromatosis form, which is six times less common than solitary osteochondroma, due to the increased risk of malignant transformation (12). In treatment protocols, asymptomatic, small, solitary masses do not typically require surgical intervention. One potential treatment option for such cases is retinoic acid receptor gamma (RARγ) agonists. Studies in mouse models have shown that these agonists can prevent heterotopic ossification and may reduce the number of osteochondromas (13,14). The incidence of osteochondromas has not been accurately determined based on histopathologically diagnosed cases, as most are detected incidentally through clinical evaluation and imaging methods, and surgical excision is not routinely performed (15).

Most cases are detected during the pediatric period. Thickening of the cartilage cap greater than 3 cm in pediatric patients and more than 2 cm in adults, along with reported pain and rapid growth of the lesion after puberty, raises suspicion for malignancy (2). The thickness of the cartilage cap can be misleading in younger patients, as this is the period when cellular proliferation peaks. Therefore, close follow-up in the clinic, along with evaluation of the mass and its behavior over time, is crucial (9). Symptoms resulting from vascular compression may include changes in skin color, loss of pulse, or alterations in blood flow. Patients may also develop arterial or venous thrombosis, aneurysms, or pseudoaneurysms. Given that the knee is the most commonly affected area, the popliteal artery, common peroneal nerve, and posterior tibial nerve are the structures most frequently involved (16).

Secondary chondrosarcomas may develop from existing osteochondromas. The onset of pain in a previously asymptomatic lesion should raise suspicion of malignant transformation (9). Transformation into chondrosarcoma occurs in approximately 5% of osteochondromas (17).

Amplification of MYC and AP-1 transcription factors plays a significant role in the pathogenesis of chondrosarcoma (18). Microscopic examination of chondrosarcoma may reveal necrosis and mitotic activity, and it can infiltrate cortical bone and the marrow space. Nuclear enlargement, hyperchromasia, size variation, and binucleation are characteristic features observed in chondrocytes. Chondrosarcomas are classified into four grades based on histopathological findings. Grade 1 chondrosarcomas closely resemble normal cartilage or enchondromas; thus, identifying an infiltrative pattern can assist in differentiation. Grade 2 exhibits more pronounced nuclear atypia, increased cellular size, and mitotic figures. In Grade 3, nuclear pleomorphism and atypia are readily apparent. Dedifferentiated chondrosarcoma has a poor prognosis and is characterized by spindle-shaped and pleomorphic cells devoid of a cartilage matrix. The IDH1 R132H antibody mutation is identified in approximately one-fifth of cases. Distinguishing Grade 1 chondrosarcoma from osteochondroma can be quite challenging, making it essential to evaluate these cases using imaging methods (19).

Osteochondromas are tumors that grow outward, manifesting as either pedunculated or sessile lesions, and are typically located in the metaphysis of bones. While direct radiography can be utilized alone for diagnosis, computed tomography (CT) and magnetic resonance imaging (MRI) are also valuable for measuring the thickness of the cartilage cap in cases where diagnosis is challenging or to predict potential complications (20).

A definitive diagnosis of osteochondroma is established through histopathological examination. Osteochondromas are characterized as hamartomatous lesions, exhibiting endochondral ossification with cartilage tissue present on the surface. Histopathologically, benign proliferation is observed with a medullary cavity, which is covered by hyaline cartilage, on the metaphyseal surface of the growth plate, known as the juxtaepiphyseal region. Expansion may be observed in the metaphyseal area where the tumor develops. Regardless of whether the tumor is pedunculated or sessile, the continuity of trabecular structures between the tumor and healthy bone is critical for diagnosis (21).

In this study, we aimed to retrospectively evaluate our cases diagnosed with osteochondroma, which presented with various localizations and clinical findings, alongside conventional cases, and to present our findings in the context of current literature.

MATERIAL and METHOD

Hematoxylin-eosin and immunohistochemically stained preparations, if available, from the materials belonging to 88 patients diagnosed with osteochondroma between January 2010 and December 2023 in Manisa Celal Bayar University Faculty of Medicine, Department of Medical Pathology were evaluated. This retrospective study was approved by the ethics committee of our institution, with approval date and number 27/12/2023/20.478.486/2172.

The hospital automation system provided information regarding the patients' ages, genders, presenting complaints, and the specific bone or bones in which the tumors were localized. Macroscopic images of the available materials in our archive concerning these cases were reviewed (sample macroscopic images are presented in Figures 1-6). The bone tissue samples, which were fixed in 10% buffered formalin and subsequently decalcified in 10% nitric acid solution, were sectioned to a thickness of 3-4 micrometers. Routine hematoxylin and eosin (H&E) stained slides, and additional immunohistochemical preparations deemed necessary were also evaluated (sample microscopic images are presented in Figure 7). In the radiology department, direct radiographs of the cases, along with available CT and MRI examinations on a case-by-case basis, were reviewed to confirm the localizations of the tumors (Figure 8).

Data analysis was conducted using SPSS version 21 (IBM, Chicago, IL, USA). The study included basic descriptive statistics such as frequency, percentage, arithmetic mean, standard deviation, and minimum and maximum values.

RESULTS

Among the 88 cases included in our study, 50 (56.8%) were male and 38 (43.2%) were female. The ages of the cases ranged from 3 to 58 years, with a mean age of 22.83 years and a median age of 20 years (Table 1).

Table 1. Distribution of Cases by Gender and Clinical Findings

Gender	**n**	**%**
Male	50	56,8
Woman	38	43,2
Total	88	100,0
Clinical Complaint	**n**	**%**
Swelling *	31	35,2
Pain	32	36,4
Pain+swelling	5	5,7
Pain+limitation of movement	18	20,5
Incidentally detected with a history of Trauma	2	2,3
Total	88	100

*Cosmetic reasons were noted in 1 of 31 cases in which swelling was detected.

Eighty-eight cases presented to the clinic, with pain being the most common symptom (n = 55, 62.5%). Among these cases, 32 (58.1%) reported pain only, 5 (9%) experienced pain accompanied by limitation of movement, and 18 (32.7%) had complaints of swelling along with pain. A history of trauma was noted in 1 of the 5 (20%) cases that had movement limitation along with pain. Additionally, in 2 cases, no symptoms were reported for the lesions; however, a mass was detected incidentally on radiographs taken due to trauma. Complaints of painless swelling were observed in 31 (35.2%) cases. In one instance, a 25-year-old male patient with an intra-articular mass reported cosmetic discomfort due to deformity as an additional complaint. Among the 5 cases with complaints of movement limitation, the lesion was located in the proximal femur in 2 cases, in the iliac region in 1 case, and intra-articularly in 2 cases (Table 1).

Of the 10 (11.3%) cases with multiple masses, 3 (27.2%) exhibited swelling, 2 (20%) had pain, and 5 (50%) presented with both pain and swelling. According to the tumor locations, the most common site was the distal femur (n = 33, 37.5%), followed by the proximal tibia (n = 14, 15.9%). It was noted that the lesions were around the knee in most of the cases (n = 47, 53.4%).

In the distribution of tumors according to localization, the humerus ranked third (n = 7, 8%), while the fingers ranked fourth (n = 6, 6.8%). Intra-articular tumors ranked fifth (n = 5, 5.7%), followed by the iliac and fibula bones (n = 4, 4.5%). The toes ranked sixth (n = 3, 3.4%), and the radius, distal tibia, and metacarpal bones each had 2 cases (n = 2, 2%). Lastly, the vertebrae, scapula, and metatarsal bones each had 1 case (n = 1, 1.1%) (Table 2, 3). Macroscopic images of tumors with different localizations and findings are presented in Figures 1-6.

Table 2. Distribution of Osteochondromas by Location and Form

Localization of osteochondroma	**n**	**%**
Distal Femur	33	37,5
Humerus	7	8,0
Proximal Femur	3	3,4
Proximal Tibia	14	15,9
Hand Phalanx	6	6,8
İliac Bone	4	4,5
İntra-Articular	5	5,7
Radius	2	2,3
Vertebra	1	1,1
Scapula	1	1,1
Fibula	4	4,5
Toe	3	3,4
Distal Tibia	2	2,3
Metacarpal	2	2,3
Metatarsal	1	1,1
Total	88	100,0
Form of osteochondromas	**n**	**%**
Solitary	78	88,6
Multiple	10	11,4
Total	88	100,0

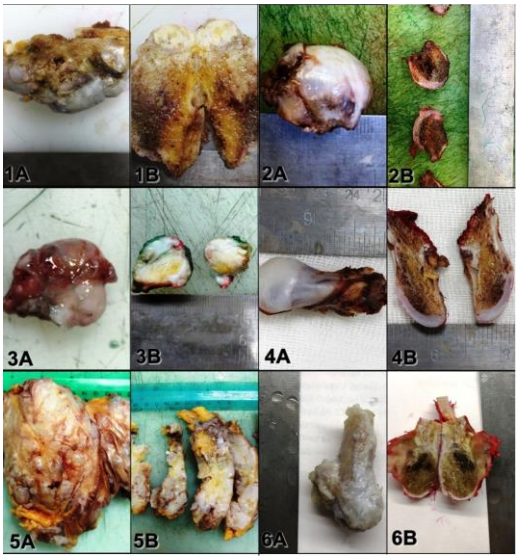

Figure 1-6: Macroscopic Samples Of Cases

1. Mass in the Proximal Tibia: (A) Excision material measuring 7 × 3.5 × 2.5 cm, with a bright pearlescent white outer surface and a lobular appearance, occasionally containing cartilage-like areas. **(B)** An area measuring 1.9 × 1.5 × 1.1 cm was observed in the distal part of the section surface, featuring a cream-colored cartilage surface; cartilage-like foci were also noted in other areas at the periphery of the lesion. **2. Mass in the Distal Femur: (A)** Hard, palpable bone excision material measuring 3.2 × 2.5 × 2.2 cm, with a shiny pearlescent white outer surface and occasional irregular brownish areas.**(B)** The cut surface was cream-brown, with a 0.3 cm thick cartilage-like area observed on the surface. **3. Mass on the 3rd Toe of the Left Foot: (A)** Bone excision material measuring 2.5 × 2 × 1.7 cm, exhibiting a bright and smooth appearance on the outside in most areas. **(B)** In the cross-sections, an area approximately 1 × 0.5 cm in the remaining half at the other end of the excision line appeared as smooth fibrous cartilage, while other areas were composed of cancellous bone. **4. Mass in the Distal Femur: (A)** Bone excision material measuring 4.7 × 2.2 × 1.8 cm, apparently excised from an area of 2.5 × 1.4 cm. Its outer surface was smooth, shiny, and white in color. **(B)** In cross-sections, the mushroom-shaped outer part was covered with 0.4 cm thick cartilage tissue, with spongiotic bone tissue visible in other areas. **5. Mass in the Distal Femur (Chondrosarcoma): (A)** Measuring 13 × 11 × 3.5 cm, this specimen exhibited a smoother appearance on one side, with a transparent-gray color and large and small nodular areas, while the opposite side contained mature fatty tissue in places and presented more irregular bone tissue. The material was composed almost entirely of tumors. **(B)** The cross-sectional surface consisted of tumoral areas with lobulated contours, appearing as transparent white-gray cartilage tissue. **(C)** Trabecular bone tissues invaded by the tumor were occasionally observed within the tumor areas, while some areas appeared to contain mature fatty tissue in the surrounding regions. **6. Left Hand 2nd Metacarpal Bone (NORA Lesion): (A, B)** Excision material of the bone measured 4 × 2.5 × 1.8 cm, cream-gray in color, and shiny. A nodular lesion was observed protruding 1.3 cm from the bone surface. **(C)** Upon incision of the lesion, the cut surface appeared dirty and cream-colored.

Table 3. Clinical Complaints of Cases and Distribution of Tumors by Location

Clinical Complaint	**LOCALIZATION**															n (t)
	1*	2*	3*	4*	5*	6*	7*	8*	9*	10*	11*	12*	13*	14*	15*	
Swelling	10	4	0	5	5	1	0	0	0	1	1	1	2	1	0	31
Pain	18	2	0	6	0	1	2	0	1	0	1	0	0	0	1	32
Pain+immobilization	0	0	2	0	0	1	2	0	0	0	0	0	0	0	0	5
Pain+Swelling	5	1	1	3	1	1	0	2	0	0	1	2	0	1	0	18
Incidental with Trauma	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	2
N (Total)	33	7	3	14	6	4	5	2	1	1	4	3	2	2	1	88

*localization: 1: distal femur, 2: humerus, 3: proximal femur, 4: proximal tibia, 5: fingers, 6: iliac, 7: intra-articular, 8: radius, 9: vertebra, 10: scapula, 11: fibula, 12:toes, 13: distal tibia 14: metacarpal 15: metatarsal

It was noted that grade II chondrosarcoma developed from osteochondroma in only 1 (1.1%) of all cases. In the case of a 45-year-old male diagnosed with chondrosarcoma, the mass was observed as a single localized mass in the distal femur. Malignant transformation was not observed in the other cases. Microscopic images of the tumors, displaying different findings, are presented in Figure 7.

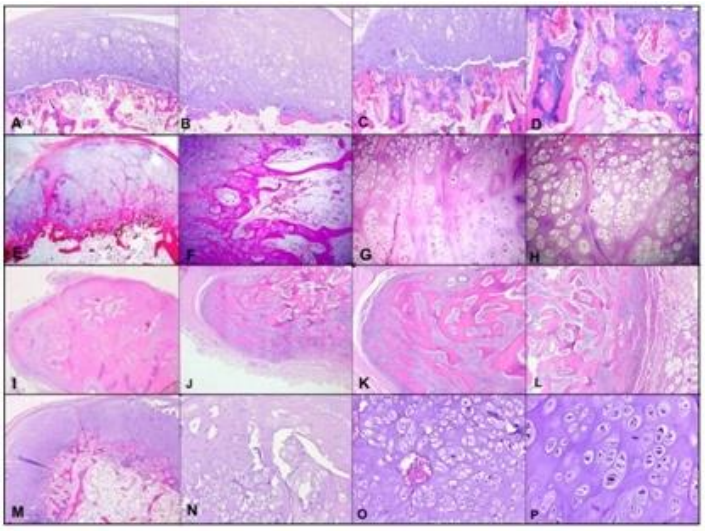

Figure 7: Microscopic Examination of the Samples

A-H: Photomicrographs of different osteochondroma cases. Osteochondroma consists of three layers; the perichondrium is visible on the outer surface, with a cartilage cap underneath that shows increased proliferation compared to normal bone. The tissue displays hyaline cartilage and irregular mature bone trabeculae passing through the cartilage. No significant atypia was observed in the proliferating chondrocytes. (H&E stained images; magnifications: x20, x40, x40, x100, x20, x100, x200, x200). **I-L:** Microscopic images from a case excised from the second metacarpal of a 15-year-old male patient, characterized by a proliferative lesion on the bone surface that is not connected to the bone cortex. The lesion, located in the stroma, is marked by spindle cell proliferation and contains limited areas of bone trabeculae and cartilage. Reactive nuclear enlargement was observed in chondrocytes within the cartilage areas. Osteoblasts and osteoclasts were noted at the periphery of the bone trabeculae. (H&E stained images; magnifications: x20, x20, x40, x40). **M-N:** Microscopic images of a 45-year-old male patient diagnosed with grade II chondrosarcoma arising from osteochondroma, localized as a single mass in the distal femur. A tumoral lesion displaying cellular hyaline cartilage morphology with lobulation was observed. The tumor showed areas of bone permeation. Foci of osteochondroma with a cartilage cap and spongy bone were noted. Most chondrocytes exhibited mild atypia, though some areas displayed more pronounced atypia with multiple chondrocytes found within the lacunae. (H&E stained images; magnifications: x20, x40, x100, x200).

In our study, a single mass was identified in 78 of the 88 cases (88.6%), while multiple masses were present in 10 cases (11.4%). Among the 78 cases with a single mass, 42 (53.8%) were male and 36 (46.2%) were female. The ages of these patients ranged from 3 to 55 years, with a median age of 20 and an average age of 23.28. In contrast, of the 10 cases with multiple masses, 8 (80%) were male and 2 (20%) were female, with ages ranging from 3 to 38 years; the median age was 20 and the average age was 19.3. Comparison of the ages of patients with single versus multiple masses revealed no statistically significant difference between the two groups ($p = 0.576$).

Among the 10 cases with multiple masses, the most common location was the distal femur (n = 3, 33.3%), followed by the humerus and proximal tibia (n = 2, 20% each), and the proximal femur, fibula, and toes (n = 1, 10% each). Radiographic images of osteochondromas, which can present as solitary or multiple masses in bone, are depicted in Figure 8.

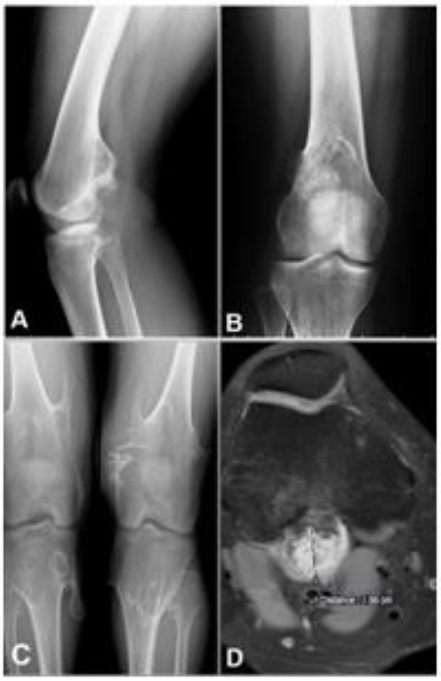

Figure 8: Direct Radiographs and MRI Examinations of The Case Were Conducted

Figure 8: A and B: Lateral and anteroposterior (AP) X-rays of the knee, showing a sessile osteochondroma located at the distal metaphysis of the femur, presenting as a bony exostosis continuous with the medullary bone. **C:** AP view X-ray of both knees demonstrating multiple pedunculated osteochondromas originating from the metaphyses of the bilateral femurs, tibias, and fibulas, typically projecting away from the epiphysis. **D:** Axial proton density (PD) fat-saturated MRI of the distal femur revealing a benign osteochondroma located at the distal metaphysis, with a cartilage cap measuring less than 2 cm in thickness.

DISCUSSION and CONCLUSION

It has been reported that osteochondromas are three times more common in men than in women (22,23). In another study, the incidence of osteochondroma in women was found to be half that of men (24). A study that focused solely on solitary osteochondromas did not identify a significant difference between male and female patients (25). In our study, we observed a higher prevalence of osteochondromas among male cases (n: 50, 56.8%) compared to female cases (n: 38, 43.2%). Additionally, we noted a greater proportion of osteochondromas in patients with multiple lesions than in those with solitary tumors.

Research indicates that osteochondromas are predominantly observed during the first and second decades of life (24,26,27). In our cohort, which included cases ranging from 3 to 58 years of age, we found that the majority fell within the first and second decades (mean age: 22.83 years; median age: 20 years), consistent with existing literature.

In a study comprising fifty-six cases, it was reported that a small subset exhibited symptoms of pain and localized swelling, while the remainder were diagnosed incidentally through radiographs taken for other reasons (28). In our study, we found that patients most frequently presented to the clinic with complaints of pain (n: 32, 58.1%), followed by swelling (n: 18, 32.7%). Among the five cases (9%) that experienced limited movement in conjunction with pain, one case had a notable history of trauma. Additionally, two cases were incidentally diagnosed with osteochondroma following trauma. Painless swelling was reported in 31 cases (35.2%), with cosmetic concerns identified in one instance.

Most of the cases associated with limited mobility involved masses located in bones related to the hip joint, specifically the iliac bone, proximal femur, and intra-articular regions. Although rare, osteochondromas can lead to compression of adjacent neurovascular structures, resulting in entrapment neuropathy of deep nerves. Neurological symptoms such as radiculopathy and myelopathy may arise in tumors that grow toward the spinal canal (29, 30).

Osteochondromas are most commonly found in the distal femur (30%), followed by the proximal tibia (15-20%), humerus (10-20%), hands and feet (10%), pelvis (5%), scapula (4%), and vertebrae (2%) (31). While the literature indicates that these tumors are predominantly detected in the knee region, one study identified the distal fibula as the third most common site, displacing the humerus from that position (24). In our study, the tumor was most frequently localized in the distal femur (n: 33, 37.5%), with the proximal tibia being the second most common site (n: 14, 15.9%). Notably, the mass was located around the knee in the majority of cases (47 cases, 53.4%).

Osteochondromas have been reported in the rib cage and pelvis in approximately 5% of cases, with an even smaller proportion found in the vertebrae (32,33). In our study, no tumors were detected in the rib cage; however, a higher incidence of tumors was noted in the iliac bone (4.5%, n: 4) compared to existing literature. Additionally, we documented one case each in the vertebra and scapula, which represent rare localizations.

In a study evaluating seven hundred and forty-eight solitary osteochondromas, tumors were identified in the bones of the foot in 10 cases, with only 2 of these located specifically in the forefoot bones (20). In our study, osteochondromas were observed in the toes in 3 cases (3.4%) and in the metatarsal bones in 1 case (1.1%). Additionally, tumors were detected in the fingers of the hands in 6 cases (6.8%) and in the metacarpal bones in 2 cases (2.3%).

According to Lichtenstein et al., the prevailing hypothesis is that osteochondromas arise spontaneously as a result of a reaction in the periosteum, triggered by rapid proliferation (34,35). Conversely, other authors propose that the development of osteochondromas may be attributed to endogenous factors (genetic predisposition) or exogenous influences (such as trauma or radiation) (11,22).

Osteochondroma can have several mimics, including subungual exostosis, bizarre parosteal osteochondromatous proliferation (BPOP), also known as Nora lesion, florid reactive periostitis, dysplasia epiphyseal hemimelica (Trevor disease), and turret exostosis (16).

The NORA lesion, also known as bizarre parosteal osteochondromatous proliferation, is a benign bone lesion characterized by a high recurrence rate and various morphological findings. It is primarily observed in the small bones of the hands, infrequently in the bones of the feet, and very rarely in larger bones (36). During our study, a case of NORA lesion that posed a challenge for differential diagnosis was identified in our archives. This case involved a 15-year-old male patient, in whom the lesion was localized to the second metacarpal region of the hand and was noted to have local recurrences during follow-up in the clinic. Histopathological examination revealed bone trabeculae and cartilage areas within the stroma, characterized by spindle cell proliferation on the bone surface, which showed no connection to the underlying bone cortex. Occasional nuclear enlargement of chondrocytes was also observed.

In addition to NORA lesion, the differential diagnosis encompasses parosteal osteosarcoma, subperiosteal hematoma, exostoses (including Dupuytren and turret exostoses), and enchondromas, all of which lack continuity with the intact bone medulla (37). The assessment of continuity with the bone medulla is crucial for making an accurate histopathological diagnosis.

Osteochondromas can lead to neurological complications in the extremities due to pressure exerted on nearby nerves, as well as vascular complications arising from pressure on vascular structures. Neurological issues may manifest as neuropathic pain or result in a loss of strength. Vascular complications can range from thrombosis to alterations in blood flow, potentially leading to ischemia due to insufficient nutritional supply to the tissues (2). The overall prognosis for osteochondromas is very favorable, with a recurrence rate estimated at approximately 2% (38). In our cases, no additional complications were reported following surgery, and no recurrences were observed.

Although a definitive diagnosis is established histopathologically, pathognomonic features of osteochondromas can often be identified through plain radiographic imaging. These lesions may appear as stalked or flat protrusions emerging from the surface of the bone and are typically located in areas where tendons attach to long bones, which can result in widening of the metaphysis. Expected radiographic findings include calcifications or linear extensions within the cartilage structure (39). In our study, the final diagnosis was achieved by analyzing the radiological images of the cases and correlating our histopathological findings with clinical and imaging data.

The periosteal reaction and the irregularity of tumor edges observed in osteosarcoma, which is included in the differential diagnosis on imaging, are significant diagnostic factors (40). Secondary osteosarcoma, which may arise from osteochondroma, is exceedingly rare (41). In our study, no instances of osteosarcoma secondary to osteochondroma were identified.

Chondrosarcoma is characterized by a low signal on diffusion-weighted MRI (26). In cases of malignant transformation, the thickness of the cartilage cap and the enhancement of septa using gadolinium are critical for diagnosis (42). Distinguishing between osteoblastic proliferation observed in chondrosarcoma and endochondral ossification seen in osteochondroma can be challenging using bone scintigraphy. Positron emission tomography (PET) may aid in grading and diagnosing chondrosarcoma; however, it is important to note that abnormal glucose retention can occur in osteochondromas, which are common in the pediatric population and continue to grow during this period (43). A study examining solitary osteochondromas over a span of 32 years reported recurrence in six cases, with secondary chondrosarcoma detected in two (43). It is estimated that 80% of secondary chondrosarcomas develop from osteochondroma. These secondary chondrosarcomas typically present at an earlier age (approximately 35 years) compared to primary chondrosarcomas, with a reported risk of malignant transformation of about 2% in cases with chondromatosis. Notably, nearly half of these cases involve the pelvic bone (9). In our study, we documented the development of grade II chondrosarcoma from osteochondroma in a 45-year-old male patient (1.1%). No malignant transformations were noted in the other cases, and the chondrosarcoma was identified as a single mass located in the distal femur.

The incidence of secondary chondrosarcomas arising from osteochondromas is estimated at 1-2%. While this rate is elevated in cases of osteochondromatosis, the actual percentage may be lower, as many solitary osteochondromas remain asymptomatic and are often discovered incidentally (26). In another study, it was determined that 81% of 151 chondrosarcoma cases developed from osteochondroma (44). In our study, no malignant transformations were observed in any of the multiple osteochondroma cases.

Secondary chondrosarcomas are typically diagnosed in individuals in their fifth and sixth decades, whereas primary chondrosarcomas are generally identified at a younger age (45). The case of grade II chondrosarcoma arising from osteochondroma that we documented in our study was in a 45-year-old patient, aligning with the typical age range for secondary chondrosarcomas.

Microscopic examination reveals several signs indicative of malignant transformation, including increased mitosis, atypical mitosis, necrosis, hypercellularity, cystic and myxoid changes, distortion of architecture, and nuclear pleomorphism (45). In the histopathological analysis of the grade II chondrosarcoma arising from osteochondroma, identified in our study, the tumor exhibited lobulated cellular morphology of hyaline cartilage with evidence of bone permeation. Mild atypia was noted in most areas, while atypical features became more pronounced in certain regions, where multiple chondrocytes were observed within the lacunae.

For symptomatic osteochondromas, particularly those with cosmetic concerns, irregular borders, radiolucent foci, or suspicious imaging characteristics such as bone destruction, the most appropriate management involves radical excision that includes the cartilage cap. This should be accompanied by close clinical follow-up to monitor for potential recurrence, and postoperative radiotherapy should be considered if necessary. Additionally, in cases where the tumor's localization may lead to instability after procedures such as laminectomy or fasciectomy, surgical stabilization is recommended. Although malignant transformation is infrequent, careful assessment is warranted in cases where the cartilage cap measures over 3 cm, particularly in conditions like Multiple Hereditary Exostoses (MHE), where the risk of malignant transformation is elevated. In such scenarios, postoperative radiotherapy should be considered alongside rigorous clinical and radiological follow-up (46,16).

Osteochondroma is primarily a benign bone tumor that is more prevalent in males and is most commonly located in the distal femur. Patients typically present with complaints of pain, although recurrence is rarely observed. While the majority of osteochondromas occur in long bones, they may manifest with atypical localizations and clinical presentations. Osteochondromas can be solitary or multiple, with most cases being solitary in nature. It is important to remain vigilant for the possibility of malignant transformation, albeit rare, occurring in association with osteochondroma.

Declaration of Ethical Code: This retrospective study was approved by the ethics committee of our institution with date and number 27/12/2023/20.478.486/2172

REFERENCES

1. Er, M.S., H. Atmaca, and L. ALTINEL, 2014. Radius başında osteokondrom. Abant Tıp Dergisi, 3(1), 81-83.
2. Tepelenis, K., et al., 2021. Osteochondromas: An updated review of epidemiology, pathogenesis, clinical presentation, radiological features and treatment options. in vivo, 35(2), 681-691.
3. Yang, C., et al., 2019. Insights into the molecular regulatory network of pathomechanisms in osteochondroma. Journal of Cellular Biochemistry, 120(10), 16362-16369.
4. Mundy C, et al., 2022. Osteochondroma formation is independent of hepa- ranase expression as revealed in a mouse model of hereditary multiple exostoses. J Orthop Res: (Epub ahead of print).
5. Tepelenis K, et al,. 2021. Osteochondromas: An updated review of epidemiology, pathogenesis, clinical presen- tation, radiological features and treatment options. In Vivo 35: 681-691.
6. Bukowska-Olech E, et al., 2021. Hereditary multiple exostoses-a review of the molecular back- ground, diagnostics, and potential therapeutic strategies. Front Genet 12: 759129.
7. Inubushi T, et al., 2018. Palovarotene inhibits osteochondroma formation in a mouse model of multiple hereditary exostoses. J Bone Miner Res 33: 658-666.
8. Ishimaru D, et al,. 2016. Large-scale mutational analysis in the EXT1 and EXT2 genes for Japanese patients with multiple osteochon- dromas. BMC Genet 17: 52.
9. Weinschenk, R.C., W.-L. Wang, and V.O. Lewis, 2021. Chondrosarcoma. JAAOS-Journal of the American Academy of Orthopaedic Surgeons, 29(13), 553-562.
10. Dahlin, D.C., Charles C, 1996. Bone Tumors. General Aspect and Data on 11087 Cases. 451-463p.
11. Garcia, R.A., C.Y. Inwards, and K.K. Unni, 2011.Benign bone tumors—recent developments. in Seminars in diagnostic pathology. Elsevier.73-85p.
12. Lotfinia, I., et al., 2010. Neurological manifestations, imaging characteristics, and surgical outcome of intraspinal osteochondroma. Journal of Neurosurgery: Spine, 12(5), 474-489.
13. Garcia SA, et al., 2020. Understanding the Effect of RARγ Agonists on Human Osteochondroma Explants. Int J. Mol Sci. 21 (8).
14. Inubushi T, et al., 2018. Prevents Osteochondroma Formation in a Multiple Hereditary Exostoses Fee Model. J Bone Miner Res. 33 (4):658-666.

15. Bovée, J.V., 2008. Multiple osteochondromas. Orphanet journal of rare diseases, 3, 1-7.
16. Alabdullrahman LW, Mabrouk A, and Byerly DW. 2024. Osteochondroma. ls (Internet). Treasure Island (FL): StatPearls Publishing; PMID: 31335016.
17. Nazeri E, et al., 2023. Chondrosarcoma: an overview of behavior, treatment mechanism, clinical drug therapy, and potential therapeutic targets. Crit Rev Oncol Hematol. Nov; 131 :102-109.
18. Sarrion P, et al. 2013. Mutations in the EXT1 and EXT2 genes in Spanish patients with multiple osteochondromas. Scientic Reports 3:1346.
19. Limaiem F, Davis DD, and Sticco KL. 2023. Chondrosarcoma. Treasure Island (FL): PMID: 30844159.
20. Mehta, M., et al., 1998. MR imaging of symptomatic osteochondromas with pathological correlation. Skeletal radiology, 27, 427-433.
21. Hill, C.E., L. Boyce, and I.D. van der Ploeg, 2014. Spontaneous resolution of a solitary osteochondroma of the distal femur: a case report and review of the literature. Journal of Pediatric Orthopaedics B, 23(1), 73-75.
22. Chatzidakis, E., et al., 2007. A rare case of solitary osteochondroma of the dens of the C2 vertebra. Acta neurochirurgica, 149, 637-638.
23. Govender, S. and A. Parbhoo, 1999. Osteochondroma with compression of the spinal cord: a report of two cases. The Journal of Bone & Joint Surgery British Volume, 81(4), 667-669.
24. Tong, K., et al., 2017. Osteochondroma: Review of 431 patients from one medical institution in South China. Journal of bone oncology, 8,. 23-29.
25. Shapiro, F., S. SIMoN, and M.J. Glimcher, 1979. Hereditary multiple exostoses. Anthropometric, roentgenographic, and clinical aspects. JBJS, 61(6), 815-824.
26. Kitsoulis, P., et al., 2008. Osteochondromas: review of the clinical, radiological and pathological features. In vivo, 22(5), 633-646.
27. Souza, A.M.G.d. and R.Z. Bispo Júnior, 2014. Osteochondroma: ignore or investigate? Revista brasileira de ortopedia, 49, 555-564.
28. Bailescu, I., et al., 2022. Diagnosis and evolution of the benign tumor osteochondroma. Experimental and Therapeutic Medicine, 23(1), 1-6.
29. Genç B, et al., 2014. Distal tibial osteochondroma causing fibular deformity and deep peroneal nerve entrapment neuropathy: a case report. Acta Orthop Traumatol Turc. 48(4):463-6. doi: 10.3944/AOTT.2014.2741. PMID: 25230273
30. Güney B, Doğan E, and Özdemir MY. 2021. Osteochondroma as a Cause of Ischiofemoral Impingement - First Case Series. Acta Med Litu. 2021;28(1):189-194. doi: 10.15388/Amed. PMC8311847.
31. Douis, H. and A. Saifuddin, 2012. The imaging of cartilaginous bone tumours. I. Benign lesions. Skeletal radiology, 41, 1195-1212.
32. Roach, J.W., J.W. Klatt, and N.D. Faulkner, 2009. Involvement of the spine in patients with multiple hereditary exostoses. JBJS, 91(8), 1942-1948.
33. Murphey, M.D., et al., 2000. Imaging of osteochondroma: variants and complications with radiologic-pathologic correlation. Radiographics, 20(5), 1407-1434.
34. Unni, K.K. and C.Y. Inwards, 2010. Dahlin's bone tumors: general aspects and data on 10,165 cases. Lippincott Williams & Wilkins.
35. Alabdullrahman LW, Mabrouk A, and Byerly DW. 2024. Osteochondroma. ls (Internet). Treasure Island (FL): StatPearls Publishing; PMID: 31335016.
36. Wittesaele, W., L. Vanbecelaere, and M. Mombert, 2021. Excision of a bizarre parosteal osteochondromatous proliferation (“Nora lesion”) in the hand: A case report. Int J Case Rep Orthop, 3(1), 1-3.
37. Yildirim, C., et al., 2010. Giant solitary osteochondroma arising from the fifth metatarsal bone: a case report. J Foot Ankle Surg, 49(3), 298.e9-298.e15.
38. Rajappa, S., M.M. Kumar, and S. Shanmugapriya, 2013. Recurrent solitary osteochondroma of the metacarpal: a case report. Journal of Orthopaedic Surgery, 21(1), 129-131.
39. RC, M., 1971. Cartilaginous tumors of the ribs. Cancer, 27, 794-801.
40. Park, Y.-K., et al., 1995. Dedifferentiated chondrosarcoma arising in an osteochondroma. Skeletal radiology, 24, 617-619.
41. Bovée, J., et al., 2002. Intermediate grade osteosarcoma and chondrosarcoma arising in an osteochondroma. A case report of a patient with hereditary multiple exostoses. Journal of clinical pathology, 55(3), 226-229.
42. Lamovec, J., M. Špiler, and V. Jevtić, 1999. Osteosarcoma arising in a solitary osteochondroma of the fibula. Archives of Pathology and Laboratory Medicine, 123(9), 832-834.
43. Hudson, T.M., F.S. Chew, and B.J. Manaster, 1983. Scintigraphy of benign exostoses and exostotic chondrosarcomas. AJR Am J Roentgenol, 140(3), 581-6.
44. Horvai, A. and K.K. Unni, 2006. Premalignant conditions of bone. J Orthop Sci, 11(4), 412-23.
45. Ahmed, A.R., et al., 2003. Secondary chondrosarcoma in osteochondroma: report of 107 patients. Clin Orthop Relat Res, (411), 193-206.
46. Kullukçu Albayrak H, et al., 2021. Solitary thoracic osteochondroma causing spinal compression: Case report. Acta Orthop Traumatol Turc. Jan;55(1):76-79. PMID: 33650517; PMCID: PMC7932743.