wjpmr, 2024, 10(2), 72-78

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

AN UP TO DATE REVIEW AND FUTURE PERSPECTIVES OF OSTEOCHONDROMA: FOCUS ON CURRENT AND EMERGING MANAGEMENT STRATEGIES

Muhzina Rahim[1]* and Sini S. G.[2]

[1]Sixth Year Pharm D, The Dale View College of Pharmacy and Research Centre Punalal PO Poovachal Thiruvananthapuram.

[2]Assistant Professor, Department of Pharmacy Practice, The Dale View College of Pharmacy and Research Centre Punalal PO, Poovachal Thiruvananthapuram.

***Corresponding Author: Muhzina Rahim**

Sixth Year Pharm D, The Dale View College of Pharmacy and Research Centre Punalal PO Poovachal Thiruvananthapuram.

Article Received on 03/12/2023 **Article Revised on 23/12/2023** **Article Accepted on 13/01/2024**

ABSTRACT

Osteochondroma is a benign tumour that appears in childhood or adolescence. Aberrant growth occur in the surface of a bone close to the growth plate. It affects the shoulder blade, the pelvis, or the long bones of the leg. Although rare, spinal osteochondromas can happen. One pathognomonic characteristic that confirms the diagnosis is the presence of cortical and medullary continuity between the tumour and the underlying bone. The most frequent type of benign bone tumour is osteochondroma. It can occur as solitary or multiple. Most solitary osteochondromas are caused by mutations in a single gene called EXT-1, which promotes the growth of the cartilage cap and the synthesis of bone. Multiple osteochondromas are a frequent side effect of growing up, as the alterations in the EXT-1 and EXT-2 genes linked to multiple hereditary exostosis. Approximately 20-50% of benign bone tumours and 9 % of all bone tumours are osteochondromas. However, In both condition solitary and multiple osteochondroma, malignant transition from osteochondroma to osteosarcoma is conceivable. However, the majority of them don't cause any symptoms, but depending on the location and size, they can produce mechanical symptoms such as hard palpable lump (most common), nerve compression, vascular compression, bursal formation, bursitis, osteoarthritis from secondary joint deformity, fracture post-trauma. Mostly treatment for the majority of osteochondromas is observation alone, as they are accidental discoveries. They can be disregarded if they are asymptomatic. As of right now, osteochondroma has no recognised medical treatment. For symptomatic lesions, excision is the preferred course of treatment. The patient can typically resume activities as tolerated in cases of osteochondromas.

KEYWORDS: Osteochondroma, Benign Bone Tumour, EXT-1, EXT-2, Hard Palpable Lump, Excision.

INTRODUCTION

An osteochondroma is a benign, cartilaginous tumour (Non cancerous) that develops enchondral bone formation during its development. The World Health Organization (Who) defines osteochondroma isa bony protrusion on the outside of a bone that is covered in cartilage.[1] They are surface bone lesions covered with hyaline cartilage caps that are made of both cortical and medullary bone. Though it can occur in any bone, it is most frequently observed around the knee and proximal humerus. Although spinal osteochondroma are rare. Among other consequences it may frequently cause osseous deformities, fractures, bursa formation with or without bursitis, vascular compromise, neurologic complaints, and malignant transformation, among other consequences.[6][11] The diagnosis is established by the pathognomonic feature of the tumor's cortical and medullary continuity with the underlying bone.[2] It is an aberrant growth that appears on a bone's surface close to the growth plate. It should develop in childhood or adolescence.[3]

It can be developed as solitary or multiple.Solitary osteochondromas are assumed to be the most prevalent type of bone tumour, because they make up 35 to 40% of all benign bone tumours. In addition to not spreading to other areas of the body. A stalk or stem protruding from the normal bone may be present on this bone protrusion. The structure is known as pedunculated if the tumour has a stalk. Sessile tumour outgrowths have a wider base and are linked to the bone.[4] Multiple Hereditary Exostosis (MHE), also known as familial osteochondromatosis, is an autosomal dominant condition that manifests as a multiple form.[2][5] Additionally, it's called as multiple osteochondromatosis, multiple osteocartilaginous exostosis, or diaphyseal aclasia.Tumours can become

sessile or pedunculated. In more extreme situations, MHE may result in aberrant bone growth.

In more serious situations, MHE may result in aberrant bone growth. For instance, a lot of patients havediminutive size, knees and ankles bent inward, abnormalities of the hands or forearms. Children with severe MHE are generally diagnosed at an early age because of these more visible symptoms. But just like isolated osteochondroma, modest MHE could not show symptoms until early adulthood. The risk of these benign tumors changing to chondrosarcoma is more common in patients with MHE, andhas having lifetime risk of approximately 10% for chondrosarcoma. In patients having single osteochondroma, risk of malignant transformation is about less than 1%.[5]

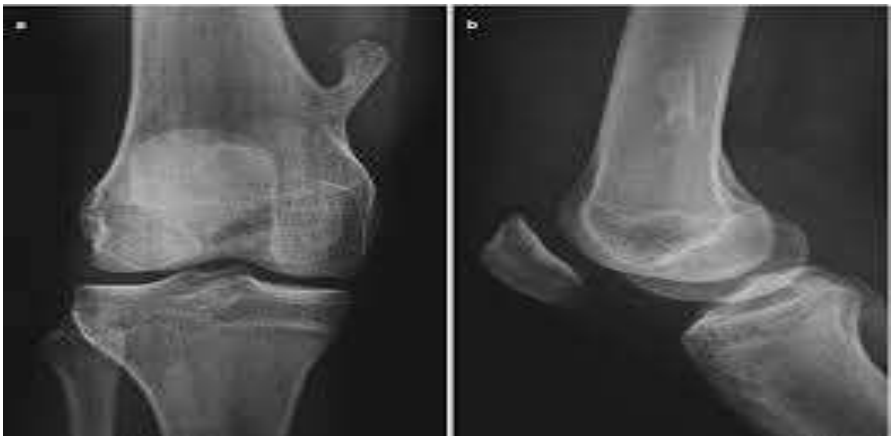
Types of osteochondroma

Osteochondromas can be classified based on various factors, including their number, location, and whether they occur as isolated (solitary) lesions or as part of a genetic condition. Following are the classifications.

1. **Solitary osteochondroma:** One kind of benign bone tumour called a solitary osteochondroma usually affects the long bones, like the tibia or femur. It is the most prevalent benign bone tumour, usually developing in childhood or adolescence but sometimes in adulthood. Approximately 35% of benign bone tumours are osteochondromas. Theyare benign tumour and often grow slowly. They never spread to other body parts.

During the growth period, the epiphyseal plate, or growth plate, of the bone, gives birth to these tumours. This is why they are frequently found in people who are still developing.Osteochondromas that are solitary usually manifest as bony protrusions or outgrowths called exostosis, which are covered in a cartilage cap. Osteochondromas are identified by their cartilage cap.Solitary osteochondromas are most frequently found in the metaphysis, or wider portion of the long bones at the growth plate, particularly in the knee region.

The first diagnosis of osteochondromas is frequently made via X-rays. A bony protrusion with a cartilage cap is one of the distinguishing features. To conduct a more thorough assessment, additional imaging modalities like MRI might be utilised. As long as there are no symptoms, the majority of solitary osteochondromas can be left untreated. That being said, surgical excision might be considered if the tumour is painful, impairs joint function, or poses a risk of consequences.[4]



Multiple hereditary exostosis

Multiple osteochondromas (MO) are a hereditary condition known as Multiple Hereditary Exostoses (MHE). Benign bone tumours called osteochondromas usually develop close to the ends of long bones. Multiple osteochondromas are developed in individuals with MHE. During childhood, these tumours typically form in the vicinity of the development plates of long bones, and they grow larger as the bones do.

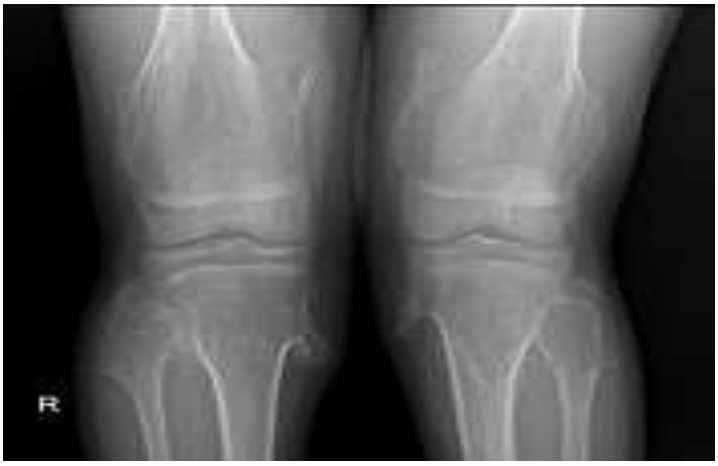
A common cause of MHE is a mutation in one of the EXT genes, which is inherited autosomally dominantly. EXT1 and EXT2 are the two primary genes linked to MHE. Even within the same family, affected people can differ greatly in the severity of MHE. While some may have several tumours causing serious functional issues, others may just have a few osteochondromas with little effect.

In MHE, osteochondromas frequently impair the metaphyses of long bones, including the humerus, tibia, and femur. Typically, the lower leg and forearm bones are affected. People with MHE have a marginally elevated risk of malignant development into chondrosarcoma, despite the fact that osteochondromas are usually benign. To find any indications of malignant change, routine monitoring is advised.

Pain, reduced joint movement, and abnormalities are possible symptoms. The number and location of osteochondromas can affect the clinical presentation.By detecting mutations in the EXT1 or EXT2 genes, genetic testing can validate the diagnosis of MHE. Imaging tests,

like MRIs and X-rays, are used to find and keep track of osteochondromas.

Surgical excision of symptomatic osteochondromas may be necessary as part of treatment to address problems, pain, and limited functional ability. Maintaining vigilant surveillance and tracking out possible issues, such as cancerous metamorphosis, is crucial.[4][24]



Epidemiology

Osteochondromas account for 20-50% of benign tumours and 9% of all bone tumours, making them the most prevalent benign bone tumours.[2] But because many osteochondromas go undiagnosed, it is unknown how frequently they actually occur. Osteochondromas occur in a genetic multiple exostosis context in around 85% of cases, with the remaining 15% being solitary.[13]Additionally, the incidence varies according to the type. In comparison to HME, solitary osteochondroma occurs around six times more frequently.[14][15] It usually appears in the first four decades of life, and 75% of these lesions appear before the age of 20 with a predominance of men.[15]

According to estimates, 1.5% of the Western population will experience MHE annually, with a 1:50,000 incidence.[3] It affects almost 80% of patients in their first ten years of life [17][18] and it is more common in Caucasian[19] and males to females (3:1).[20][21]

An epidemiological study conducted in South China relatively recently revealed that osteochondromas are more common in the first two decades of life and are more common in men. However, compared to the reported rate in Western countries, only 14.7% of individuals with HME have a positive family history.[22]

The area around the knee is home to over half of them.[23] The humerus accounts for 10–20%, the proximal tibia for 15%, the distal femur for 30%, and the hands and feet for 10%. Long bones are the ideal location. Osteochondromas grow away from the joint and are located at the metaphysis in these bones.

Etiology

However the exact aetiology of these aberrant growth remains unknown, a peripheral section of the physis is hypothesised to herniate from the growth plate. This herniation could be caused by trauma, a perichondrial ring deficiency or it could be idiopathic.[5] In individuals with multiple hereditary exostoses (MHE), osteochondroma may manifest as a single lesion or as a component of many osteochondromas.[6] Most solitary osteochondromas are caused by mutations in a single gene called EXT-1, which promotes the growth of the cartilage cap and the synthesis of bone. This alteration does not impact the rest of the body or the person's family because it might happen randomly during growth. In contrast, the alterations in the EXT-1 and EXT-2 genes linked to multiple hereditary exostosis are inherited from parents at conception and impact every cell in an individual. As a result, it is typical for a child or adolescent to develop many osteochondromas as they grow.[7] Based on their aetiology, isolated osteochondromas are classified as primary or secondary osteochondromas. Primary osteochondroma develops naturally without any precipitating events. While secondary osteochondroma can develop as a result of trauma (Such as surgery or Salter-Harris fractures) or radiation exposure during childhood.[8][9]

Clinical manifestations

Most solitary osteochondromas are asymptomatic lesions that are unintentionally found on radiographs taken for symptoms that are not related.A mass, which may or may not be connected to pain, is the second most frequent appearance. For the most part, asymptomatic lesions can be safely disregarded and do not require treatment. Still, they need to be appropriately assessed when they hurt. Lesions exhibiting symptoms could besecondary to fracture, malignant transformation, compression of adjacent neurovascular structures, bursal formation and/or bursitis, or palpable mass.[2][5][6]

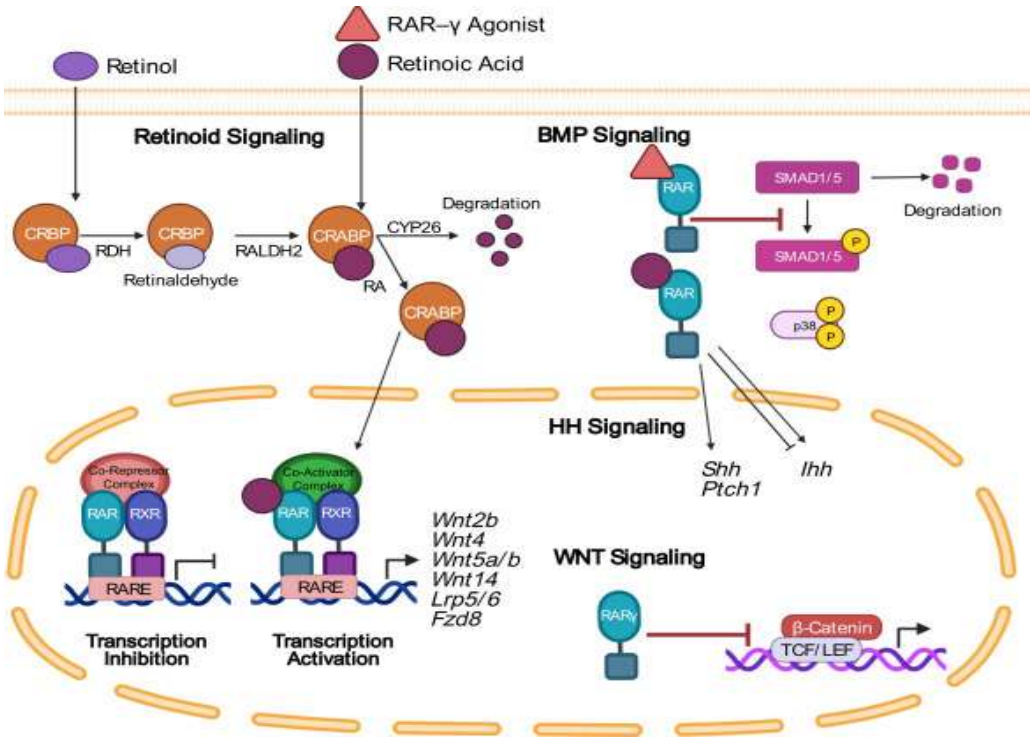
However most of the solitary osteochondromas are present as asymptomatic having painless mass. Most of them can grow until they reach skeletal maturity and may exhibit mechanical or neurovascular compression symptoms.

While Multiple hereditary exostosis (MHE) presented with deformity of knee, forearm, and ankle (Such asfemoral shortening and limb-length discrepancy, ankle valgus, coxa valga, knee valgus and patellar dislocation), Deformities of the upper extremities are usually tolerated and cause minimal function loss(Ulnar shortening, radial bowing and radial head dislocation) and having joint pain whichmay exhibit early OA symptoms. Adults with MHE who experience sudden start of pain should be suspicious for cancer.[10]

Pathophysiology

Osteochondroma is a type of hamartoma, with individuals often presenting in their second decade of life. Instead of being a true neoplasm, isolated osteochondromas could be the consequence of a developmental defect. The theory puts forth is that a piece of the growth plate herniates through the periosteum and then keeps growing, producing a sessile or pedunculated lesion, most frequently in the metaphysis region. Growth plate fragments can separate spontaneously (primary osteochondroma) or secondary (secondary osteosarcoma) as a result of radiation, surgery, or fractures. However, because researchers have discovered genetic abnormalities in the gene producing exostosin, subsequent investigations indicate that isolated osteochondromas actually represent benign neoplasms.[6][11]

The tumour suppressor genes EXT1 and EXT2, which are in charge of synthesising heparan sulphate proteoglycans (HSPG), have a loss-of-function type of mutation linked to the hereditary form of osteochondroma (HME). This mutation causes HSPG deficiency, which in turn leads to the development of multiple osteochondromas. Because of its capacity to interact with bone morphogenetic proteins (BMPs), which are crucial for controlling the production of new bone and cartilage, HSPG plays a significant role in the development of osteochondromas. HME is inherited in an autosomal dominant manner, with a male predominance and incomplete penetrance. HME is caused by a wide range of EXT mutations linked to the EXT1 and EXT2 genes. Patients that have EXT1 mutations typically have more severe symptoms (Such as osteochondromas and severe osseous abnormalities). It's interesting to note that different family members with the same EXT mutations display the HME severity differently, pointing to a complicated pathophysiology that is still poorly understood.



Diagnostic methods

The diagnosis of osteochondromas is usually achieved by a combination of imaging techniques, clinical examination, and occasionally biopsy. The following are typical techniques used to diagnose osteochondroma.

1. **Clinical examination**

- Medical history: The physician will obtain a thorough medical history, encompassing all symptoms, their duration, and any pertinent family history of such ailments.

- Physical examination: Using a thorough examination technique, the doctor will palpate the problematic area and look for any indications, such as a bony lump or restricted joint movement.

2. Imaging techniques

- X rays: Often, the initial imaging technique utilised to see bone structures is an X-ray. Usually, osteochondromas show up as a bony protrusion covered in cartilage.
- Computed Tomography (CT)scan: CT scans can be used to assess the extent of a lesion and its relationship to surrounding structures, and they offer more detailed images than X-rays.
- Magnetic resonance imaging (MRI): When evaluating soft tissues and distinguishing osteochondromas from other bone pathologies, magnetic resonance imaging (MRI) can offer valuable insights into the cartilaginous cap.

3. Occasionally biopsy

- Needle biopsy: A biopsy may be necessary in certain circumstances in order to remove tissue for analysis. This is not always required, though, as imaging tests and clinical observations can frequently be used to diagnose osteochondromas.
- Surgical excision biopsy: Resection of the lesion may be necessary if it is causing symptoms or if the diagnosis is unclear. After removal, the tissue is inspected under a microscope.

4. Genetic testing

Genetic testing may be considered in certain cases, particularly if there is a family history or several osteochondromas are present. Mutations in the EXT1 and EXT2 genes can be found through genetic testing, and hereditary multiple exostoses (HME) is a disorder linked to the formation of numerous osteochondromas.

Treatment

Osteochondroma is usually treated primarily with surgical removal, particularly if the lesion is painful, restricts movement of the affected joint, or results in additional problems. It is important to remember, though, that not all osteochondromas need to be treated; in fact, some cases may be watched without requiring emergency surgery.

An outline of the osteochondroma therapy options is provided below

1. **Observation:** Over time, osteochondromas that are asymptomatic and not causing discomfort or impairment to function may be monitored, particularly if they are not expanding or creating issues.

2. **Surgical excision**

- Osteochondromas that are troublesome or symptomatic are frequently surgically removed. The cartilaginous cap of the bony protrusion is removed during the surgical process.
- Relieving symptoms, enhancing joint function, and averting complications are the three main objectives of surgery. It is typically regarded as a therapeutic method for isolated osteochondromas.

3. **Physical therapy:** In the course of treatment, particularly following surgery, physical therapy may be advised. Strength, flexibility, and function of the joints can all be enhanced by it.

4. **Pain management:** Osteochondroma-related discomfort may be treated with over-the-counter or prescription painkillers, particularly if surgery is not scheduled right away or if the lesion is not producing significant symptoms.

5. **Monitoring and Follow UP:** Orthopaedic specialists should be seen on a frequent basis to monitor the growth of lesions that already exist and spot any new ones in people with multiple osteochondromas or disorders such as multiple hereditary exostoses (MHE).

Not to mention that less than 1% of osteochondromas will develop into malignant transformations, which is an incredibly unusual occurrence. Continuous monitoring is still advised, though, particularly if there is a family history of hereditary multiple exostosis or if numerous lesions are present.[4][5]

Surgical therapy of osteochondroma

Resection is the treatment for osteochondromas that present symptoms. If any cartilage cap or perichondrium is left in the resection bed, it needs to be carefully removed to prevent a recurrence. The tumour is removed in its entirety, together with its fibrous covering, when the line of resection passes through the base of the stalk. To rule out the rare chance of cancer, unusual or very large lesions should be thoroughly examined. Assessing cartilage-cap thickness can be done with MRI.

In patients with underdeveloped skeletons, caution needs to be exercised to prevent harm to the growth plate when exposing and excising the lesion. In a small study assessing the surgical outcomes of paediatric patients (average age, 3.6 years) with digital osteochondroma, early surgical intervention was advised to improve motion and prevent further deformity in the fingers in those with nonepiphyseal metaphysis of the bone; for laterally oriented tumours involving less than one third of the joint surface, tumour excision, possibly including part of the articular surface, was advised.[25][26]

Before beginning surgical treatment for these patients, it may be wise to take into account the likelihood that some occurrences of spontaneous regression of solitary osteochondromas in children have been documented.

Surgical preparation

Careful consideration of local anatomic restrictions is necessary to ensure that adjacent structures are not damaged during the approach and resection. For lesions originating from flat bones or situated in challenging regions, like lesions around the hip or scapula, computed tomography (CT) and magnetic resonance imaging (MRI) may be beneficial.

Operative details

Dissection of the osteochondroma is restricted to the lesion's base once it has been made visible, allowing an osteotome to be used to shear off the base at the level of the host bone cortex. It is important to take precautions to make sure the excision doesn't go too deep and compromise the normal host cortex or leave a residual lesion. The lesion and the bursa should be removed by slicing away the loose sticky tissue, leaving the overlying bursa intact.

If necessary, bone wax can be placed onto the sliced surface of the host bone to halt the bleeding after the resected surface has been rasped smooth.

The wound needs to be well-irrigated when the material is removed and pathologic confirmation is obtained. A surgical drain that exits in line with the wound might be inserted if necessary.[26]

Emerging therapy

Surgical excision is the main therapy for osteochondroma. Benign bone tumours called osteochondromas typically don't need to be treated unless they result in discomfort, strain on blood vessels or nerves, or other problems.Still, medical research and treatment modalities are always changing. There's a chance that osteochondroma management will progress and new treatments will appear. For the most recent information on new treatments, it is imperative to speak with an orthopaedic specialist or healthcare professional.

Research and Development in the following areas could be useful in treating osteochondroma

1. **Non surgical interventions:** To control symptoms or stop the formation of osteochondromas, researchers may look into non-surgical approaches such targeted therapy or pharmaceutical interventions.

2. **Genetic and Molecular therapies:** Targeted treatments that target the underlying factors that contribute to tumour formation may result from knowledge of the genetic basis of osteochondromas. Molecular interventions as well as gene treatments may be investigated.

3. **Minimally invasive techniques:** Technological developments in minimally invasive surgery could result in less intrusive methods for removing osteochondromas, which would shorten recovery times and minimise consequences.

4. **Biological therapies:** Researchers may look at biological therapies, which aim to improve bone healing and prevent tumour growth by utilising growth hormones, stem cells, or other biological agents.

5. **Imaging and Diagnosis:** Advances in imaging technologies should help identify osteochondromas earlier and more accurately, which could result in faster and more efficient therapies.

DISCUSSION AND CONCLUSION

Osteochondroma is a benign tumor projecting from external surface of a bone. It mainly occurs in the metaphyseal region of the long bones. In majority of cases, it will appears as a solitary lesion. In 15% of cases, it presents as multiple lesions due to EXT1 and EXT2 genes. Currently, the clinical approach is a careful follow up for osteochondroma until the masses grow to meet surgery application criteria. The tumor appears as a protuberance on the bone surface while calcified flakes can be present as well. Asymptomatic lesions require no treatment, whereas surgical indications encompass symptoms, complications, cosmetic reasons, malignant transformation or uncertain diagnosis. If complete resection is achieved, the recurrence rate is less than 2%.

REFERENCE

1. Ostensen H, Pettersson H, Davies AM, et al. The WHO manual of diagnostic imaging: radiographic anatomy and interpretation of the musculoskeletal system. World Health Organization, 2023; 31.
2. Alabdullrahman LW, Byerly DW. *Osteochondroma*. Treasure Island, FL: StatPearls, 2023.
3. Ryckx A, Somers JF, Allaert L. Hereditary multiple exostosis. Acta Orthop Belg, 2013.
4. https://orthoinfo.aaos.org/en/diseases--conditions.
5. https://emedicine.medscape.com/article.
6. Murphey MD, Choi JJ, Kransdorf MJ, Flemming DJ, Gannon FH. Imaging of osteochondroma: variants and complications with radiologic-pathologic correlation. Radiographics, 2000; 20.
7. Heinritz W, Hüffmeier U, Strenge S, Miterski B, Zweier C, Leinung S, et al. New mutations of EXT1 and EXT2 genes in German patients with Multiple Osteochondromas. *Ann Hum Genet*, 2009.
8. Douis H, Saifuddin A. The imaging of cartilaginous bone tumours. I. Benign lesions. Skeletal Radiol, 2012. Mavrogenis AF, Papagelopoulos PJ, Soucacos PN. Skeletal osteochondromas revisited. Orthopedics, 2008.
9. Mavrogenis AF, Papagelopoulos PJ, Soucacos PN. Skeletal osteochondromas revisited. Orthopedics, 2008; 31.
10. https://www.orthobullets.com/pathology

11. Garcia RA, Inwards CY, Unni KK. Benign bone tumors--recent developments. Semin Diagn Pathol, 2011.
12. Pacifici M. The pathogenic roles of heparan sulfate deficiency in hereditary multiple exostoses. Matrix Biol, 2018.
13. Tepelenis K, Papathanakos G, Kitsouli A, Troupis T, Barbouti A, Vlachos K, et al. Osteochondromas: An Updated Review of Epidemiology, Pathogenesis, Clinical Presentation, Radiological Features and Treatment Options. *In Vivo*, 2021.
14. Bovee JV*:* Multiple osteochondromas. *Orphanet J Rare Dis*, 2008; 3*:* 3.
15. Kostas tepelenis, georgios papathanakos, aikaterini kitsouli: Osteochondromas: An Updated Review of Epidemiology, Pathogenesis, Clinical Presentation, Radiological Features and Treatment Options Ryckx A, Somers JF, Allaert L. Hereditary multiple exostosis. Acta Orthop Belg, 2013.
16. Hennekam RC: Hereditary multiple exostoses. J MedGenet, 28(4).
17. Nawata K, Teshima R, Minamizaki T and Yamamot o K: Knee deformities in multiple hereditary exostoses. A longitudinal radiographic study. Clin Orthop Relat Res, 313: 194-199.
18. Kitsoulis P, Galani V, Stefanaki K, Paraskevas G, K aratzias G, Agnantis NJ and Bai M: Osteochondrom as: review of the clinical, radiological and pathological features. In Vivo, 2008; 22(5): 633-646.
19. Chatzidakis E, Lypiridis S, Kazdaglis G, Chatzikons tadinou K and Papatheodorou G: A rare case of solitary osteochondroma of the dens of the C2 vertebra. Acta Neurochir (Wien), 2007; 149(6): 637-638. PMID: 17450439.
20. Govender S and Parbhoo AH: Osteochondroma with compression of the spinal cord. A report of two cases. J Bone Joint Surg Br, 1999; 81(4): 667-669.
21. Tong K, Liu H, Wang X, Zhong Z, Cao S, Zhong C, Yang Y and Wang G: Osteochondroma: Review of 431 patients from one medical institution in South China. J Bone Oncol, 2017; 30: 23-29.
22. Galasso O, Mariconda M and Milano C: An enlarging distal tibia osteochondroma in the adult patient. J Am Podiatr Med Assoc, 2009; 99(2): 157-161.
23. https://www.hss.edu/conditions
24. Ohnishi T, Horii E, Shukuki K, Hattori T. Surgical treatment for osteochondromas in pediatric digits. *J Hand Surg Am*, 2011.
25. Kim JI, Kwon JH, Park YJ, D'Almeida VR, Soni SM, Nha KW. Arthroscopic Excision of Solitary Intra-articular Osteochondroma of the Knee. *Knee Surg Relat Res*, 2013; 25.