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World J Clin Cases 2022 September 6; 10(25): 8808-9179



Contents

Thrice Monthly Volume 10 Number 25 September 6, 2022

MINIREVIEWS

- 8808** Ear, nose, and throat manifestations of COVID-19 and its vaccines
Al-Ani RM
- 8816** Potential influences of religiosity and religious coping strategies on people with diabetes
Onyishi CN, Eseadi C, Ilechukwu LC, Okoro KN, Okolie CN, Egbule E, Asogwa E

ORIGINAL ARTICLE

Case Control Study

- 8827** Effectiveness of six-step complex decongestive therapy for treating upper limb lymphedema after breast cancer surgery
Zhang HZ, Zhong QL, Zhang HT, Luo QH, Tang HL, Zhang LJ

Retrospective Study

- 8837** Hospital admissions from alcohol-related acute pancreatitis during the COVID-19 pandemic: A single-centre study
Mak WK, Di Mauro D, Pearce E, Karran L, Myintmo A, Duckworth J, Orabi A, Lane R, Holloway S, Manzelli A, Mossadegh S
- 8844** Indocyanine green plasma clearance rate and 99mTc-galactosyl human serum albumin single-photon emission computed tomography evaluated preoperative remnant liver
Iwaki K, Kaihara S, Kita R, Kitamura K, Hashida H, Uryuhara K
- 8854** Arthroscopy with subscapularis upper one-third tenodesis for treatment of recurrent anterior shoulder instability independent of glenoid bone loss
An BJ, Wang FL, Wang YT, Zhao Z, Wang MX, Xing GY
- 8863** Evaluation of the prognostic nutritional index for the prognosis of Chinese patients with high/extremely high-risk prostate cancer after radical prostatectomy
Yang F, Pan M, Nie J, Xiao F, Zhang Y

Observational Study

- 8872** Chlorine poisoning caused by improper mixing of household disinfectants during the COVID-19 pandemic: Case series
Lin GD, Wu JY, Peng XB, Lu XX, Liu ZY, Pan ZG, Qiu ZW, Dong JG
- 8880** Mental health of the Slovak population during COVID-19 pandemic: A cross-sectional survey
Kralova M, Brazinova A, Sivcova V, Izakova L

Prospective Study

- 8893** Arthroscopic anatomical reconstruction of lateral collateral ligaments with ligament advanced reinforcement system artificial ligament for chronic ankle instability
Wang Y, Zhu JX

SYSTEMATIC REVIEWS

- 8906** How to select the quantitative magnetic resonance technique for subjects with fatty liver: A systematic review
Li YW, Jiao Y, Chen N, Gao Q, Chen YK, Zhang YF, Wen QP, Zhang ZM
- 8922** Lymphocytic choriomeningitis virus: An under-recognized congenital teratogen
Ferenc T, Vujica M, Mrzljak A, Vilibic-Cavlek T

CASE REPORT

- 8932** Alagille syndrome associated with total anomalous pulmonary venous connection and severe xanthomas: A case report
Zeng HS, Zhang ZH, Hu Y, Zheng GL, Wang J, Zhang JW, Guo YX
- 8939** Colo-colonic intussusception with post-polypectomy electrocoagulation syndrome: A case report
Moon JY, Lee MR, Yim SK, Ha GW
- 8945** Portal vein gas combined with pneumatosis intestinalis and emphysematous cystitis: A case report and literature review
Hu SF, Liu HB, Hao YY
- 8954** Quadricuspid aortic valve and right ventricular type of myocardial bridging in an asymptomatic middle-aged woman: A case report
Sopek Merkaš I, Lakušić N, Paar MH
- 8962** Treatment of gastric carcinoma with lymphoid stroma by immunotherapy: A case report
Cui YJ, Ren YY, Zhang HZ
- 8968** Gallstone associated celiac trunk thromboembolisms complicated with splenic infarction: A case report
Wu CY, Su CC, Huang HH, Wang YT, Wang CC
- 8974** Extracorporeal membrane oxygenation for lung cancer-related life-threatening hypoxia: A case report
Yoo SS, Lee SY, Choi SH
- 8980** Multi-disciplinary treatment of maxillofacial skeletal deformities by orthognathic surgery combined with periodontal phenotype modification: A case report
Liu JY, Li GF, Tang Y, Yan FH, Tan BC
- 8990** X-linked recessive Kallmann syndrome: A case report
Zhang P, Fu JY
- 8998** Delayed complications of intradural cement leakage after percutaneous vertebroplasty: A case report
Ma QH, Liu GP, Sun Q, Li JG

- 9004** Coexistent Kaposi sarcoma and post-transplant lymphoproliferative disorder in the same lymph nodes after pediatric liver transplantation: A case report
Zhang SH, Chen GY, Zhu ZJ, Wei L, Liu Y, Liu JY
- 9012** Misdiagnosis of pancreatic metastasis from renal cell carcinoma: A case report
Liang XK, Li LJ, He YM, Xu ZF
- 9020** Discoid medial meniscus of both knees: A case report
Zheng ZR, Ma H, Yang F, Yuan L, Wang GD, Zhao XW, Ma LF
- 9028** Simultaneous laparoscopic and arthroscopic excision of a huge juxta-articular ganglionic cyst compressing the sciatic nerve: A case report
Choi WK, Oh JS, Yoon SJ
- 9036** One-stage revision arthroplasty in a patient with ochronotic arthropathy accompanied by joint infection: A case report
Wang XC, Zhang XM, Cai WL, Li Z, Ma C, Liu YH, He QL, Yan TS, Cao XW
- 9044** Bladder paraganglioma after kidney transplantation: A case report
Wang L, Zhang YN, Chen GY
- 9050** Total spinal anesthesia caused by lidocaine during unilateral percutaneous vertebroplasty performed under local anesthesia: A case report
Wang YF, Bian ZY, Li XX, Hu YX, Jiang L
- 9057** Ruptured splenic artery aneurysms in pregnancy and usefulness of endovascular treatment in selective patients: A case report and review of literature
Lee SH, Yang S, Park I, Im YC, Kim GY
- 9064** Gastrointestinal metastasis secondary to invasive lobular carcinoma of the breast: A case report
Li LX, Zhang D, Ma F
- 9071** Post-bulbar duodenal ulcer with anterior perforation with kissing ulcer and duodenocaval fistula: A case report and review of literature
Alzerwi N
- 9078** Modified orthodontic treatment of substitution of canines by first premolars: A case report
Li FF, Li M, Li M, Yang X
- 9087** Renal cell carcinoma presented with a rare case of icteric Stauffer syndrome: A case report
Popov DR, Antonov KA, Atanasova EG, Pentchev CP, Milatchkov LM, Petkova MD, Neykov KG, Nikolov RK
- 9096** Successful resection of a huge retroperitoneal venous hemangioma: A case report
Qin Y, Qiao P, Guan X, Zeng S, Hu XP, Wang B
- 9104** Malignant transformation of biliary adenofibroma combined with benign lymphadenopathy mimicking advanced liver carcinoma: A case report
Wang SC, Chen YY, Cheng F, Wang HY, Wu FS, Teng LS

- 9112** Congenital hepatic cyst: Eleven case reports
Du CX, Lu CG, Li W, Tang WB
- 9121** Endovascular treatment of a ruptured pseudoaneurysm of the internal carotid artery in a patient with nasopharyngeal cancer: A case report
Park JS, Jang HG
- 9127** Varicella-zoster virus meningitis after spinal anesthesia: A case report
Lee YW, Yoo B, Lim YH
- 9132** Chondrosarcoma of the toe: A case report and literature review
Zhou LB, Zhang HC, Dong ZG, Wang CC
- 9142** Tamsulosin-induced life-threatening hypotension in a patient with spinal cord injury: A case report
Lee JY, Lee HS, Park SB, Lee KH
- 9148** CCNO mutation as a cause of primary ciliary dyskinesia: A case report
Zhang YY, Lou Y, Yan H, Tang H
- 9156** Repeated bacteremia and hepatic cyst infection lasting 3 years following pancreatoduodenectomy: A case report
Zhang K, Zhang HL, Guo JQ, Tu CY, Lv XL, Zhu JD
- 9162** Idiopathic cholesterol crystal embolism with atheroembolic renal disease and blue toes syndrome: A case report
Cheng DJ, Li L, Zheng XY, Tang SF
- 9168** Systemic lupus erythematosus with visceral varicella: A case report
Zhao J, Tian M

LETTER TO THE EDITOR

- 9176** Imaging of fibroadenoma: Be careful with imaging follow-up
Ece B, Aydın S

ABOUT COVER

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The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

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Chondrosarcoma of the toe: A case report and literature review

Li-Bo Zhou, He-Cheng Zhang, Zai-Gang Dong, Chao-Chao Wang

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Abstract

BACKGROUND

Chondrosarcoma of the foot is a rare malignant bone tumour, and it is even rarer when it originates in a toe bone. Surgical excision is the only effective treatment. The osteolytic destruction of the tumour severely affects limb function and carries the risk of distant metastasis. Most such tumours are removed surgically to minimize local recurrence and distant metastases, maximize limb function, and prolong the patient's tumour-free survival time. The main objective of this article is to present the case of a chondrosarcoma that invaded the first phalanx of the left foot and formed a large phalangeal mass with osteolytic destruction of the distal bone.

CASE SUMMARY

A 74-year-old man suffered from swelling of his left toe for six months, with pain and swelling for two months. Computed tomography and magnetic resonance imaging showed that the tumour on the first phalanx of the left foot was approximately 54.9 mm × 44.6 mm, surrounded by a significant soft tissue signal mass, with osteolytic destruction of the distal phalanx and a speckled bone-like high-density shadow within it.

CONCLUSION

Chondrosarcoma occurring in a toe bone is extremely rare. In this case, extensive surgical resection of the large low-grade chondrosarcoma, which showed osteolytic destruction and invaded the distal metatarsal bone, was safe and effective.

Key Words: Chondrosarcoma; Phalanges tumour; Diagnosis; Surgery; Case report

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Core Tip: The main objective of this article is to present a case of chondrosarcoma that invaded the first phalanx of the left foot and formed a sizeable phalangeal mass with osteolytic destruction of the distal bone. Chondrosarcoma originating in a toe bone has only been sporadically reported, and this case report will help clinicians better understand this rare lesion.

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INTRODUCTION

Chondrosarcoma is the second most common primary malignant tumour of bone, accounting for approximately 25% of all primary bone tumours. It has an annual incidence of approximately 6.63 per 1 million people and is characterized by the production of tumourigenic cartilage[1-3]. Chondrosarcoma can occur at any age, with a mean age of 50 years, and it affects slightly more men than women (55%: 45%)[4]. The anatomical sites most commonly involved in chondrosarcoma include the long tubular bone (40%), pelvis (25%), and scapula[3,5].

Chondrosarcoma of the foot is a rare malignant bone tumour. One study found that the prevalence of chondrosarcoma of the foot is approximately 3.0%, with the highest prevalence in the metatarsal bone, and the overall survival of chondrosarcoma of the foot is better than that of chondrosarcoma of other anatomical sites[6]. It is even rarer when it arises in phalanges, the incidence of which has not been clearly established and has rarely been reported in the literature. Chondrosarcoma is insensitive to radiation and chemotherapy; thus, surgery remains the preferred treatment modality. This case report expands the literature on chondrosarcoma of the toe and will help clinicians better understand this rare lesion.

CASE PRESENTATION

Chief complaints

A 74-year-old man suffered from swelling of his left toe for six months, with pain and swelling for two months.

History of present illness

A painless left calcaneal mass observed over six months presented with a rapidly enlarging mass, a significant increase in size, and localized symptoms of pain and swelling for two months.

History of past illness

He reported that he had noticed a mass on the lesser toe of his left foot that had gradually increased in size over the past six months and was not taken seriously.

Personal and family history

He had no family history of chondrosarcoma disease or any other disease.

Physical examination

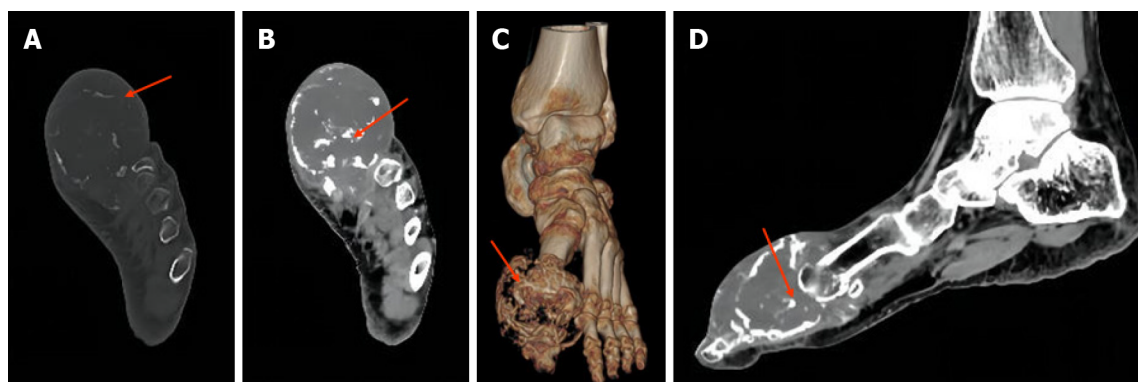
Physical examination showed swelling of the left calcaneus and a palpable round mass of approximately 60.0 mm × 50.0 mm in size with a mallet-like appearance. The mass was soft, with tenderness on palpation and indistinct borders. The movement of the interphalangeal joint and the metatarsophalangeal joint was limited. Other physical examination findings were normal.

Laboratory examinations

The results of routine blood tests and biochemical tests were normal.

Imaging examinations

Computed tomography (CT) and magnetic resonance imaging (MRI) showed a large tumour in the first phalanx of the left foot. A CT scan showed osteolytic destruction of the distal bone of the first phalanx of the left foot, with a local soft tissue density mass of approximately 54.9 mm × 44.6 mm, a local CT value of approximately 21 HU, and a speckled bone-like high-density shadow within it (Figure 1). MRI +



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Figure 1 Computed tomography imaging of chondrosarcoma of the toe. A: Osteochondrosarcoma of the first phalanx of the left foot (arrow) [computed tomography (CT) axial bone window] shows osteolytic destruction of the distal bone of this phalanx; B: Osteochondrosarcoma of the first phalanx of the left foot (arrow) (CT axial soft tissue window) shows the longest diameter of the local soft tissue mass with speckled bony hyperintensity; C: Osteochondrosarcoma of the first phalanx of the left foot (arrow) (CT 3D view) showing osteolytic destruction of the distal bone of this phalanx; D: Osteochondrosarcoma of the first phalanx of the left foot (arrow) (CT sagittal soft tissue window) shows the widest diameter of the local soft tissue mass and the relationship of the lesion to the adjacent phalanx with a speckled bony hyperdense shadow.

enhancement showed that the typical shape of the first phalanx of the left foot had disappeared, and a large soft tissue signal mass with equal length T1 Weighted Image (T1WI) signals was seen around it (Figure 2).

FINAL DIAGNOSIS

The final diagnosis was chondrosarcoma.

TREATMENT

The preoperative imaging findings were suggestive of malignant occupancy of the first phalanx of the left foot with the possible distal invasion of the adjacent metatarsals. All routine blood tests, biochemical tests, and chest radiographs were within normal limits, and parallel CT examinations of the head, chest, abdomen, and pelvis revealed no metastatic lesions or other tumourigenic lesions.

The patient and his family were informed of his condition based on the imaging findings and clinical symptoms. Due to the possibility of invasion of the adjacent distal metatarsal bone, the patient was advised to undergo extensive resection, and the patient and his family agreed. A joint surgeon performed the surgical treatment. The surgeon performed an osteotomy of the first phalanx of the left foot and distal bone removal of the adjacent metatarsal. The tumour tissue was excised and sent for histopathological examination.

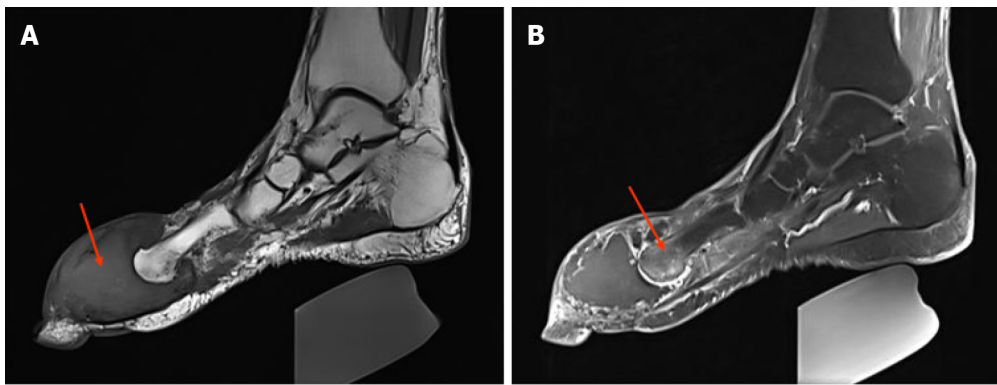
OUTCOME AND FOLLOW-UP

The pathological result was reported as highly differentiated cartilaginous sarcoma (low-grade malignancy) (Figure 3). The patient was followed up for 30 mo after surgery, and the patient was in good condition with no tumour recurrence or distant metastasis (Figure 4).

DISCUSSION

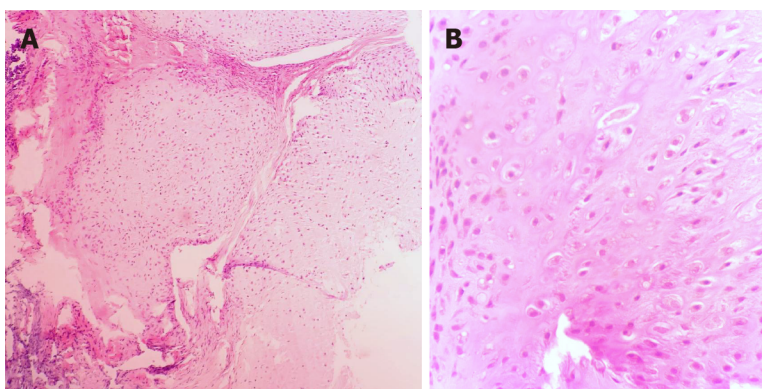
Clinical manifestations

Chondrosarcoma is a malignant tumour of mesenchymal cell origin that can be primary or secondary to benign cartilage tumours[7]. A common clinical symptom of chondrosarcoma is localized pain with or without a significant mass. Local pain is an essential feature for distinguishing chondrosarcoma from benign cartilage tumours. This pain is thought to be caused by invasive growth of the chondrosarcoma, and the pain increases with increasing malignancy. At first, the pain is often intermittent and mild, and then it gradually develops into persistent severe pain, nocturnal pain, and tenderness. When the



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Figure 2 Magnetic resonance imaging of chondrosarcoma of the toe. A: T1 weighted imaging shows a low-signal shadow of the mass (arrow); B: The mass enhances heterogeneously and is seen to strengthen with intracompartmental separation-like enhancement and a high-signal shadow distal to the metatarsal bone (arrow).



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Figure 3 Pathology of chondrosarcoma of the toe. A: Haematoxylin and eosin-stained section of the tumour ($\times 20$ magnification). Microscopically, there are many slightly heterotopic chondrocytes with large cell densities and binucleated and multinucleated types; B: Haematoxylin and eosin-stained section of the tumour ($\times 40$ magnification). Most of the tumour cells are well differentiated, and some hypertrophic nuclear, large, binucleated cells can be seen in the background of the tumour cartilage tissue, with differing degrees of cell heterogeneity and rare nuclear schizoporenia.



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Figure 4 Postoperative photos of the patient. The patient underwent resection of the first phalanx of the left foot + distal bone tumour of the adjacent metatarsal and was followed up for 30 mo after surgery.

tumours is located close to the joint, the movement of the joint can be limited, and the surrounding soft tissue mass can be easily palpated.

Imaging and pathology

Early diagnosis facilitates effective treatment and improves the prognosis of patients with chondrosarcoma. In addition to the above nonspecific symptoms and signs, the diagnosis of chondrosarcoma mainly relies on imaging evaluation and histopathological characterization. Compared with X-rays, CT is more reliable and sensitive for diagnosing chondrosarcoma, especially with small tumours or tumours that have complex anatomical locations. CT is superior to X-rays for the detection of calcifications[8]. The most common manifestations of chondrosarcoma on X-ray or CT are "ring", "arc," or "popcorn" calcifications and invasive growth; osteolytic changes are also common[9]. The specific imaging signs depend on the type and grade of the chondrosarcoma. Calcification of high-grade chondrosarcoma is rare.

For example, intramedullary chondrosarcoma often presents with osteolytic changes and osteosclerosis, often accompanied by calcification. In clear cell chondrosarcoma, calcification occurs in only 30% of cases. Dedifferentiated chondrosarcoma shows a "biphasic sign" on X-ray or CT. Its imaging manifestations are closely related to the two pathological components in the tumour and depends on the proportion of low-grade and high-grade areas of the lesion[8,10]. MRI is superior to the other techniques in terms of soft-tissue contrast. In typical cases, the edges of the lesion may show lobulated changes with a low or medium signal on T1WI and a high signal on T2 Weighted Image. The combination of MRI diffusion-weighted imaging and enhancement also allows for accurate staging of the lesion. Low-grade lesions tend to show interval and peripheral enhancement, whereas high-grade lesions tend to show diffuse enhancement of the solid component of the lesion, mostly accompanied by a large nonenhancing necrotic shadow[11].

Pathological classification of chondrosarcoma, according to the WHO classification of bone and soft tissue tumours in 2020, is divided into conventional, periosteal, and clear cell mesenchymal and dedifferentiated chondrosarcoma. Conventional chondrosarcoma is divided into grades I, II, and III[12]. Eighty-five percent of chondrosarcomas are primary and of the conventional type[1]. Chondrosarcomas are central (intramedullary), periosteal, or peripheral according to their location in the bone. Chondrosarcomas are classified into primary and secondary chondrosarcomas by the source[13]. Since the recurrence rate and prognosis of tumours after surgery for intermediate (locally invasive) atypical cartilaginous tumour/chondrosarcoma grade I (atypical cartilaginous tumour, ACT/chondrosarcoma grade I, CS1) differ significantly from site to site, mainly because the location of the tumour determines the prognosis, the new version of the guidelines split atypical cartilaginous tumour/chondrosarcoma grade I into ACT and CS1 based on the anatomical location, with the former retained in the intermediate type and the latter upgraded to malignant disease. The diagnosis of ACT occurring in the tubular bones of the extremities and the diagnosis of CS1 occurring in the mesial bones, such as the skull base, pelvis, and scapula, suggest the need for complete surgical resection[14].

Chondrosarcoma histological grade (Evans grade) is categorized as grade I (low grade), grade II (intermediate grade), or grade III (high grade). Grade I and II chondrosarcoma have a good prognosis, while grade III chondrosarcoma has a high recurrence and metastasis rate[15]. Grossly, the growth is lobulated, the cut surface is translucent or white with hyaline brittle tissue or even gel-like mucus, and cystic changes can be seen. It can be sandy due to calcification and can be rigid or soft. Microscopically, the density of grade I chondrocytes is low, the nucleus is fat and deeply stained, binucleate cells are occasionally seen, and there are no mitotic images. The density of grade II chondrocytes is increased, the nucleus is increased, the chromatin is thickened, heteromorphism and binucleate cells appear, and mitotic images can be seen. Grade III has a high cell density, with prominent atypia, pleomorphism, and mitotic images. Spindle cells around the leaflets are immature. Mutations of isocitrate dehydrogenase type 1 (IDH1) or isocitrate dehydrogenase type 2 (IDH2) may exist in primary central chondrosarcoma and periosteal chondrosarcoma[16].

Secondary chondrosarcoma

Secondary chondrosarcoma originates from osteochondroma or endogenous chondrosarcoma. Clinically, they present as new painful episodes of existing lesions, and their histological presentation is indistinguishable from that of primary conventional chondrosarcoma. Osteochondroma is one of the most common benign tumors of bone. Multiple cases often have a family history called hereditary multiple osteochondromas (HMOs), also known as hereditary multiple exostoses. HMO is an autosomal dominant inherited abnormality of skeletal development[17]. Osteochondromas account for approximately 80% or more of secondary chondrosarcomas. The average age at diagnosis is 35 years, which is much younger than that for primary chondrosarcoma.

For patients with isolated exophytic warts, the lifetime risk of malignant transformation is approximately 0.4%-2%, compared to 5%-25% for patients with HMO[18]. The cartilage cap indicates tumour malignancy, and MRI can show this structure. A larger cartilage cap can indicate malignancy, but there is no significant correlation between the thickness of the cartilage cap and the malignancy rate in young patients[19]. One study showed that for cartilage caps of approximately 2 cm, the sensitivity and specificity of MRI and CT were 100% and 98% and 100% and 95%, respectively[20]. However, imaging and clinical aspects are vital because marginal cartilage caps with stable clinical and imaging presentation are unlikely to be cancerous, whereas rapid enlargement may indicate malignant changes.

Chondroma is a common benign tumour of bone. Cases that occur in the bone marrow cavity are called endogenous chondroma, and those that occur on the bone surface are called periosteal chondroma. This disease can have single or multiple lesions, and cases with multiple lesions are called endogenous chondromatosis. Endogenous chondromatosis combined with skeletal deformities is called Ollier's disease, whereas endogenous chondromatosis combined with soft tissue (and occasionally visceral) haemangiomas of the limbs is called Maffucci syndrome[21].

Both diseases are nonhereditary benign diseases and are related to gene mutations of IDH1 or IDH2 [22]. Solitary endophytic chondroma has a 1-9% risk of malignant transformation. Approximately 40% of Ollier's disease cases and more than 50% of Maffucci syndrome cases can be secondary to chondrosarcoma[23]. Almost all patients with Maffucci syndrome will develop malignant transformation. In addition to secondary skeletal system tumours, pancreatic cancer or biliary tract cancer can also occur[24].

Özmanevra *et al*[25] reported a patient initially diagnosed with endogenous chondroma who received curettage and bone grafting. The tumour recurred locally seven months after the operation and was then diagnosed as grade 2 chondrosarcoma, followed by resection of the proximal phalanx of the third toe. At the one-year follow-up, the patient survived tumour-free. Therefore, lifelong monitoring is required for patients with endogenous chondromatosis.

Prognosis

It remains controversial which factors affect the prognosis of chondrosarcoma, but tumour grading has clear prognostic significance. The survival and metastatic potential of chondrosarcoma are closely related to histological grade. Evans *et al*[15] found 10-year survival rates of 83%, 64%, and 29% for grade I, II, and III chondrosarcomas, respectively. There were 40%, 60%, and 47% local recurrence rates for low, medium, and high grades, respectively. The metastasis rate is low for low-grade chondrosarcomas, 10% for intermediate-grade metastases, and 71% for high-grade metastases. Patients undergoing margin-negative surgery have a reduced risk of local tumour recurrence and improved survival. However, even if they undergo margin-negative surgery, patients with grade III chondrosarcoma will eventually die from recurrence and metastasis[26].

The current case is a 74-year-old male patient with a disease course of 8 mo. Although most of the tumour cells were well differentiated (mildly heterogeneous chondrocytes) and mitotic images were rare, cortical destruction and soft tissue expansion were apparent. Therefore, the patient underwent extensive surgical resection. The patient was free of tumor tumour recurrence and distant metastasis at the 30 mo postoperative follow-up. The most current version of the guideline diagnoses ACT/CS1 occurring in tubular bones of the extremities as ACT because of its relatively short anatomy, relatively easy surgical resection, maximum negative margins, and significantly lower tumour recurrence rate. Hence, patients have a longer tumour-free survival time.

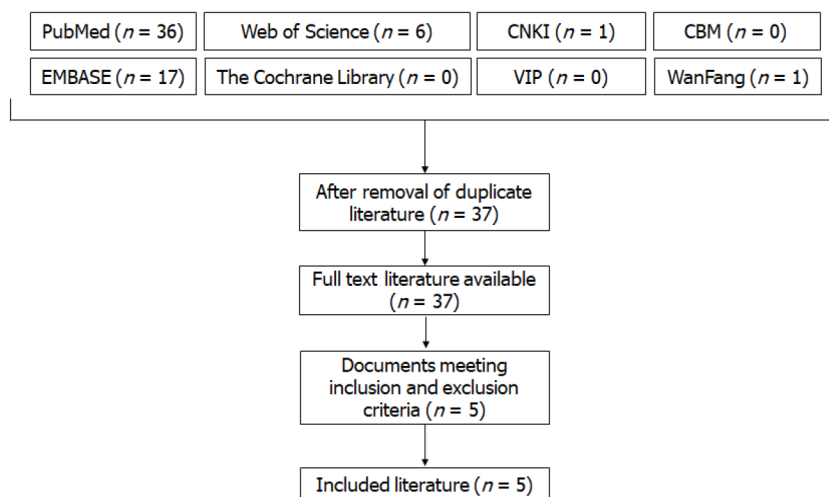
Treatment modality

Surgical resection remains the treatment of choice for primary or secondary chondrosarcoma. According to the Enneking staging[27], surgical resection is classified as local, extensive, or radical resection. Local resection includes intracapsular curettage and marginal resection, intracapsular curettage is used for central tumours, and marginal resection is used for peripheral tumours. Local excision is used when the tumour is distant from the joint when cortical destruction and soft tissue invasion are not severe. Extensive resection is used when the tumour is close to the joint, has cortical destruction, or has severe soft tissue invasion. When anatomically permitted, the critical treatment for chondrosarcoma is a radical operation; that is, the margin of the resected malignant tumour is negative under the microscope. According to Laitinen *et al*[28], complete surgical resection reduces the risk of local recurrence of the tumour.

Chondrosarcoma originating in the toe bone is usually of low grade (grade I), but controversy still exists regarding the surgical approach to grade I chondrosarcoma. According to the latest guidelines, some surgeons suggest that intrathecal curettage and local adjuvant treatment should be adopted for treating the tubular bones of limbs, such as electric knife cauterization, bone cement, high-speed grinding, drilling, ethanol, phenol, and liquid nitrogen[2,29].

We searched the following 8 databases: four English medical databases [MEDLINE (PubMed), EMBASE, The Cochrane Central Register of Controlled Trials (Cochrane Library)], Web of Science Database, and four Chinese medical databases [the China National Knowledge Database (CNKI), Journal Integration Platform (VIP), WanFang Database and SinoMed (CBM)]. We also manually searched the additional relevant studies using the references of the systematic reviews that were published previously. All of the searches were performed from inception to April 2022 and did not impose restrictions on language, population or country. The following search strategy was used for PubMed and was modified to suit other databases.

- #1 (chondrosarcoma[Title/Abstract])
- #2 (Toe [Title/Abstract])
- #1 AND #2



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Figure 5 Flow diagram of the search process.

Literature inclusion and exclusion criteria were as follows: (1) The site of the disease was in the toe; (2) Pathologically diagnosed as chondrosarcoma; (3) Chondrosarcoma was the main lesion; and (4) Not combined with other malignant diseases. Figure 5 illustrates the study selection process.

Searching the relevant database, there were 5 cases of chondrosarcoma of the phalanx. Two of the patients had grade 1 chondrosarcoma. The patients underwent resection of the first phalanx of the right foot or resection of the mass on the first phalanx of the left foot with scraping of the proximal phalanx. At the 1-year postoperative follow-up, none of the patients had local recurrence or distant metastases [30,31]. Masuda *et al* [32] reported a case of primary grade 2 chondrosarcoma in which the patient underwent resection of the distal half of the second proximal phalanx of the right foot. There was no evidence of recurrence or metastasis at two years of follow-up. Özmanevra *et al* [25] reported a secondary grade 2 chondrosarcoma case with proximal phalangeal resection of the lesser toe. At the one-year follow-up, the patient was tumour-free. We found that patients with grade 2 chondrosarcoma of the toe bone had a better prognosis than those with chondrosarcoma of other sites. In addition, studies have shown that the prognosis of secondary chondrosarcoma is similar to that of primary chondrosarcoma, and the 5-year survival rate is approximately 90% [19]. It has been suggested that the flexor and extensor tendon sheaths are natural barriers that limit the spread of toe tumours; thus, metastases are uncommon [24]. The recurrence rate and metastasis rate of grade 3 chondrosarcoma are relatively high. Rafi *et al* [33] reported that a patient with grade 3 chondrosarcoma of the right foot and toe underwent amputation treatment. Left orbital and left infratemporal metastasis occurred, causing swelling and pain and gradual vision loss in the left eye.

A literature review showed that the local recurrence rate was only 0%-7.7% when intracapsular curettage was used for the resection of central low-grade chondrosarcoma of the limbs [34]. Chen *et al* [3] showed that intracapsular curettage was a safe and functional method for treating central primary grade I chondrosarcoma. Lesenský *et al* [35] concluded that curettage is the treatment of choice for ACT/Grade I tumours; however, surgeons should be aware of the potentially high local recurrence and recurrence rates. Resection is recommended for Grade II and Grade III chondrosarcomas. However, the Dierselhuis *et al* [36] meta-score noted that the current level of evidence does not yet adequately support local excision as a treatment modality for low-grade chondrosarcoma of the extremities. For grade II and III chondrosarcomas, extensive resection with negative margins should be performed [37]. Although chondrosarcoma of the foot has a low risk of recurrence and metastasis, all patients require long-term follow-up. The previously reported cases are listed in Table 1.

Chondrosarcomas are considered radiation-resistant tumours. However, the exact mechanism has not been clarified. Several ideas have been proposed, such as the ability to inhibit reactive oxygen species and the high expression of antiapoptotic genes [38,39]. Goda *et al* [40] showed that preoperative or postoperative radiotherapy as an adjuvant treatment could reduce local tumour recurrence. Therefore, radiotherapy can be administered to patients with inoperable or incomplete resection and tumour recurrence, but its therapeutic significance is not yet supported by high-level clinical evidence. Chemotherapy is usually ineffective for chondrosarcoma, especially for conventional and dedifferentiated types. In the future, protein inhibitors targeting altered molecular pathways and mutated genes may become a focus for targeted therapies.

Table 1 Review of the literature of cases of chondrosarcoma of the toe bone

Ref.	Gender	Age, yr	Symptoms	Tumor Location	Histological grading	Treatment	Follow-up
Mondal[30]	Male	37	The right big toe was gradually swollen and painful for nearly two years	Distal end of the first phalanx of the right foot	Grade I	Excision of the big toe at the metatarsophalangeal joint	Followed up for 1 yr, there was no tumor recurrence or metastasis
Haliloglu <i>et al</i> [31]	Female	19	Painless swelling of the left big toe for 6 yr	First phalanx of the left foot	Grade I	The mass was completely removed and the proximal phalanx was scraped	Followed up for 1 yr, there was no tumor recurrence or metastasis
Özmanevra <i>et al</i> [25]	Female	52	Swelling of the left big toe	First phalanx of the left foot	Grade II	Excision of the proximal phalanx	Followed up for 1 yr, there was no tumor recurrence or metastasis
Masuda <i>et al</i> [32]	Female	32	Pain, swelling and nail deformity of the second toe of the right foot for 6 mo	Second phalangeal bone of the right foot	Grade II	Resection of the distal part of the second proximal phalanx	Followed up for 2 yr, there was no tumor recurrence or metastasis
Rafi <i>et al</i> [33]	Male	56	Pain, swelling and ill defined mass on the right toe	First phalangeal bone of the right foot	Grade III	Amputation (specific location unknown)	Left orbital and left infratemporal metastasis

CONCLUSION

Chondrosarcoma is a rare malignant bone tumour, and it is even rarer when it occurs in a toe. Local excision is feasible for low-grade chondrosarcoma of the phalanx, which can minimize surgical trauma while preserving the function and aesthetics of the limb. However, considering the risk of tumour recurrence and metastasis, clinicians should carefully select cases that are not obviously aggressive on imaging, and for patients with chondrosarcoma of grades I (aggressive), II, and III, extensive excision with negative margins is the preferred initial treatment.

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FOOTNOTES

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