Review

DOI: https://doi.org/10.17816/PTORS676913

EDN: PEHSLH

Vol. 13 (2) 2025



Enchondromas of Hand in Children: Current Concepts in Etiopathogenesis, Diagnosis, and Treatment: **A Review**

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ABSTRACT

The prevalence of benign bone tumors among pediatric patients highlights the relevance of such investigations for orthopedic practice. This article focuses on hand enchondromas in children. Despite the relative frequency of this condition, the lack of clinical guidelines for this disease area underscores the relevance of the publication. A total of 69 full-text articles were selected from 387 sources identified through searches in CyberLeninka, eLibrary, PubMed, and Scopus from 1990 to 2023. This review presents current views on the etiopathogenesis, diagnostic and therapeutic challenges, and prognosis of hand enchondromas in children. Radiography and computed tomography are the primary diagnostic methods for hand enchondromas. Histological verification of diagnosis is mandatory. Particular attention should be given to surgical treatment strategies, including the optimal timing and extent of intervention, selection of grafting material, risk factors, and frequency of recurrence. The scientific data analysis enabled the systematization of data on the etiopathogenesis of hand enchondromas, identification of diagnostic priorities, clarification of diagnostic and differential diagnostic criteria, and refinement of approaches to treatment strategy and methods. The choice of treatment strategy, including the method and timing of intervention, should be individualized, taking into account tumor localization and histogenesis, as well as any additional diagnostic findings and the risk of complications. In recent years, specialists have tended to favor early surgical intervention over wait-and-see approaches, with the choice between autograft and allograft being determined by the clinical context. Autografts are considered the gold standard; however, the use of allografts for restoring the structural and functional integrity of bone in cases of injury is a reasonable and well-substantiated alternative, even in the light of the high risks of donor site morbidity. Such decisions should be made collaboratively, considering the opinions of the involved specialists, including orthopedic oncologists, radiologists, pathologists, and rehabilitation physicians.

Keywords: enchondroma; hand; etiology; diagnosis; classification; graft; bone defect; surgical treatment.

To cite this article

Cherdantseva LA, Duginova MV, Gubina EV, Kirilova IA. Enchondromas of Hand in Children: Current Concepts in Etiopathogenesis, Diagnosis, and Treatment: A Review. Pediatric Traumatology, Orthopaedics and Reconstructive Surgery. 2025;13(2):192-201. DOI: 10.17816/PT0RS676913 EDN: PEHSLH

Submitted: 07.03.2025 Accepted: 07.05.2025 Published online: 24.06.2025



Научный обзор

DOI: https://doi.org/10.17816/PTORS676913

EDN: PEHSLH

Энхондромы кисти у детей: современные представления об этиопатогенезе, диагностике и лечении. Обзор литературы

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Распространенность доброкачественных опухолей костей у пациентов детского возраста определяет актуальность их изучения для ортопедов. Данная статья посвящена энхондромам кисти у детей. Несмотря на частоту встречаемости этой патологии, отсутствие клинических рекомендаций по указанной нозологии объясняет актуальность темы публикации. На основе баз данных полнотекстовых публикаций сайтов CyberLeninka, eLibrary, PubMed, Scopus за период с 1990 по 2023 г. из 387 источников в анализ были взяты 69 полнотекстовых рукописей. В обзоре отражены современные представления об этиопатогенезе, сложностях диагностики и лечения и прогнозе при энхондромах кисти у детей. В диагностике энхондром кисти приоритетные методы — рентгенография и компьютерная томография. Обязательный метод — гистологическая верификация диагноза. Особое внимание уделено тактике хирургического лечения: выбору оптимального срока и объема хирургического вмешательства, выбору материала для замещения костных дефектов, факторам риска развития рецидивов и их частоты. Проведенный анализ литературы позволил систематизировать данные об этиопатогенезе энхондром кисти, определить приоритетность диагностических мероприятий, упорядочить данные о критериях диагностики и дифференциальной диагностики энхондром кисти, а также подходах к выбору тактики и способов лечения. Решение о выборе тактики лечения, способе и сроках лечения должно быть персонализированным и учитывать локализацию и гистогенез опухолевого процесса, а при необходимости данные дополнительных методов исследования и риски развития осложнений. В последние годы специалисты склоняются к раннему началу хирургического лечения, а не к выжидательной тактике, а выбор между аутокостью и аллокостью зависит от клинического контекста. Аутокость — «золотой стандарт», но использование в целях восстановления структурно-функциональной целостности костей при повреждениях именно аллокости — разумная и обоснованная альтернатива, даже с учетом высоких рисков донорской морбидности. Данное решение должно быть коллегиальным — с учетом мнения привлеченных специалистов: врача-онкоортопеда, врача-рентгенолога, врача-патологоанатома, врача-реабилитолога.

Ключевые слова: энхондрома; кисть; этиология; диагностика; классификация трансплантат; костный дефект; хирургическое лечение.

Как цитировать

Черданцева Л.А., Дугинова М.В., Губина Е.В., Кирилова И.А. Энхондромы кисти у детей: современные представления об этиопатогенезе, диагностике и лечении. Обзор литературы // Ортопедия, травматология и восстановительная хирургия детского возраста. 2025. Т. 13. № 2. С. 192—201. DOI: 10.17816/PTORS676913 EDN: PEHSLH



科学审查

DOI: https://doi.org/10.17816/PTORS676913

EDN: PEHSLH

儿童手部软骨内瘤:病因机制、诊断与治疗的现代认识。 文献综述

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摘要

儿童良性骨肿瘤的较高发病率决定了其对骨科医生的研究价值。本文聚焦于儿童手部软骨内瘤。尽管该病相对常见,但目前缺乏专门针对该疾病的临床指南,凸显了该议题的现实意义。作者基于CyberLeninka、eLibrary、PubMed和Scopus等数据库中1990年至2023年的全文资料,在387篇文献中筛选出70篇纳入分析。综述内容涵盖儿童手部软骨内瘤的最新病因机制观点、诊断和治疗难点及疾病预后。在诊断方面,首选方法为X线检查和计算机断层扫描。确诊必须依赖组织病理学验证。特别强调了外科治疗策略,包括最佳手术时机与手术范围的选择、骨缺损替代材料的使用、复发风险因素及其发生率。文献分析有助于系统梳理儿童手部软骨内瘤的病因机制,明确诊断措施的优先顺序,整理诊断与鉴别诊断标准,并理清治疗策略与方法选择的原则。治疗策略、方法和时机的选择应个体化,考虑肿瘤过程的解剖部位和组织发生特征,并在必要时结合辅助检查结果及并发症发生的风险。近年来,专家更倾向于尽早开展外科治疗,而非采取观望策略;在自体骨与异体骨的选择上,则取决于具体的临床情境。自体骨被视为"金标准",但在骨损伤后的结构和功能重建中,异体骨的应用也是一种合理且有据的替代方案,尽管存在较高的供区并发症风险。此类决策应由多学科专家共同商议决定,涉及肿瘤骨科医生、影像科医生、病理科医生及康复科医生等专业人员的意见。

关键词: 软骨内瘤; 手部; 病因学; 诊断; 分类; 移植物; 骨缺损; 外科治疗。

引用本文

Cherdantseva LA, Duginova MV, Gubina EV, Kirilova IA. 儿童手部软骨内瘤: 病因机制、诊断与治疗的现代认识。文献综述. Pediatric Traumatology, Orthopaedics and Reconstructive Surgery. 2025;13(2):192–201. DOI: 10.17816/PTORS676913 EDN: PEHSLH



INTRODUCTION

The prevalence of benign hand tumors in pediatric patients indicates the relevance of their investigation by orthopedic specialists. In pediatric orthopedics, tumors and tumor-like diseases account for 3.5%-8.2% of all hand conditions [1-3]. Among these, enchondromas are the most common hand tumors in children, comprising 10%-27% of all benign neoplasms in this localization [3, 4]. Enchondromas may be solitary or multiple, as seen in Ollier disease [1, 5, 6] and Maffucci syndrome [6, 7], often in combination with other developmental anomalies of organs and systems. Typically, the clinical presentation of multiple hand enchondromas includes bone shortening and multiplanar deformities, particularly affecting the phalanges [3, 5, 8]. Up to 40%-60% of solitary enchondroma diagnoses are made as incidental radiological findings, often in the context of a pathological fracture [9-11]. The prolonged absence of complaints and clinical symptoms can be attributed to the slow tumor growth [8, 12].

Despite the relatively high incidence of enchondromas in children and abundance of scientific publications on this topic, there are currently no established criteria for selecting the method and timing of surgical treatment, type of fixation, use of adjuvant agents, or choice of bone graft material for defect reconstruction following tumor resection. Particular attention is required when determining the management strategy for patients with pathological fractures associated with enchondromas [2, 6, 12]. There are no current clinical guidelines for the management of this nosological entity.

The work aimed to review and systematize data from Russian and international scientific data addressing the etiopathogenesis, classification, diagnosis, and treatment of hand enchondromas in children.

The electronic databases CyberLeninka, PubMed, Scopus, and eLibrary were searched for publications in Russian, English, and French using the following keywords: *hand enchondroma*, *etiology*, *diagnosis*, and *treatment*. The search covered the period from 1990 to 2023 and yielded 387 articles. After exclusion of duplicate publications and case reports, 69 full-text manuscripts were analyzed.

PREVALENCE AND ETIOPATHOGENESIS

An enchondroma is a benign intraosseous neoplasm composed of hyaline cartilage. Enchondromas of the small bones of the hands and feet are characterized by lobules of differentiated chondrocytes with large nuclei, areas of calcification, and foci of myxoid changes in the hyaline cartilaginous matrix, with possible destruction of the cortical layer but without signs of invasion in surrounding tissues [13]. Enchondroma prevalence accounts for 10%–27% of all benign

hand tumors [13–15]. This tumor is most commonly diagnosed between the first and fourth decades of life, with no significant difference in incidence between males and females [1, 13, 16]. A considerable proportion of asymptomatic enchondromas precludes accurate assessment of their true prevalence.

The most frequent localization of enchondromas is the short tubular bones of the hands and feet [1, 17, 18], including the proximal and middle phalanges, especially of the fourth and fifth fingers, accounting for 70% [6, 9, 18], and the metacarpal bones (30%) [1, 3, 6]. This distribution pattern of enchondromas among various bones and skeletal regions was noted as early as the 1940s [19].

In pediatric patients, enchondroma usually begins to develop in the metadiaphyseal regions of the metacarpal bones and phalanges, originating from residual growth plate anlagen with subsequent proliferation and the formation of hypertrophic cartilage tissue foci, which may persist throughout life [6]. In 2019, Miwa et al. [12] proposed a hypothesis regarding the etiopathogenesis of hand enchondromas. Differentiation of the hand, with the emergence of the anlagen of tubular bones (metacarpals and phalanges), occurs between days 33 and 54 of intrauterine development. The digit rays are visible by day 41 of gestation, and the separation of the distal, middle, and proximal phalanges and metacarpal bone is completed by day 54 of intrauterine development. The sequential occurrence of multiple enchondromatous lesions along the same digit ray in the studied cases led the authors to indicate that lesion formation precedes the segmentation of the hand bones [12, 19]. According to studies [12, 19], based on genetic studies, tumor formation depends particularly on the PTPN11 gene, located on the long arm of chromosome 12 at locus 12q24.13. This gene encodes the tyrosine phosphatase protein SHP2, which is involved in signal transduction pathways regulating the cell cycle, differentiation, migration, and apoptosis during embryonic and postnatal development. Mutations in this gene are associated with oncogenic cell transformation and carcinogenesis [12, 19, 20].

CLASSIFICATION AND CLINICAL PRESENTATION OF HAND ENCHONDROMAS

Currently, there is no unified (clinical and radiological) classification system for hand enchondromas. Moreover, a radiological classification of hand enchondromas is relevant, reflecting the localization, shape, and type of the tumor (Fig. 1). The most common variants of enchondroma are monostotic type I(A) by type, non-expansile type II(A) by shape, and central type III(A) by localization [21, 22].

The initial stage of enchondroma development is characterized by slow growth and absence of clinical

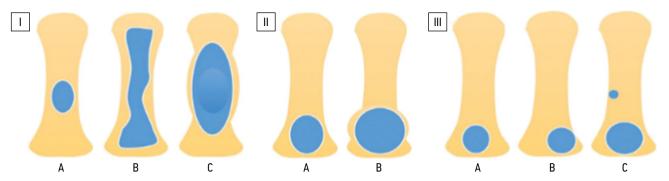


Fig. 1. Hasselgren classification of hand enchondromas. I: tumor type, namely, monostotic (A), polyostotic (B), and giant (C); II: tumor shape, namely, non-expansile (A) and expansile/spreading (B); III: tumor localization, namely, central (A), eccentric (B), and associated (C). © Orman O. et al., 2022. Licensed under CC BY-NC 4.0. Source: adapted from [DOI: 10.14744/SEMB.2022.00483].

symptoms. A nonspecific complaint may be pain of varying intensity, which is observed in approximately one-third of patients [15, 17, 18].

DIAGNOSIS OF HAND ENCHONDROMAS

The first stage of diagnosis is inspection and palpation of the hand and wrist, during which the range of active and passive movements in the interphalangeal and metacarpophalangeal joints and presence of angular and torsional deformities of the phalanges of the hand are assessed [5, 7, 12]. The clinical manifestations of enchondromas of the distal phalanges may include deformation of the nail plate and injury to the extensor tendon of the finger against the background of a pathological fracture, followed by a mallet finger deformity. This results in a limitation of active extension in the distal interphalangeal joint [23, 24]. Another clinical manifestation may be impaired active flexion in the distal interphalangeal joint, which is associated with destruction of the palmar cortical layer of the distal phalanx by the enchondroma and flexor digitorum profundus tendon damage [25-27].

The main instrumental diagnostic method at the patient's initial visit for hand trauma, pain syndrome, and finger deformity is radiography in two standard projections (anteroposterior and lateral). If a neoplasm is suspected, additional radiography is performed in an oblique projection [15, 18]. Radiographic signs of enchondroma in the tubular bones of the hand can be detected in the metaphysis, diaphysis, or epiphysis and, in some cases, may totally replace the entire phalanx.

On radiographs, the intraosseous location of the pathological lesion can be identified as a homogeneous radiolucency of irregular round or oval shape with polycyclic contours, demarcated from the unaffected bone. Within the radiolucent area, single shadows are visualized as rings and arcs, which correspond to areas of cartilage calcification. In some cases, calcified cartilage foci in the deformed short tubular bone of the hand are surrounded by a minimal sclerotic rim, and the cortical

layer appears thinned. The contour of the endosteum at the enchondroma level is usually smooth, although slight deformation may be present. If a pathological fracture is associated with the enchondroma, disruption of the integrity of the thinned cortical layer can be observed. Intra-articular involvement or soft tissue extension is rarely detected [28–30]. Computed tomography visualizes cortical thinning and discontinuity with greater precision and allows for assessing the lobulated architecture of the lesion [31].

Magnetic resonance imaging (MRI) complements the information obtained from radiographic and computed tomography examinations. MRI plays an important role in the differential diagnosis from malignant cartilaginous neoplasms, namely, chondrosarcomas [31-33]. On T1-weighted MR images, a characteristic sign of enchondroma is a decrease in bone density, whereas T2-weighted images demonstrate increased density with high signal intensity. Moreover, a lobulated structure of the lesion is identified [34, 35]. A significant diagnostic criterion distinguishing enchondromas from chondrosarcomas is the presence of high-signal-intensity areas on T1-weighted images in chondrosarcomas [31, 35]. In addition, according to Janzen et al. [32] and Fayad et al. [33], MRI enables the visualization of peritumoral bone marrow edema and trabecular edema of the adjacent cancellous bone, which are characteristic of malignant tumors, including chondrosarcomas (with 13 cases of chondrosarcomas observed by Janzen and 6 of 7 cases by Favad). No prospective studies with sufficient number of observations confirming the reliability of these diagnostic criteria were found in the available Russian and international scientific data.

Additionally, intravenous gadolinium-based contrast agents may be used to differentiate enchondroma from chondrosarcoma. This was reported by Büyükceran et al. [30] and Geirnaerdt [36], who observed an arc-like enhancement of MRI signal in cases of chondrosarcoma. However, other studies [34, 35] did not confirm the diagnostic value of contrast enhancement compared to standard MRI. Although MRI is not a first-line diagnostic modality for enchondromas, it contributes to a more accurate and efficient assessment

of the pathological process when used in combination with other methods, particularly in cases requiring differential diagnosis with malignant lesions.

Histological examination of biopsy (or surgical) specimens obtained by curettage during surgical treatment is mandatory for diagnosing enchondroma. During clinical and radiological evaluation, if differentiation from an atypical cartilaginous tumor/chondrosarcoma grade 1 (low-grade malignancy) is required, an open or incisional biopsy is performed [37]. Macroscopically, enchondroma appears as translucent areas of hyaline cartilage with a lobular architecture, grayish-white in color, containing yellowish or brownish-yellow inclusions of calcified interstitial substance. Gray bulging areas may be detected in the cortical layer during subperiosteal dissection [13, 29].

Histologically, the tumor may exhibit a multicentric lobular structure, with lobules located within the bone marrow cavity and separate from the main lesion, without signs of destruction within the lobules. The cartilage lobules are composed of groups of mature chondrocytes located in lacunae and separated by solid hyaline cartilage matrix, with a moderate amount of myxoid changes. The tumor cells are predominantly distributed discretely; however, hypercellular areas may also be present [6, 38]. Multicellularity is typical for enchondromas of small bones. The cells are uniform and round, with dense, large nuclei of regular form and few mitotic figures [13, 39]. Binucleated chondrocytes are frequently observed. Cortical layer destruction may be identified, without signs of tumor invasion into the bone marrow cavity or intertrabecular spaces of preexisting bone (Fig. 2) [40, 41].

In some enchondroma cells and in atypical cartilaginous tumor/chondrosarcoma grade 1, nuclear polymorphism and hyperchromasia with coarse chromatin distribution and prominent nucleoli may be observed, which complicates histological diagnosis [37, 42]. In such cases, the presence or absence of other histological features characteristic of atypical cartilaginous tumor/chondrosarcoma grade 1 should be considered: increased cellularity and binucleated cells, presence of cellular atypia, bone marrow cavity invasion with tumor infiltration into the spaces between adjacent trabecular bone structures, and destructive changes in the form of endosteal erosion foci and small foci of necrosis with loss of nuclear staining [13]. If necessary, immunohistochemical analysis may be used for differential diagnosis. In biopsy samples, enchondromas are typically positive for the S-100 protein marker, similar to other cartilaginous tumors. Alpha-methylacyl-CoA racemase marker expression is detected in 88.9% of enchondroma cases, whereas periostin protein expression is more commonly observed in atypical cartilaginous tumor/chondrosarcoma grade 1 [13, 29, 43, 44]. Considering the lack of specificity of this method for the diagnosis of enchondroma, the results

should be interpreted in conjunction with an extended clinical history, radiological findings, and histological examination data.

Molecular genetic testing may be an additional method for the differential diagnosis of cartilaginous tumors. According to a multicenter study, important diagnostic criteria include detectable somatic heterozygous point mutations in the IDH1 (isocitrate dehydrogenase 1) gene or, in rare cases, the IDH2 gene. These mutations alter normal cellular metabolism, promoting uncontrolled growth of cartilaginous tissue, disrupting differentiation, and leading to enchondroma formation. These mutations were found in 81% of patients with Ollier disease and in 77% of patients with Maffucci syndrome. Furthermore, *IDH1* and *IDH2* gene mutations have been identified in solitary central and periosteal enchondromas and chondrosarcomas. Somatic heterozygous mutations IDH1 (R132C and R132H) or IDH2 (R172S) are associated with enchondroma formation in 87% of cases and may contribute to the development of spinal hemangiomas that is, benign vascular tumors, in 70% of cases [45].

INTERVENTIONS

When choosing a treatment for patients with enchondromas, some studies recommend over-time observation for solitary enchondromas in the absence of clinical symptoms (pain, swelling, deformity, and functional impairment of the hand), despite a confirmed diagnosis [14, 46–48]. However, this approach may lead to delayed histological verification of the diagnosis and, consequently, to complications (e.g., pathological fracture), delayed surgical intervention with greater tissue trauma, and a longer rehabilitation period [1, 3, 12].

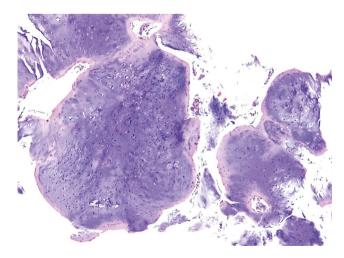


Fig. 2. Enchondroma. Lobules of hyaline cartilage with a thin fibrous tissue capsule surrounding the lobules. Hematoxylin and eosin staining, magnification ×50. © Academy of Medical Sciences, Romanian Academy Publishing House, Bucharest, 2022. Licensed under CC BY-NC 4.0. Source: adapted from [DOI: 10.47162/RJME.63.4.04].

Surgical treatment allows for ensuring mechanical stability of the bone, reducing the risk of pathological fractures, and relieving clinical symptoms and achieving accurate morphological identification of the pathological process [15, 49]. Additionally, the choice of surgical treatment is justified by the risk of malignant transformation of enchondromas, which occurs in 4% of cases [3, 46, 50]. According to Adam Sasson [2] and Kadar et al. [3], malignant transformation of enchondromas ranges from 0.4% in children to up to 5% in adults. Moreover, dedifferentiation and malignant progression of chondroma cells may occur with each recurrence after surgical treatment [45, 51, 52].

The standard surgical treatment method is isolated intralesional resection of the tumor, either alone or combined with immediate bone grafting [49, 54]. Moreover, intraoperative resection may be supplemented with cryoablation or chemical cauterization of the resection cavity [2, 47, 54] and cauterization using a high-speed burr [50, 55, 56]. Adjuvant therapy for enchondromas is considered unnecessary [1, 2, 57].

The optimal approach to surgical management of enchondromas complicated by pathological fracture remains controversial and includes the following:

- Early surgical intervention
- Delayed surgical intervention.

Fig. 3a (a patient with a pathological fracture of the proximal phalanx of the fourth finger caused by an enchondroma) shows an example of early surgical treatment. Radiographically, rarefaction of the bone structure is observed in the central portion of the proximal phalanx of the fourth finger, with thinning and bilateral disruption of the cortical layer. Surgical treatment was performed (Fig. 3b): curettage of the enchondroma with defect reconstruction using an autograft harvested from the iliac crest and fixation with a plate and screws.





Fig. 3. A 17-year-old patient with displaced pathological fracture of the proximal phalanx. © Çapkin S. et al., 2020. Licensed under CC BY-NC 4.0. Source: adapted from [D0I: 10.7759/cureus.7497].

Early surgical intervention allows for a shorter period of temporary disability, earlier histological verification of the pathological lesion, and reduced risk of malunion. However, this approach carries the risk of complications such as secondary displacement of fragments, hardware failure, and bone graft material migration into soft tissues [2, 46, 58].

Currently, there is ongoing debate regarding the optimal materials for bone defect reconstruction after enchondroma excision [14, 18, 51]. Autogenous bone grafting demonstrates the best outcomes for bone restoration. However, complications at the donor site (bone harvest area) cannot be ruled out, including hematoma formation, inflammation due to infection, pain syndrome, and paresthesias [19, 58].

The most common donor sites for autologous bone graft harvesting are the iliac crest and/or the distal metaphysis of the radius. According to the clinical and radiographic studies by Orman et al. [21], there is no difference in the timing of bone defect healing and autograft remodeling in the area of defect reconstruction after phalangeal enchondroma removal when using autologous bone from the iliac crest or the distal metaphysis of the radius. However, harvesting autografts from the iliac crest is associated with prolonged hospital stay because of persistent severe pain [21]. In their study, Teache et al. [60] found a 1.5-fold decrease in the duration of pain persistence in pediatric patients when using autografts from the distal metaphysis of the radius, regardless of the analgesia protocol, compared to the duration of pain observed when using autografts from the iliac crest.

Proponents of allogeneic bone grafting justify their choice by noting that the use of this type of grafting material avoids additional trauma to the patient, which is particularly important in pediatric patients [3, 61]. Furthermore, it helps shorten operative time and hospital stay [62].

Comparative analysis of autograft and allograft remodeling following bone defect reconstruction after enchondroma curettage demonstrated that remodeling occurs in 100% of cases, regardless of graft type [53, 54]. No significant differences were found in bone healing time when using autografts, allografts, and synthetic bone substitutes [1, 2, 63]. Furthermore, publications reporting randomized study results on this topic noted that the choice of bone graft material may be based on the operating surgeon's preference [17, 41, 64]. The choice between autograft and allograft depends on the clinical context. Autograft remains the gold standard, but allograft, including in combination with adjuvants, is a reasonable alternative in cases of high donor site morbidity risk.

Synthetic bone substitutes based on phosphate and calcium sulfate are used as graft materials.

The disadvantages of these materials are delayed integration, potential host foreign body reaction, incomplete bone defect filling, and insufficient mechanical strength [54]. In 2013, Lin et al. described the effectiveness of bone cement use in cases of phalangeal pathological fracture caused by enchondroma, noting early recovery of hand function and working ability and the lack of the need for internal or external fixation methods [65]. Meanwhile, Yasuda et al. [61] reported that the use of bone cement in cases of phalangeal pathological fracture caused by enchondroma may lead to partial absorption of the material, improper healing, and, consequently, repeat surgery in the form of corrective osteotomy, which adversely affects hand function. Similar complications with the use of bone cement were described by Lu et al. [67], who recommended its use only for unicortical defects to avoid graft migration into soft tissues. A common drawback of any non-biological material is the absence of vascularization and remodeling capability and the need for complete removal in the event of infection or tumor recurrence [62, 66].

Joosten et al. [66] reported favorable outcomes with hydroxyapatite bone defect reconstruction after enchondroma excision, confirmed by complete radiographic bone integration of the material within 6–8 weeks. Based on a retrospective study in 1991–2008, Sasson et al. [2] concluded that full recovery of the structural and functional characteristics of the hand was achieved in 96% of patients, regardless of the bone graft material used in the surgical treatment of enchondromas.

Scientific sources reported that the recurrence rate in this condition is independent of the type of bone graft material used [1, 3, 9, 17, 25, 68].

CONCLUSION

Scientific data review allowed for systematizing the data on the etiopathogenesis of hand enchondromas, identifying the priorities in diagnostic procedures, organizing the criteria for diagnosis and differential diagnosis of hand enchondromas, and summarizing the approaches to treatment

strategy selection and therapeutic techniques. The decision on treatment strategy, method, and timing should be individualized and consider the localization and histogenesis of the tumor process and, when necessary, the data from additional diagnostic methods and risk of complications.

In recent years, specialists have increasingly favored early surgical intervention over watchful waiting. The choice between autograft and allograft depends on the clinical context. Autograft remains the gold standard; however, the use of allograft for restoring the structural and functional integrity of bone in lesions is a reasonable and well-justified alternative, even considering the high risks of donor site morbidity. This decision should be collectively made, with input from a multidisciplinary team (including an orthopedic oncologist, radiologist, pathologist, and rehabilitation specialist).

ADDITIONAL INFORMATION

Author contributions: I.A. Kirilova: conceptualization, writing—review & editing; M.V. Duginova: investigation, writing—original draft; E.V. Gubina: writing—original draft, writing—review & editing; L.A. Cherdantseva: investigation, writing—original draft, writing—review & editing. All authors approved the version of the manuscript to be published and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding sources: The authors declare no external funding was received for conducting the study or publishing the article.

Disclosure of interests: The authors have no relationships, activities, or interests for the last three years related to for-profit or not-for-profit third parties whose interests may be affected by the contents of the article.

Statement of originality: The authors used previously published materials (texts, illustrations, etc.) from full-text databases including CyberLeninka, eLibrary, PubMed, and Scopus from 1990 to 2023 to analyze and systematize data from Russian and international scientific sources on the etiopathogenesis, classification, diagnosis, and treatment of hand enchondromas in children.

Data availability statement: All data generated during this study are available in this article.

Generative Al: No generative artificial intelligence technologies were used to prepare this article.

Provenance and peer-review: This paper was submitted unsolicited and reviewed following the standard procedure. The review process involved two in-house reviewers.

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