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Prikaz slučaja
Case report

FORTY YEARS FOLLOWING PAEDIATRIC CHONDROMYXOID FIBROMA OF THE DISTAL FEMUR: A CASE REPORT AND REVIEW OF THE LITERATURE

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Background: Chondromyxoid fibroma (CMF) is a rare type of benign bone tumour comprising less than 2% of all benign bone neoplasms; it predominantly affects young individuals and typically arises in the metaphysis of long bones. Despite its benign nature, CMF poses diagnostic and therapeutic challenges due to its potential for local recurrence and its radiological resemblance to chondrosarcoma.

Case Presentation: We report the case of a 9-year-old girl diagnosed with CMF of the distal femur in 1985. She underwent curettage twice, three years apart, with histological confirmation of CMF. Following surgical management, the patient remained asymptomatic and functionally unrestricted for nearly four decades. At the age of 49, she presented with medial knee pain, unrelated to tumour recurrence. Imaging studies, using magnetic resonance imaging and computed tomography (MRI and CT), revealed multiple small, well-defined lesions in the left femoral diaphysis, radiologically consistent with residual CMF. The lesions were asymptomatic and biologically inactive. A multidisciplinary evaluation supported conservative management and follow-up imaging.

Discussion: This case highlights the importance of long-term monitoring in patients with CMF and raises the question of whether late-appearing lesions represent true recurrence or, more likely in this case, post-surgical residuals with no biological activity. Positron emission tomography and computed tomography (PET/CT) may offer additional insights into the metabolic activity of such lesions, aiding in differentiation and treatment planning. Our case underscores the relevance of a tailored, patient-centred approach that leverages modern imaging and minimally invasive diagnostics.

Conclusion: CMF requires careful long-term follow-up, due to the potential for recurrence and rare malignant transformation. This case demonstrates that residual lesions may persist without clinical consequences for decades and that advanced imaging techniques play a crucial role in ongoing evaluation and management.

Keywords: CHONDROMYXOID FIBROMA, FIBROMA, BENIGN NEOPLASMS, RECURRENCE, RESIDUAL NEOPLASM, MAGNETIC RESONANCE IMAGING, POSITRON EMISSION TOMOGRAPHY, COMPUTED TOMOGRAPHY, LONG-TERM FOLLOW UP, CASE REPORT

Introduction

Chondromyxoid fibroma (CMF) is among the rarest primary bone tumours, accounting for less than 2% of all benign and under 1% of all primary bone neoplasms; it was named based on its histological architecture, characterised by a mixture of cartilaginous, myxoid, and fibrous tissue components (1-4). CMF was first described as a distinct pathological entity in 1948 by Dr Henry L. Jaffe and Dr Louis Lichtenstein, in the journal Archives of Pathology (5). A subsequent article by Dr Lichtenstein in the American Journal of Pathology further elaborated upon the clinical, pathological, and radiological characteristics of CMF; at that time, differentiating this benign tumour from malignant chondrosarcoma posed a significant diagnostic challenge (5, 6).

In a study of 36 cases published by Zillmer and Dorfman in 1989, misdiagnosis occurred in 22% of patients, with limb amputation mistakenly performed in two cases due to the erroneous diagnosis of chondrosarcoma (2). As of today, a PubMed search using the keyword "chondromyxoid fibroma" yields 612 articles, the majority of which are case reports (n=370) and case series, along with 89 review articles. Although CMF remains diagnostically challenging, several well-established features are recognised; for example, CMF most commonly arises in the metaphysis of long bones especially the tibia and femur typically affecting children and young adults during their second or third decades of life, and it has a higher prevalence in males (1, 5, 7, 8).

We present a rare case of CMF located in the distal femur of a 9-year-old girl, as well as the diagnostic and clinical challenges observed four decades after the initial diagnosis and surgery.

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Case Presentation

This case was reconstructed based on the original medical documentation from 1985 and 1988, as well as heteroanamnesis from the patient's parents and anamnesis from the patient herself, who is now a physician.

In 1985, a previously healthy 9-year-old girl presented to the Division of Orthopaedic Surgery, General Hospital of Split, with limping and localised pain in the distal left femur. Radiographic evaluation revealed a large cystic lesion, located in the metaphyseal-lateral aspect of the distal femur. At that time, advanced imaging modalities such as CT (computed tomography) and MRI (magnetic resonance imaging) were not available at the hospital. A bone biopsy and curettage were performed in June 1985. Histopathological examination by two institutions the General Hospital of Split and the Department of Pathology at the School of Medicine, University of Zagreb confirmed the diagnosis of chondromyxoid fibroma. Unfortunately, histopathological slides from the original surgical procedures (1985 and 1988) are no longer available in the hospital archives; however, both diagnoses were confirmed by independent pathology departments at the time, and the clinical course strongly supports the initial diagnosis. The term "fibromyxoid chondroma" was used in the report (historically, CMF was sometimes referred to as "fibromyxoid chondroma", a term that is now considered obsolete but may still appear in older literature). The postoperative course was uneventful, and the patient returned to regular activities within a short period of time. Marginal resection and spongioplasty were discussed but not pursued.

Three years later, during a routine follow-up, a small cortical lesion was identified on an X-ray in the same metaphyseal region, and repeated curettage and biopsy were performed in June 1988. Histopathology once again confirmed the original diagnosis. Notably, no adjuvant therapy (such as phenol application, cryotherapy, or high-speed burring) was administered during either surgical procedure, which was consistent with the standard of care at the time.

The patient underwent annual follow-up in the subsequent years; growth and development were normal, and there were no activity limitations. She maintains an active professional and social lifestyle, with regular engagement in cycling, swimming, brisk walking, yoga, and Pilates.

At the age of 49, following stair climbing and repetitive squats, she experienced mild medial left knee pain, which worsened over two weeks. A physical medicine and rehabilitation specialist, during clinical examination, noted mild swelling and tenderness at the pes anserinus region of the left limb and suspected overuse syndrome and bursitis. Treatment with Etoricoxib (90 mg/day), proton pump inhibitors, rest (RICE protocol), and physical therapy (magnetic and interferential currents) was initiated.

Given the prolonged interval since her last imaging evaluation, modern radiologic investigations were conducted. A CT scan and plain radiograph (X-ray) of the left femur were conducted (Figure 1, Figure 2). An MRI showed no abnormalities in the knee's soft tissues but revealed focal grade 2 patellar chondromalacia and minimal effusion in the suprapatellar recess. Importantly, four distinct lesions were identified in the left femoral diaphysis: three sharply demarcated round lesions (7-9 mm), and one subcortical lesion with sclerotic margins and imaging characteristics (low T1 signal,

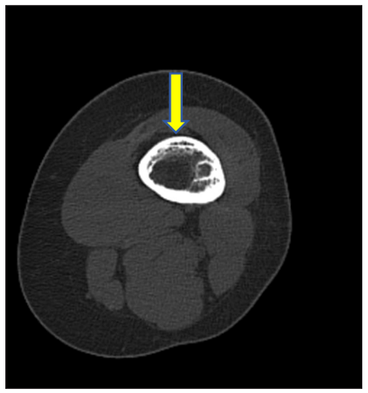

Figure 1.
Axial CT image of the left femoral diaphysis, showing a sharply demarcated, round lesion, with a sclerotic border and thickened cortical bone. No cortical breakthrough or periosteal reaction is observed, consistent with a benign, residual, post-surgical lesion.

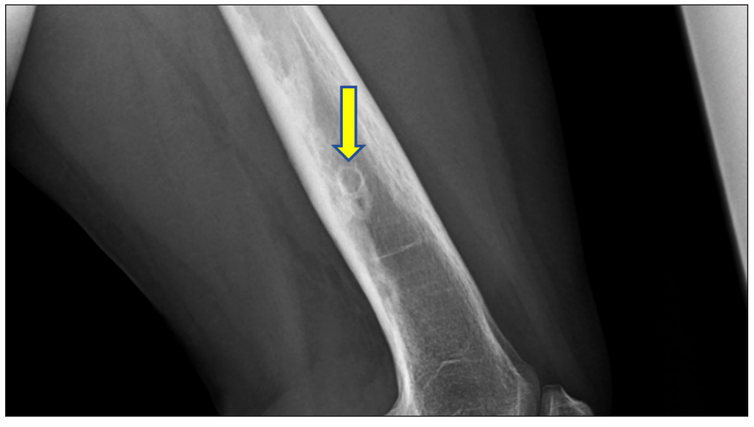

Figure 2.
Plain radiograph (X-ray) of the left femur, displaying a well-defined, sclerotic-bordered lesion in the diaphyseal cortex, without periosteal reaction or soft tissue involvement. Findings are consistent with a stable, residual lesion.

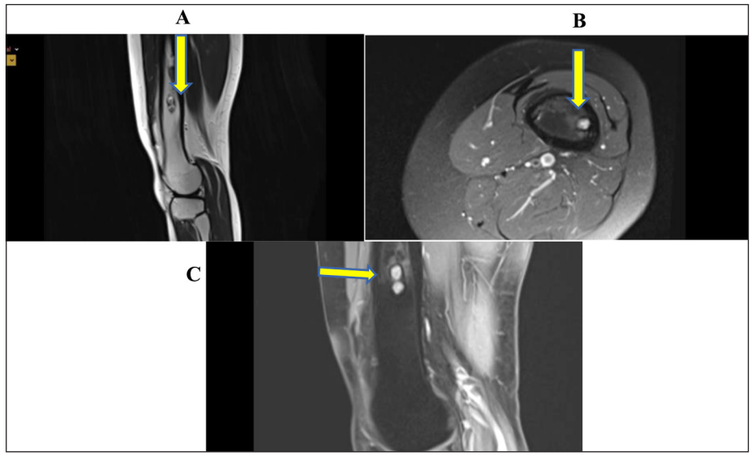

Figure 3.
MRI images of the left femur, showing residual CMF lesions. The changes are marked with a yellow arrow.
(A) T2-weighted sagittal image sharply demarcated lesion with a sclerotic border, high signal intensity on T2, low signal on T1, thickened cortical bone, and no signs of aggressive periosteal reaction. (B) Proton density (PD)-weighted axial image lesion with similar morphology, high signal intensity on PD, low signal on T1, and preserved cortical contour. (C) PD-weighted sagittal image subcortical lesion with high PD signal, sclerotic margin, no cortical breakthrough, and no soft tissue involvement.

mixed T2 and PD signals with chondroid/fibrous components) consistent with residual CMF (Figure 3). Low-dose PET/CT (positron emission tomography and computed tomography) revealed postoperative, metabolically inactive (without pathological accumulation) lesions consistent with residual CMF (Figure 4). Importantly, the imaging studies were conducted for unrelated medial knee pain and incidentally revealed small lesions radiologically consistent with residual CMF, which had remained clinically silent and biologically inactive for nearly four decades.

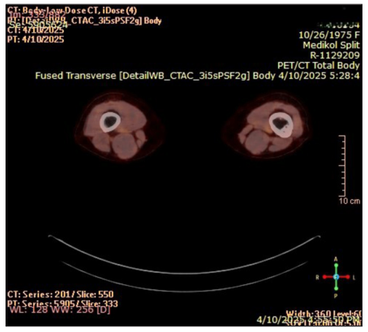

Figure 4.
PET/CT scan demonstrating no significant fluorodeoxyglucose (FDG) uptake in the residual femoral lesions, confirming their metabolic inactivity. Findings support a diagnosis of longstanding, asymptomatic residuals, rather than recurrence.

These lesions showed no signs of biological activity and were considered residual findings from childhood CMF. A follow-up MRI in three months was recommended to monitor potential changes.

To better localise the current pain, diagnostic injections of corticosteroids and local anaesthetics were applied to the pes anserinus area. The patient reported immediate relief, confirming the clinical diagnosis of bursitis. This case represents a highly instructive long-term example of chondromyxoid fibroma management, with both classical and atypical elements. The initial surgical approach intralesional curettage without adjunctive bone grafting was consistent with the standard of care in the mid-1980s. Given the absence of CT or MRI availability at the time, histopathologic confirmation was crucial, and the dual-centre verification added diagnostic robustness. The subsequent recurrence, observed three years later, reflects the well-documented biological behaviour of CMF, which often includes local recurrence if intralesional excision is not combined with adjuvant measures, such as high-speed burring, phenolization, or cryotherapy. Interestingly, in this case, the residual lesions identified four decades later remain radiologically inactive and clinically silent, further confirming the benign nature of CMF in the absence of additional triggers such as mechanical trauma or radiation. The patient's presentation with medial knee pain at age 49 was biomechanically unrelated to the residual CMF lesions, and instead attributable to pes anserinus bursitis confirmed both clinically and therapeutically via targeted corticosteroid and anaesthetic injection. However, renewed imaging revealed small residual CMF-like lesions, highlighting the value of modern MRI/CT and PET/CT technology in distinguishing tumour residues from active disease. Considering current knowledge and imaging, no immediate orthopaedic surgical intervention is warranted. Conservative observation, with short-interval follow-up MRI, is a sound strategy. Should any of the lesions demonstrate growth or signal characteristics suggesting aggressive behaviour, percutaneous ablative techniques (cryoablation or radiofrequency ablation) could be reconsidered as minimally invasive alternatives to open surgery. This case illustrates the importance of long-term vigilance in CMF cases and confirms that not all residual lesions require surgical excision; furthermore, it emphasises the need for patient-centred, function-preserving decision making, particularly in individuals with high physical activity levels and excellent quality of life.

Discussion

Chondromyxoid fibroma is a rare type of benign cartilaginous tumour, most frequently arising in the metaphysis of long bones, with the proximal tibia being the most affected site (9). Karaca et al. reported on 31 CMF cases over 35 years, identifying the pelvis (25.8%), proximal tibia (22.6%), and distal femur (12.9%) as the most prevalent localisations, with less frequent involvement of the fibula, calcaneus, ribs, clavicle, olecranon, and bones of the hands and feet (4). In their cohort, pain was reported in 96.8% of patients, swelling in 41.9%, and the recurrence rate was 16.1%, with no malignant transformation observed. However, their methodology raises important questions: it remains unclear which imaging modalities were used to distinguish true recurrence from residual post-surgical lesions, and whether any early postoperative imaging confirmed complete clearance of the lesion after surgery. Without such baseline imaging for comparison, it is difficult to determine whether follow-up findings represented true recurrence or simply long-standing residuals. Establishing a standardised radiological follow-up protocol including MRI or PET/CT would greatly assist in resolving this ambiguity in future studies.

Standard treatment options for CMF include intralesional curettage, with or without bone grafting or cementing, wide resection, or segmental resection. The highest recurrence rates are associated with curettage performed without adjuvant techniques (7, 8, 10, 11). In the present case, intralesional curettage without grafting was performed, consistent with the practices of the 1980s. Recurrence was observed three years later, requiring a second surgical intervention. Remarkably, the patient remained asymptomatic and functionally unrestricted for more than three decades thereafter. The radiologically visible lesions, identified through modern imaging nearly 40 years later, present an important diagnostic dilemma: do these findings represent true late recurrences of CMF, or more likely in this case residual tumour remnants that remained biologically inactive over time?

The above distinction is clinically significant. The lesions identified by MRI and CT were small, sharply demarcated, subcortical in location, and surrounded by sclerotic margins, without signs of cortical breakthrough or soft tissue invasion. Their imaging characteristics low signal on T1 and mixed or intermediate signals on T2 and PD sequences are consistent with CMF. Importantly, there was no peri-lesional oedema or enhancement to suggest active inflammation or growth. Differential diagnosis of post-curettage residual lesions should also consider the possibility of low-grade chondrosarcoma, especially given the overlapping imaging features. Radiologically, both CMF and low-grade chondrosarcoma may show well-demarcated lytic lesions with chondroid matrices. However, low-grade chondrosarcomas often demonstrate endosteal scalloping, cortical breakthrough, soft tissue extension, and pain progression. In our case, the absence of aggressive features, together with a stable, asymptomatic course and negative PET/CT uptake, strongly supports the interpretation of benign residual CMF, rather than low-grade malignancy. Nonetheless, the radiologic similarities reinforce the importance of combining imaging with clinical and metabolic data to avoid over-treatment. Given the patient's long symptom-free interval and excellent functional status, the current findings are most consistent with residual, inactive lesions, rather than true recurrence. To further assess the metabolic activity of the lesions, a low-density PET/CT scan was performed, and the results showed no significant fluorodeoxyglucose (FDG) uptake in the femoral lesions, which strongly supports the interpretation that these are quiescent residuals rather than active or recurrent tumour tissue. Although CMF is typically a tumour of low metabolic activity, PET/CT can serve as a useful adjunct in ambiguous cases, especially when MRI findings are indeterminate or clinical suspicion persists. The absence of FDG activity in this case provided additional reassurance and justified a conservative management approach with short-interval follow-up imaging. In this context, we believe the term "recurrence" would be misleading, as there is no radiologic, metabolic, or clinical evidence to support active disease; rather, this case illustrates incidental, asymptomatic residuals persisting after non-adjuvant curettage. This case illustrates that not all post-treatment CMF lesions require excision, especially when they remain asymptomatic and radiologically stable. The patient's current symptoms were unrelated to tumour recurrence and were instead due to pes anserinus bursitis, as confirmed through clinical improvement following targeted corticosteroid injection. To our knowledge, only two cases of CMF have been reported in Croatia to date, both involving atypical locations: the mandible and the second metacarpal bone (12, 13). This case is the first Croatian report describing CMF of a long bone with long-term follow-up; it also underscores the importance of individualised, function-preserving decision-making and the value of a multidisciplinary approach. Contemporary management of CMF should involve orthopaedic oncologists, radiologists, and, where appropriate, interventional radiologists, especially in the era of minimally invasive and image-guided techniques. While malignant transformation of CMF is exceedingly rare, it has been described. In their clinicopathologic review of 278 patients with chondromyxoid fibroma, Wu et al. provided valuable insights into the natural history and biological behaviour of this rare tumour, which is considered to have an extremely low risk of malignant transformation (1). Radiotherapy has been cited as a potential risk factor. Yadav et al. recently described a high-grade secondary chondrosarcoma developing in previously treated CMF of the proximal tibia, reinforcing the importance of careful monitoring over time (14). Conversely, Berenstein-Weyel et al. reported successful treatment of a paediatric CMF case using percutaneous radiofrequency ablation (RFA), and Gowda et al. described cryoablation in a case of recurrent CMF, both highlighting promising, less invasive therapeutic alternatives (15, 16).

Although the histopathological diagnosis in our case was based on the conventional morphological criteria available at the time, we recognise that the molecular understanding of CMF has significantly advanced in recent years. Unfortunately, as no archival tissue has been preserved, retrospective molecular analysis was not possible in our case; however, in current clinical practice, genetic testing may provide additional diagnostic confidence in challenging or borderline cases.

In summary, this case exemplifies the benign but persistent nature of CMF, the utility of modern imaging including PET/CT in guiding management decades

after initial treatment, and the ongoing importance of long-term surveillance; it also raises critical questions about the interpretation of residual lesions and demonstrates how multimodal assessment can help resolve clinical uncertainty.

Importantly, this case further exemplifies the pivotal role that modern radiological techniques play in differentiating between active disease and benign residual lesions, especially in the context of long-term follow-up for benign bone tumours such as chondromyxoid fibroma (CMF). In previous decades, when advanced modalities such as MRI or PET/CT were unavailable or limited, surgical re-intervention was often required not only for treatment but also for diagnostic confirmation. In contrast, current non-invasive imaging strategies-when interpreted within the clinical and metabolic context-can offer a high degree of diagnostic confidence, potentially avoiding unnecessary procedures.

In this case, the absence of metabolic activity on PET/CT, combined with stable and well-demarcated imaging findings and a four-decade symptom-free interval, strongly supported the conclusion that the lesions were biologically inactive. Had there been any radiologic or metabolic indication of disease activity, such as increased FDG uptake, lesion progression, cortical breakthrough, or surrounding oedema, a biopsy would have been clearly warranted. However, none of these features was present.

Notably, the decision to forego biopsy was not based solely on imaging but resulted from a comprehensive multidisciplinary evaluation involving orthopaedic oncology, radiology, and nuclear medicine. This collaborative, patient-centred approach allowed for a nuanced management plan that minimised risk while preserving diagnostic integrity.

We believe this case reflects a broader shift in musculoskeletal oncology toward precision medicine and minimally invasive care, where advanced imaging modalities can, in selected low-risk cases, reliably serve as a surrogate for histopathological confirmation. Ultimately, it highlights the clinical and educational value of applying modern imaging techniques in evaluating late-appearing bone lesions, guiding appropriate follow-up strategies while avoiding unnecessary surgical morbidity.

Conclusions

This case highlights several key points: knowledge of chondromyxoid fibroma has significantly improved over recent decades; long-term, biologically inactive, residual lesions may persist for decades following intralesional curettage alone, without any adjuvant therapy; advanced imaging modalities, such as MRI and PET/CT, are essential for distinguishing such residuals from active disease; lifelong clinical and radiologic surveillance is warranted, due to the potential for late recurrence; malignant transformation, though rare, underscores the need for continued vigilance; and a multidisciplinary approach, involving orthopaedic surgeons, radiologists, and interventional radiologists, is essential for optimal management.

Abbreviations:

CMF - chondromyxoid fibroma
MRI - magnetic resonance imaging
CT - computed tomography
PET/CT - Positron emission tomography and computed tomography
RFA - radiofrequency ablation
FDG - fluorodeoxyglucose

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INSTITUTIONAL REVIEW BOARD STATEMENT: This study's protocol was reviewed and approved by the ethics committee of the Clinical Hospital Centre in Split; class: 520-03/25-01/83; registry number:2181-147-01-06/LJ.Z.-25-02, 02 April 2025. Written informed consent was obtained from the patient for publication of the details of her medical case and any accompanying images.

INFORMED CONSENT STATEMENT: Written informed consent was obtained from the patient.

DATA AVAILABILITY STATEMENT: All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

CONFLICTS OF INTEREST: The authors declare no conflicts of interest.

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Sažetak

ČETRDESET GODINA NAKON PEDIJATRIJSKOG HONDROMIKSOIDNOG FIBROMA DISTALNOG FEMURA: PRIKAZ SLUČAJA I PREGLED LITERATURE

Ivana Jukic, Ante Bandalovic, Kresimir Bukarica, Ana Krnic, Jonatan Vukovic

Hondromiksoidni fibrom (CMF) je rijedak tip benignog tumora kostiju koji čini manje od 2% svih benignih neoplazmi kostiju. Pretežito pogađa mlade osobe i obično se javlja u metafizi dugih kostiju. Unatoč svojoj benignoj prirodi, CMF stvara dijagnostičke i terapijske izazove zbog potencijala za lokalni recidiv i radiološke sličnosti s hondrosarkomom.

Prikaz slučaja: Izvještavamo o slučaju 9-godišnje djevojčice kojoj je 1985. godine dijagnosticiran CMF distalnog femura. Dva puta je podvrgnuta kiretaži, u razmaku od tri godine, s histološkom potvrdom CMF-a. Nakon kirurškog liječenja, pacijentica je ostala asimptomatska i funkcionalno neograničena gotovo četiri desetljeća. U dobi od 49 godina, javila se s bolovima u medijalnom dijelu koljena, koji nisu povezani s recidivom tumora. Slikovne studije, korištenjem magnetske rezonancije i kompjutorizirane tomografije (MRI i CT), otkrile su više malih, dobro definiranih lezija u dijafizi lijeve femura, radiološki konzistentnih s rezidualnim CMF-om. Lezije su bile asimptomatske i biološki neaktivne. Multidisciplinarna evaluacija podržala je konzervativno liječenje i slikovno praćenje.

Rasprava: Ovaj slučaj ističe važnost dugoročnog praćenja pacijenata s CMF-om i postavlja pitanje predstavljaju li kasno nastale lezije pravi recidiv ili, što je u ovom slučaju vjerojatnije, postoperativne ostatke bez biološke aktivnosti. Pozitronska emisijska tomografija i kompjutorizirana tomografija (PET/CT) mogu pružiti dodatne uvide u metaboličku aktivnost takvih lezija i pomažu u diferencijaciji i planiranju liječenja. Naš slučaj naglašava važnost prilagođenog pristupa usmjerenog na pacijenta, koristeći moderno snimanje i minimalno invazivnu dijagnostiku.

Zaključak: CMF zahtijeva pažljivo dugoročno praćenje zbog mogućnosti recidiva i rijetke maligne transformacije. Ovaj slučaj pokazuje da rezidualne lezije mogu perzistirati bez kliničkih posljedica desetljećima te da napredne tehnike snimanja igraju ključnu ulogu u kontinuiranoj evaluaciji i liječenju.

Ključne riječi: HONDROMIKSOIDNI FIBROM, FIBROM, BENIGNE NEOPLAZME, REZIDUALNA LEZIJA, MAGNETSKA REZONANCIJA, PET/CT, DUGOROČNO PRAĆENJE, PRIKAZ SLUČAJA

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