Intratendinous Calcified Chondroid Mesenchymal Neoplasm: A Case Report

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Learning Point of the Article:

This case report provides an example of the clinical findings, along with diagnostic imaging and histopathology used to identify an intratendinous calcified chondroid mesenchymal neoplasm of hamstring tendon origin.

Abstract

Introduction: We present a case report concerning calcified chondroid mesenchymal neoplasms (CCMN), a novel category of tumors that exhibit chondroid formation and contain fibronectin 1-receptor tyrosine kinase fusions.

Case Report: Our report focuses on a 73-year-old female patient who presented with pain in her right hip and gluteal region. Initially, the condition was misdiagnosed as calcific tendinitis based on X-ray imaging. However, a subsequent magnetic resonance imaging (MRI) revealed a solid lobulated mass originating from the right hamstring tendon origin, exhibiting heterogeneously hypointense T1-weighted signal, heterogeneously isointense proton density fat-suppressed signal, and heterogeneous contrast-enhancement compared to skeletal muscle. Further, investigation through computed tomography (CT) demonstrated intratumoral calcifications accompanied by erosive changes in the adjacent right ischial tuberosity. Histologic examination of a CT-guided biopsy confirmed the presence of large calcium pyrophosphate crystal deposits, along with benign chondroid tissue, thus supporting the diagnosis of CCMN. Notably, there is considerable overlap in the imaging characteristics of CCMN and the more commonly encountered calcific tendinitis (calcium hydroxyapatite depositional disease). Contrast-enhanced MRI findings play a crucial role in distinguishing between these two conditions.

Conclusion: To the best of our knowledge, this is the first documented report describing the imaging features of CCMN across multiple modalities, including radiography, CT, and MRI.

Keywords: Tumor, mass, hip.

Introduction

"Calcified chondroid mesenchymal neoplasm" (CCMN) is a newly coined term used to classify a group of chondroid-forming neoplasms that harbor fibronectin 1 (FN1)-receptor tyrosine kinase fusions. These neoplasms encompass entities such as chondroblastoma-like soft-tissue chondromas and chondroid tenosynovial giant cell tumors (TGCTs) [1]. Histologically,

CCMNs exhibit a lobular, multinodular architecture characterized by irregular and lace-like calcifications, as well as increased cellularity at the periphery of the nodules. The tumor cells demonstrate a stellate to polygonal shape, with moderate eosinophilic cytoplasm and nuclei eccentrically located within the chondroid matrix. Notably, certain cases of grungy calcifications exhibit features consistent with calcium



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Figure 1: Axial magnetic resonance imaging of the right hip. (a) Axial T1-weighted (T1W) image demonstrates a lobulated soft-tissue mass within the hamstring tendon origin (white arrow), with cortical irregularity of the adjacent ischial tuberosity (red arrow). (b) Axial T1W fat-suppressed image demonstrates areas of intratumoral hyperintense signal relative to muscle (white arrow), as well as cortical irregularity of the adjacent ischial tuberosity (red arrow). (c) Axial post-contrast T1W image without fat suppression and (d) axial post-contrast T1W fat-suppressed images demonstrate diffuse heterogeneous solid enhancement of the mass.

pyrophosphate deposition (CPPD) [1].

In this report, we aim to describe the imaging findings of CCMNs as observed through radiography, computed tomography (CT), and magnetic resonance imaging (MRI). These imaging modalities play a crucial role in distinguishing intratendinous CCMNs from calcific tendinitis (intratendinous hydroxyapatite depositional disease [HADD]). By elucidating the distinct imaging characteristics, this study provides valuable insights into the differentiation of these two conditions.

Case Report

A 73-year-old female patient was referred to our orthopedic oncology clinic for further evaluation of a "right sacral mass." She reported a 6-month history of lower back and right gluteal pain, which radiated down her right leg and was accompanied by numbness and tingling. Despite taking non-steroidal antiinflammatory medications and gabapentin, she experienced minimal pain relief. The patient denied experiencing fevers, changes in appetite, weight loss or gain, recent trauma, or previous surgery in the affected area. Her family history was unremarkable.

On physical examination, tenderness was noted on palpation of the right gluteal region and the upper leg around the hamstring origin of the ischial tuberosity. Hip flexion exacerbated her symptoms and restricted the range of motion in her right hip. No apparent skin changes or gross deformities were observed. Neurovascular and motor examination did not reveal any additional weakness or sensory deficits beyond those mentioned above. The radiating pain, numbness, and tingling in the right gluteal region were likely attributed to compression of the sciatic nerve by the tumor mass in various hip positions.





Figure 2: Coronal magnetic resonance imaging (MRI) of the right hip. (a) Coronal T1-weighted (T1W) MRI demonstrates a lobulated soft-tissue mass within the hamstring tendon origin (white arrow), with cortical irregularity and erosion of the adjacent ischial tuberosity (red arrow). (b) Coronal post-contrast T1WMRI demonstrates heterogeneous solid enhancement of the mass.

X-rays taken at an external medical institution displayed softtissue calcification in the region of the ischial tuberosity, extending just distally into the right ischial tuberosity. This prompted further investigation through MRI. A review of the axial MRI findings (Fig. 1) revealed a well-defined, lobulated heterogeneous soft-tissue mass measuring $6.9 \times 3.1 \times 2.7$ cm within the origin of the right hamstring tendon. The mass exhibited intermediate signal intensity on T1-weighted (T1W)sequences, resembling the signal intensity of skeletal muscle, with some areas of decreased signal intensity. Post-contrast T1W fat-saturated sequences showed intermediate signal intensity with no surrounding edema (Fig. 1d). The lesion extended toward and caused cortical irregularity of the adjacent right ischial tuberosity, which was evident on coronal MRI (Fig. 2). Post-contrast imaging demonstrated solid heterogenous enhancement of the soft-tissue mass, along with scattered areas of low signal intensity on T1W sequences, due to intralesional calcifications (Fig. 1 and 2). To further investigate the mass, a CT-guided biopsy was performed, and the scout view (Fig. 3) showed lobulated calcified mass near the right ischial tuberosity. Axial CT images (Fig. 4) revealed that the calcified mass was located within the hamstring tendon origin, with cortical irregularity of the adjacent right ischial tuberosity. The presence of intratumoral calcifications was consistent with an internal chondroid matrix. Histological analysis of the biopsy (Fig. 5) revealed significant deposits of calcium pyrophosphate crystals associated with benign chondroid tissue. Polarized microscopy was performed and revealed small rhomboidal

geometrically shaped crystals. Immunohistochemistry for the pan-TRK antibody yielded negative results, while S100 staining highlighted a few chondroid cells. These findings were indicative of a CCMN. Following histological analysis of the mass, the mass was excised surgically, ensuring that the entire tumor mass and its gross pathology were removed . Negative tumor margins were determined intraoperatively by the pathologist. Our institution's standard is to have pathology evaluate the tumor on resection to determine negative margins before closing the patient. Postoperatively, a standard hamstring tendon tear physical therapy regimen was employed for rehabilitation. Following surgical resection, the patient proceeded with follow-up care at another institution closer to her home. However, as far as the orthopedic surgeon who excised the tumor at our institution is aware, the patient has not returned for any new or recurring symptoms.

Discussion

CCMN is a recently introduced term by Liu et al. in 2021 to provide a comprehensive understanding of chondroid matrixproducing neoplastic entities with FN1-receptor tyrosine kinase fusions [1]. Liu et al. observed that CCMN exhibits overlapping morphologic and genetic features of chondroblastoma-like soft-tissue chondromas and chondroid TGCTs, along with variable calcium pyrophosphate crystal deposition [1,2,3].

On one end of the spectrum, CCMN shares similarities with



Figure 3: Scout view of computed tomography (CT)-guided biopsy. Scout view CT shows a calcified mass, along the inferolateral margin of the right ischial tuberosity.



Figure 4: Axial view computed tomography (CT)-guided biopsy. Axial image from the CT-guided biopsy shows an intratendinous calcified mass within the right hamstring tendon origin (white arrow), with cortical irregularity of the adjacent ischial tuberosity (red arrow).

chondroid TGCTs. Histologically and morphologically, chondroid TGCTs display sheet-like proliferation of large epithelioid to histiocytoid mononuclear cells. Some cases exhibit hemosiderin deposition in a ring-like fashion around the cytoplasm, as well as multinucleated giant cells, which are typical of conventional TGCTs. In addition, chondroid TGCTs demonstrate the presence of geographic or nodular areas of chondroid matrix, often associated with grungy, lace-like calcifications, akin to chondroblastoma-like soft-tissue tumors, as described by Liu et al. [1]. While some chondroid TGCTs are reported to result from CSF1 fusion, others harbor the FN1 fusion [1], which prompts the consideration of reclassifying FN1 fusion subtypes of chondroid TGCTs and those exhibiting significant histological overlap with chondroblastoma-like soft-tissue tumors as CCMN.

CCMN also encompasses features of chondroblastoma-like soft-tissue tumors, which histologically manifest as cellular foci consisting of epithelioid chondrocytes of varying sizes admixed with osteoclast-like giant cells within a variable amount of chondroid matrix, frequently accompanied by lace-like calcifications [4]. However, certain FN1 fusion subtypes of chondroblastoma-like soft-tissue tumors reported by Liu et al.



Figure 5: Histology of the mass. (a) Low power microscopy image (H&E stain, ×100) shows vaguely lobular architecture with extensive basophilic calcium pyrophosphate crystal deposition. (b) High power microscopy image (H&E stain, ×200) shows epithelioid to differentiated chondrocytes within crystalline deposits at high power.

also exhibit TGCT features and calcium pyrophosphate deposition. The spectrum of these features is encompassed by the recently defined CCMN classification.

In the past, chondroblastoma-like soft-tissue chondromas were distinguished from TGCTs based on the absence of specific cell types, such as siderophages, foamy macrophages, and lymphocytes intermixed with mononuclear cells [4]. Chondroid TGCTs, on the other hand, feature a collagenous and hyalinized background stroma



not observed in chondroblastoma-like chondromas [4]. However, Liu et al. have demonstrated that these entities are better characterized as part of a spectrum of chondroid matrixforming tumors with translocations involving FN1 and receptor tyrosine kinase domains, including FGFR1 (without Ig domain), FGFR2, MERTK, TEK1, and NTRK11. Previously, tumors with tyrosine kinase domains containing FGFR1 (without Ig domain) and FGFR2 were categorized as a subset of soft-tissue chondromas. However, Liu et al. introduced the term CCMN to expand the classification and encompass these entities within a broader spectrum of chondroid-producing neoplasms [1,5,6].

In our case, the imaging findings of the CCMN revealed an amorphous calcified mass projecting inferiorly to the right ischial tuberosity on radiographs. MRI showed cortical irregularity of the ischial tuberosity and demonstrated a calcified low to intermediate T1W signal intensity intratendinous soft-tissue mass within the hamstring tendon origin. The mildly increased T1W signal within the tumor may be attributed to a combination of intratumoral protein content and T1 shortening due to surface interactions between microcalcifications and protons [7,8]. In addition, intralesional foci of high signal intensity were observed on proton density images, which likely corresponded to the chondroid/cartilaginous matrix of the neoplasm. Notably, there was minimal perilesional edema on fluid-sensitive sequences, which serves as a distinguishing feature from acute calcific tendinitis. Post-contrast imaging revealed a heterogeneously enhancing solid soft-tissue mass. The scattered internal foci with low signal intensity on both T1 and PD sequences were suggestive of internal mineralization within the mass. CT images (Figs. 3 and 4) further revealed mass-like amorphous calcifications within the right hamstring tendon origin, causing cortical irregularity in the adjacent ischial tuberosity.

The differential diagnosis included CCMN, HADD (calcific tendinitis), tophaceous CPPD, and calcifying aponeurotic fibroma. In this case, HADD was the primary consideration due to the presence of extra-articular, intratendinous mineralization. HADD is a common cause of intratendinous mineralization, typically affecting women between the ages of 30 and 50, primarily involving the shoulders [7, 9, 10, 11, 12, 13]. The underlying pathophysiology of calcium hydroxyapatite deposition within tendons remains unclear but may be related to repeated microinjury, leading to tendon ischemia and subsequent remodeling [14, 15]. CCMN and HADD share overlapping features on plain film and CT, such as intratendinous amorphous calcifications and cortical erosions. However, on MRI, HADD can exhibit a variable appearance

depending on the phase of the process. In the acute or resorptive phase, HADD presents with a globular low T1W signal and a low T1-FS signal due to mineralization, accompanied by increased perilesional edema and surrounding enhancement due to inflammation [11, 14]. In contrast, this case of CCMN did not demonstrate perilesional edema. Due to the similar imaging findings between HADD and CCMN, histological evaluation was essential for an accurate diagnosis. Histological studies of calcific tendinitis have revealed the presence of macrophages and multinucleated cells surrounding fragmented calcium deposits, often in proximity to capillary channels. Chondrocyte-like cells have also been reported to surround calcium deposits, which are identified as calcium hydroxyapatite crystals [15, 16]. In the present case of CCMN, histological examination differed from HADD in terms of the absence of surrounding macrophages, and the calcium deposits were composed of calcium pyrophosphate crystals. However, chondrocytes were evident in both conditions.

Tophaceous CPPD, also known as tumoral pseudogout, is a rare form of CPPD that can mimic the appearance of chondroid tumors [16]. These tophaceous masses are typically periarticular and can cause erosive changes in the adjacent bones. Radiographs and CT scans demonstrate amorphous mass-like calcifications [16]. MRI findings can vary, with reported findings of low T1W signal and uniformly high or heterogeneous intermediate T2-weighted (T2W) signal [16]. Interestingly, Liu et al. also suggested the possibility that tophaceous pseudogout may be a neoplastic process involving FN1 translocations, potentially falling within the CCMN spectrum [1]. However, further research on the molecular and genetic aspects of tophaceous pseudogout is needed for confirmation.

Calcifying aponeurotic fibroma is a rare fibroblastic tumor that primarily occurs in the hands and feet of children [17, 18]. While it is most commonly located within the subcutaneous layer, it has also been reported to present as an intermuscular mass [19]. Radiographically, it appears as an ill-defined softtissue mass with or without stippled calcifications [18, 19]. CT is more sensitive in detecting calcified areas and possible bony erosions. On MRI, it typically demonstrates intermediate T1W signal intensity and heterogeneous high and low T2W signal intensity, along with intense heterogeneous contrastenhancement [18, 19].

The preferred treatment for chondroid TGCTs and soft-tissue chondromas is surgical excision [5, 20]. This suggests that CCMN, which encompasses both entities, would also be amenable to surgical excision. However, as research on molecular targeted inhibitors progresses, targeted therapy of the receptor tyrosine kinases may become an alternative



treatment option for CCMN [1]. These treatment approaches differ from those for intratendinous HADD, which is typically a self-limiting process managed with pain control using aspirin, non-steroidal anti-inflammatory drugs, or acetaminophen, and resolves within a few weeks [21]. Non-operative treatments, including ultrasound-guided and CT-guided barbotage, as well as steroid injections, have been shown to provide pain relief and functional recovery [22, 23, 24, 25, 26]. Surgical treatment is reserved for cases where minimally invasive techniques are unsuccessful.

CCMN represents a spectrum of chondroid-producing neoplasms with FN1-receptor tyrosine kinase fusion, as first described by Liu et al. in 2021. This review provides the first comprehensive evaluation of the imaging characteristics of CCMN using radiography, MRI, and CT. In our case, there was a significant overlap in the radiographic and CT imaging findings between CCMN and intratendinous HADD. Contrast-enhanced MRI plays a crucial role in the diagnosis by revealing distinctive imaging features. CCMN exhibited a mass-like appearance within the tendon, minimal perilesional edema, and diffuse heterogeneous intralesional contrast enhancement. In contrast, HADD during the acute phase displayed minimal intralesional contrast-enhancement with extensive surrounding perilesional edema. The final diagnosis of CCMN is confirmed through tissue biopsy, with surgical excision being the preferred treatment. However, further investigation into targeted therapies is imperative, as surgical excision alone may not provide a definitive cure, and recurrence is possible.

Conclusion

CCMN is a new classification capturing the spectrum of chondroid-producing neoplasms with FN1-receptor tyrosine kinase fusions. Although rare, in an elderly female with nonspecific unilateral gluteal and lower back pain with associated soft-tissue calcifications on X-ray imaging, it is important to consider a CCMN on the differential diagnoses. To the best of our knowledge, this case is one of the first reported CCMN tumors identified after the Lie et al. classification.

Clinical Message

When a patient presents with soft-tissue calcifications on X-ray, an MR image along with histological analysis of the calcified mass can be useful to diagnose the mass as a chondroid tumor under the recently coined CCMN tumor spectrum and provide an appropriate treatment plan. Although rare, CCMN should be included on the differential of an elderly patient presenting with non-specific localized tenderness with radiating pain, especially if X-ray imaging demonstrates a soft-tissue calcification in the associated region.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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