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CASE REPORT

Osteolipoma: radiological, pathological, and cytogenetic analysis of three cases

Karen J. Fritchie · Jordan B. Renner · Kathleen W. Rao · Robert J. Esther

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Abstract Osteolipoma is a rare variant of lipoma consisting of mature adipose tissue and mature lamellar bone. The presence of non-fatty elements may lead to a wide differential diagnosis on radiology including benign and malignant lipomatous and nonlipomatous entities. The pathological diagnosis is also confounded by the presence of heterologous differentiation. Fortunately, most lipomas harbor classic cytogenetic aberrations, and the finding of translocations involving 12q13-15 may aid in the correct diagnosis. We report three cases of osteolipoma with radiological, histological, and cytogenetic correlation.

Keywords Magnetic resonance imaging · Neoplasm · Lipoma · Chromosome aberrations

Introduction

Lipoma is the most common soft tissue tumor and typically causes few clinical problems. Most lipomas are superficial (subcutaneous) and present during middle age in locations such as the upper back, shoulder, abdomen, and extremities [1]. Occasionally, lipomas occur in deep soft tissue (subfascial), and tend to be larger and less well circumscribed compared with their superficial counterparts. While superficial fatty tumors are almost always benign, deep well-differentiated lipomatous neoplasms are more diagnostically challenging because the distinction between atypical lipomatous tumors and lipomas can be difficult radiologically and microscopically. This is compounded by the fact that some lipomas contain other mesenchymal elements such as fibrous connective tissue (fibrolipoma), an abundance of blood vessels (angiolipoma), and cartilaginous/osseous metaplasia (chondrolipoma, osteolipoma). Fortunately, cytogenetic analysis can be helpful since lipomas harbor distinct karyotypic abnormalities. We report three cases of osteolipoma with clinical, radiological, microscopic, and cytogenetic correlation.

K. J. Fritchie (✉)
Department of Laboratory Medicine and Pathology, Mayo Clinic,
200 First Street SW,
Rochester, MN 55905, USA
e-mail: karenfritchie@gmail.com

J. B. Renner
Radiology, University of North Carolina Hospitals,
Chapel Hill, NC, USA

K. W. Rao
Cytogenetics, University of North Carolina Hospitals,
Chapel Hill, NC, USA

R. J. Esther
Orthopedic Surgery, University of North Carolina Hospitals,
Chapel Hill, NC, USA

Case report

Case 1

A 60-year-old woman with a remote history of a left wrist fracture presented with a 2- to 3-year history of a progressively enlarging left wrist mass. Physical examination revealed a nontender mobile distal radial mass approximately 3 cm proximal to the distal wrist crease. Her sensation was intact to light touch over the mass and throughout the superficial radial nerve distribution.

Radiographs showed a large partially calcified soft tissue mass without evidence of bone erosion (Fig. 1). Deformity of the distal radius indicating an old comminuted fracture was also noted. MR imaging showed a soft tissue mass

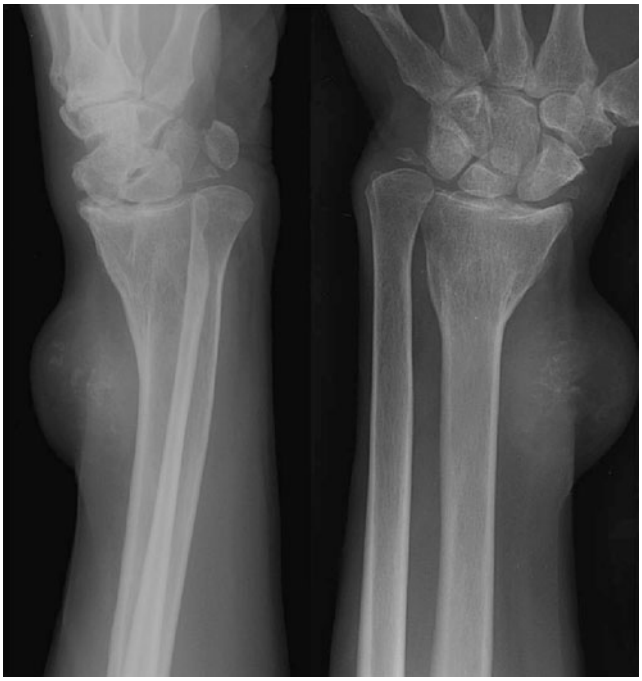

Fig. 1 Semisupinated oblique (*left*) and posteroanterior (*right*) radiographs of the left wrist from Case 1 show a partially and faintly calcified mass adjacent to the distal radius. There is an old, healed fracture of the distal radius, but there is no erosion of the underlying radius. Small ossicles at the radial and ulnar styloid processes also indicate previous trauma

along the radial side of the distal forearm abutting and displacing the extensor carpi radialis longus and brevus and abductor pollicis longus tendons (Fig. 2). The mass closely approximated but did not involve the radial artery and vein. The mass appeared to contain some adipose tissue and demonstrated heterogeneous T1 and T2 signal and intense heterogeneous enhancement following the administration of IV contrast material (Fig. 3).

Gross examination revealed a well-circumscribed partially calcified 4×3×2 cm tan-pink fatty soft tissue mass with cartilaginous/osseous foci at the periphery of the lesion (Fig. 4a). Histological examination showed a lipomatous lesion with large foci of cartilage undergoinging endochondral ossification (Fig. 4b). No atypical hyperchromatic stromal cells or cytological atypia were identified within the fatty component (Fig. 4c). Fresh tissue was sent for cytogenetic analysis. The tissue was set up in monolayer culture and harvested by standard cytogenetic protocols. Slides were G-banded and 20 cells from each case were analyzed thoroughly. Cytogenetic analysis showed a translocation between chromosome 3 and 12 (46,XX,t(3;12)(q27;q15)[20]).

Seven months after excision the patient is doing well without recurrence.

Case 2

A 51-year-old man presented with a 3-month history of a painless right knee mass. Physical examination revealed a nontender, minimally mobile mass over the lateral anterior infrapatellar knee. The knee had range of motion from 0–120° and was stable to varus, valgus, and anterior/posterior drawer stress.

Radiographs showed a soft tissue mass projecting over Hoffa's fat pad and partially over the infrapatellar tendon (Fig. 5). Calcific stippling suggestive of chondroid matrix calcification or dystrophic calcification was identified. MR images showed the mass encircling the lateral retinaculum of the patella and encasing the lateral patellar tendon. The

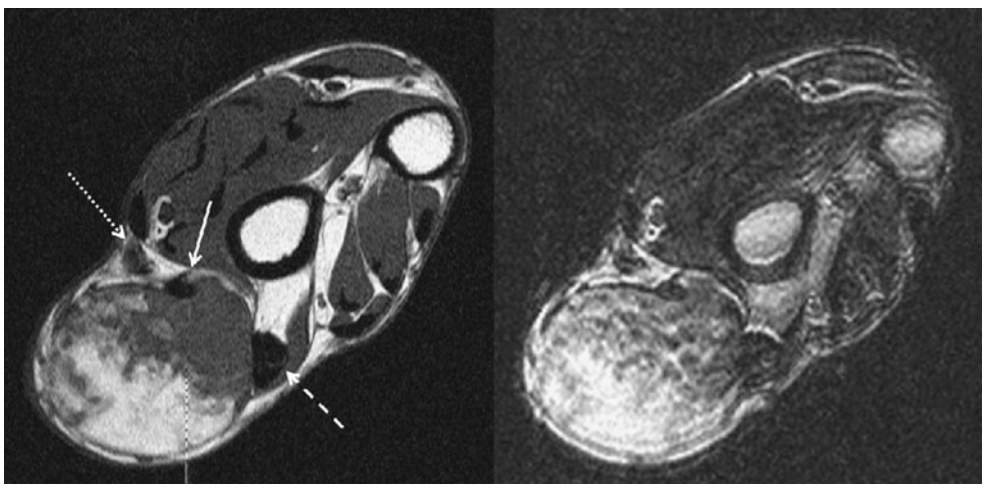

Fig. 2 Transverse T1- (*left*) and T2-weighted (*right*) images of the distal forearm from Case 1 demonstrate a heterogeneous mass along the lateral aspect of the forearm. The mass is partially interposed between the abductor pollicis longus tendon (*solid arrow*) and the extensor carpi radialis longus and brevis tendons (*dashed arrow*) and is posterior to the radial artery (*dashed arrow*). There is no underlying bone erosion. Laterally, much of the mass contains fat, whereas, particularly between the tendons, the signal intensity is isointense to muscle

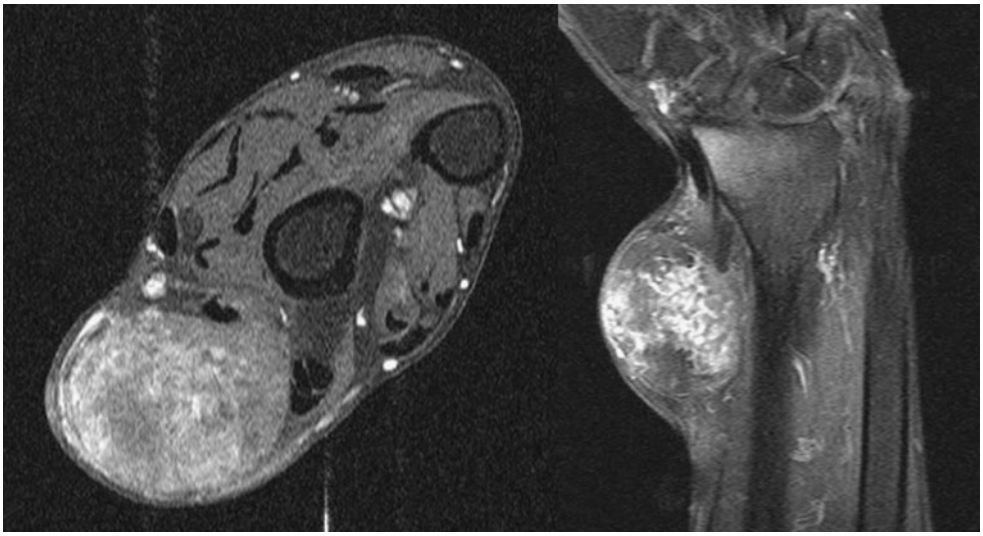

Fig. 3 Transverse (*left*) and coronal (*right*) fat-suppressed T1-weighted images after the intravenous administration of gadolinium show heterogeneous enhancement of the mass demonstrated from Case 1. Enhancement is present in portions of the lipomatous and soft tissue components of the mass

mass had heterogeneous low T1 signal and heterogeneous low and high T2 signal. Post-gadolinium images demonstrated intense heterogeneous enhancement (Fig. 6). There was no evidence of bone involvement.

Gross examination revealed multiple fragments of yellow tissue measuring up to 4.2×4×2.8 cm. The cut surfaces showed yellow-tan glistening fat intermixed with bony fragments. Microscopic examination revealed a lipomatous proliferation of mature adipose tissue studded with islands of mature bone and cartilage (Fig. 7a). Osteoblastic rimming was identified at the edge of new bone formation (Fig. 7b). No atypical hyperchromatic stromal cells or cytological atypia were identified. Cytogenetic analysis showed a translocation involving the long

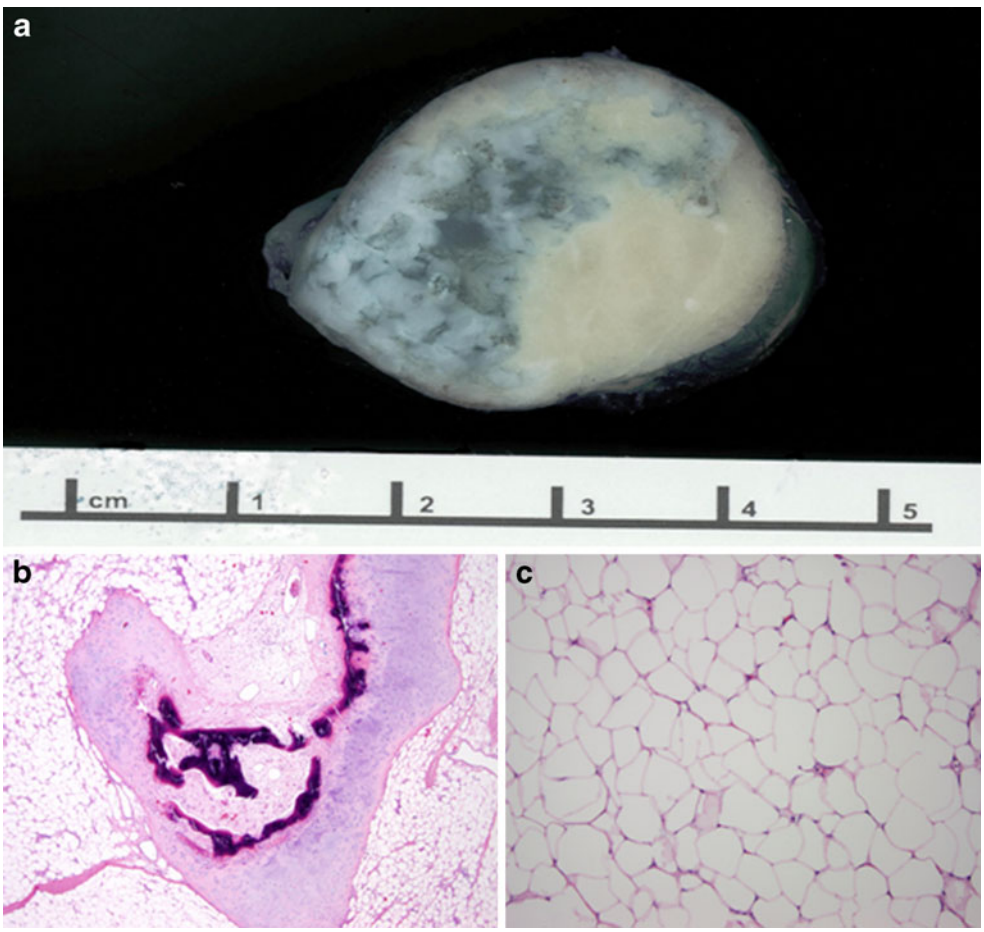

Fig. 4 **a** Gross examination of the specimen from Case 1 reveals a well-circumscribed lipomatous lesion with a large gray-white chondro-osseous component. **b** Histological review demonstrates a large central area of chondroid metaplasia with focal bone formation surrounded by mature adipose tissue (H&E stain; ×40 original magnification). **c** Microscopic examination of the fatty component reveals mature adipocytes without fibrous bands or cytological atypia (H&E stain; ×100 original magnification)

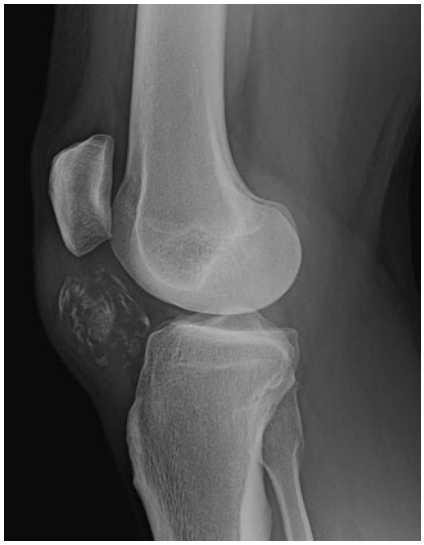

Fig. 5 A lateral radiograph of the knee from Case 2 demonstrates a heterogenous, densely calcified mass projecting within the infrapatellar soft tissue. The mass is inseparable from the infrapatellar tendon, but is well removed from the adjacent bones

arms of chromosomes 3 and 12 (46,XY,t(3;12) (q27;q14-15).[15] / 46,XY[4]).

Eight months following excision of the mass the patient is doing well without recurrence.

Case 3

A 31-year-old woman presented with a 1-year history of a slowly enlarging right knee mass. The mass was generally nontender, but mechanically irritating. Physical examination revealed a firm, rubbery mass adherent to the patellar tendon. The knee was otherwise stable with a good range of motion.

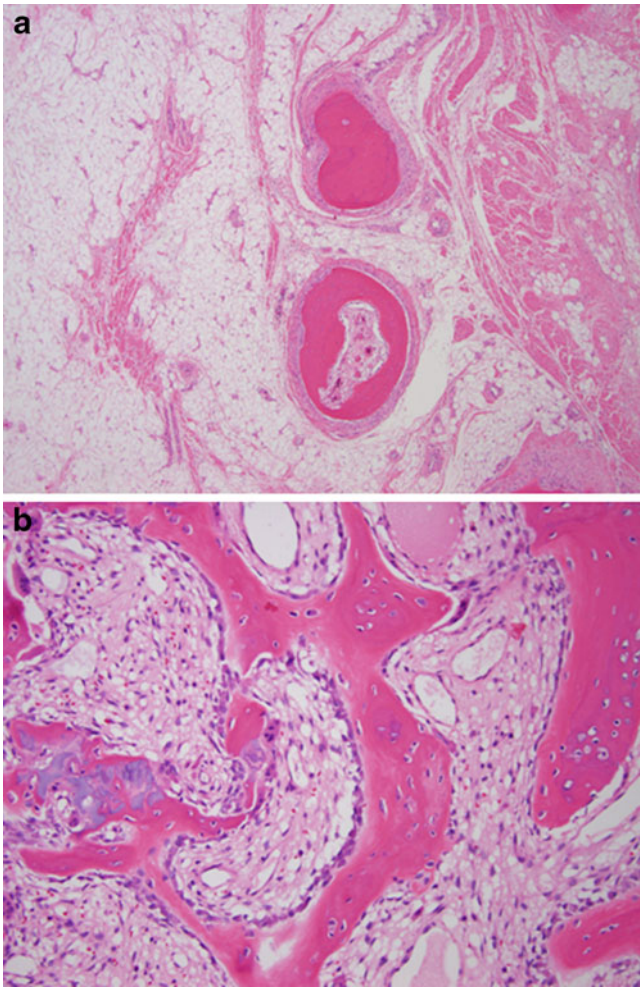

Fig. 7 **a** Histological review of Case 2 shows islands of mature bone within a background of mature adipose tissue (H&E stain; ×40 original magnification). **b** Numerous osteoblasts are identified rimming the bony trabeculae (H&E stain; ×100 original magnification)

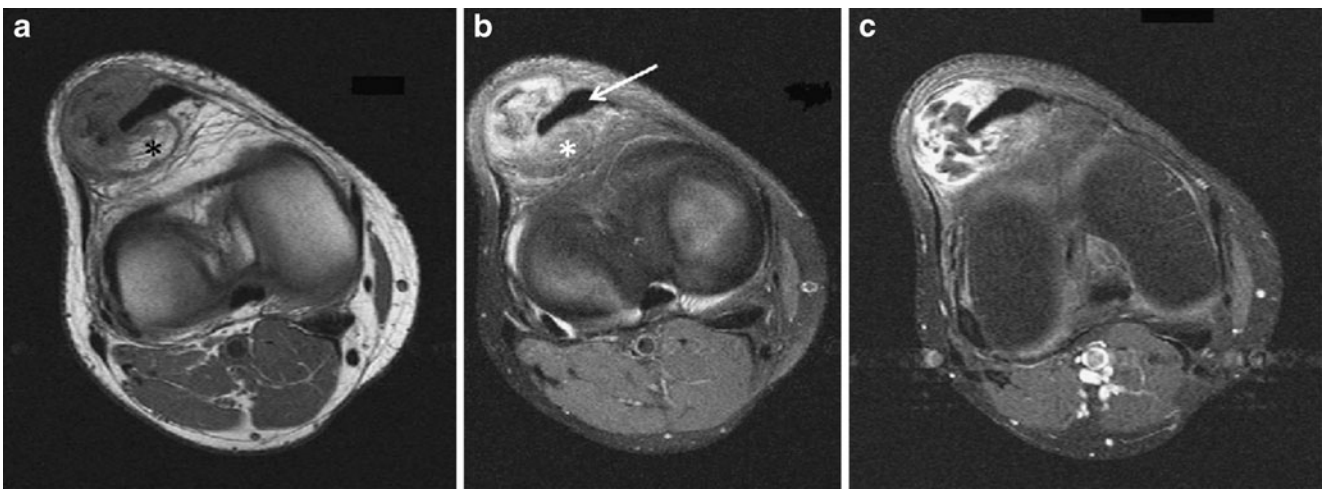

Fig. 6 Transverse **a** T1-weighted, **b** fat-suppressed T2-weighted and **c** fat-suppressed T1-weighted images from Case 2 with intravenous gadolinium enhancement show the heterogeneous soft tissue mass lateral to and partially enveloping the infrapatellar tendon (*arrow* in **b**). Posterior to the infrapatellar tendon, a portion of the mass is isointense to fat (*asterisk*), but anteriorly much of the mass is hypointense to fat on T1 imaging and hyperintense to muscle on fat-suppressed T2 imaging. After gadolinium administration, much of the mass enhances briskly anteriorly and posteriorly. Persistently hypointense material just lateral to the infrapatellar tendon represents calcification in the mass

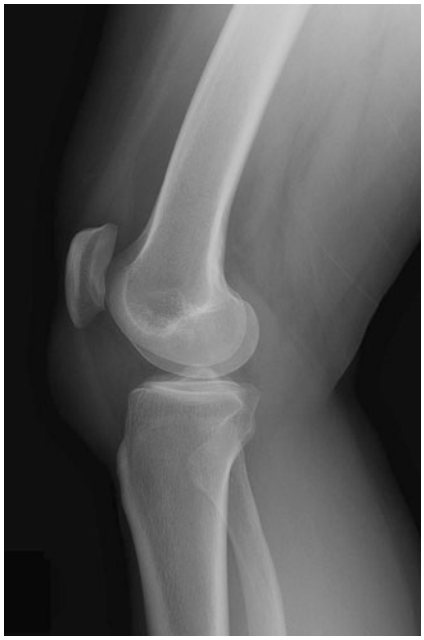

Fig. 8 A lateral radiograph of the knee from Case 3 reveals thickening of the infrapatellar tendon as well as a vague soft tissue density posterior to the patella and infiltrating Hoffa's fat pad

Anteroposterior/lateral images revealed thickening of the infrapatellar tendon as well as a vague soft tissue density posterior to the patella and infiltrating Hoffa's fat pad (Fig. 8). MR imaging showed a moderately large soft tissue mass arising from and partially enveloping the lateral aspect of the infrapatellar tendon and extending into the infrapatellar fat pad (Fig. 9). A portion of the mass anteriorly was isointense to fat, although the remainder of the mass was heterogeneously hypointense to fat. A fat-suppressed T1-weighted image after intravenous gadolinium enhancement showed that the signal intensity in the fatty component anterior to the infrapatellar tendon was suppressed with fat, while there was brisk enhancement posterior to the infrapatellar tendon

Gross examination revealed a well-defined encapsulated mass that measured 5.2×4.3×4.1 cm. Sectioning revealed a solid whorled cut surface with a small amount of fibrofatty tissue at the edge of the mass. Microscopic examination revealed a lipomatous neoplasm composed of mature adipose tissue, significant cartilaginous metaplasia and focal osseous differentiation. No atypical hyperchromatic stromal cells or cytological atypica were present. Cytogenetic analysis showed a translocation involving the long arms of chromosomes 3 and 12 (46,XX,t(3;12) (q27;q13) [18] /46,XX[2]) (Fig. 10).

The patient is doing well 25 months after excision.

Discussion

All three patients described in this report had an osteolipoma composed of mature adipose tissue and mature lamellar bone. Most prior reports of lipomatous tumors with osseous elements have had some connection to bone (parosteal lipoma). In contrast, there have been relatively few cases of osteolipoma independent of bone [2–6]. While lipoma is a common soft tissue neoplasm, osteolipoma is a rare variant that can cause diagnostic difficulty on many levels.

It is generally accepted that superficial (subcutaneous) fatty lesions are more likely to be benign, while deep-seated (subfascial, retroperitoneal) lipomatous masses may be

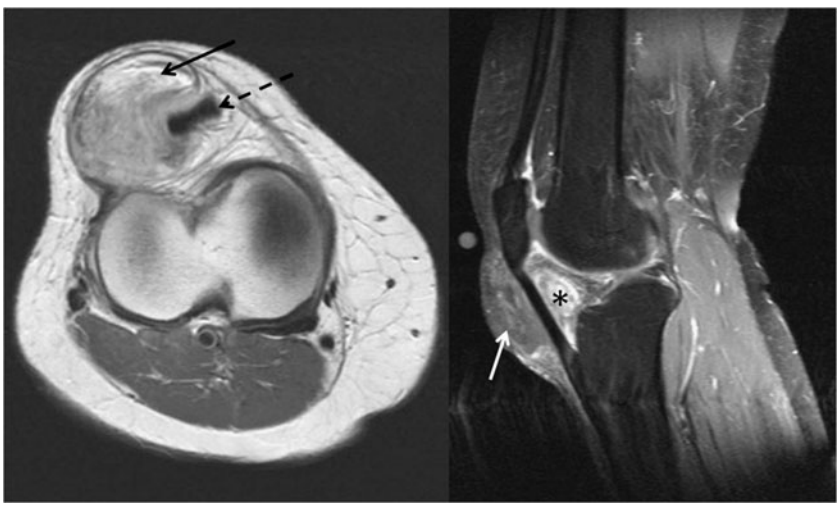

Fig. 9 A transverse T1-weighted image (*left*) from Case 3 demonstrates a soft tissue mass lateral to and partially encircling the infrapatellar tendon (*dashed arrow*). A portion of the mass anteriorly is isointense to fat (*solid arrow*), although the remainder of the mass is heterogeneously hypointense to fat. A fat-suppressed T1-weighted image after intravenous gadolinium enhancement (*right*) shows that the signal intensity in the fatty component anterior to the infrapatellar tendon suppresses with fat (*arrow*), while there is brisk enhancement posterior to the infrapatellar tendon (*asterisk*)

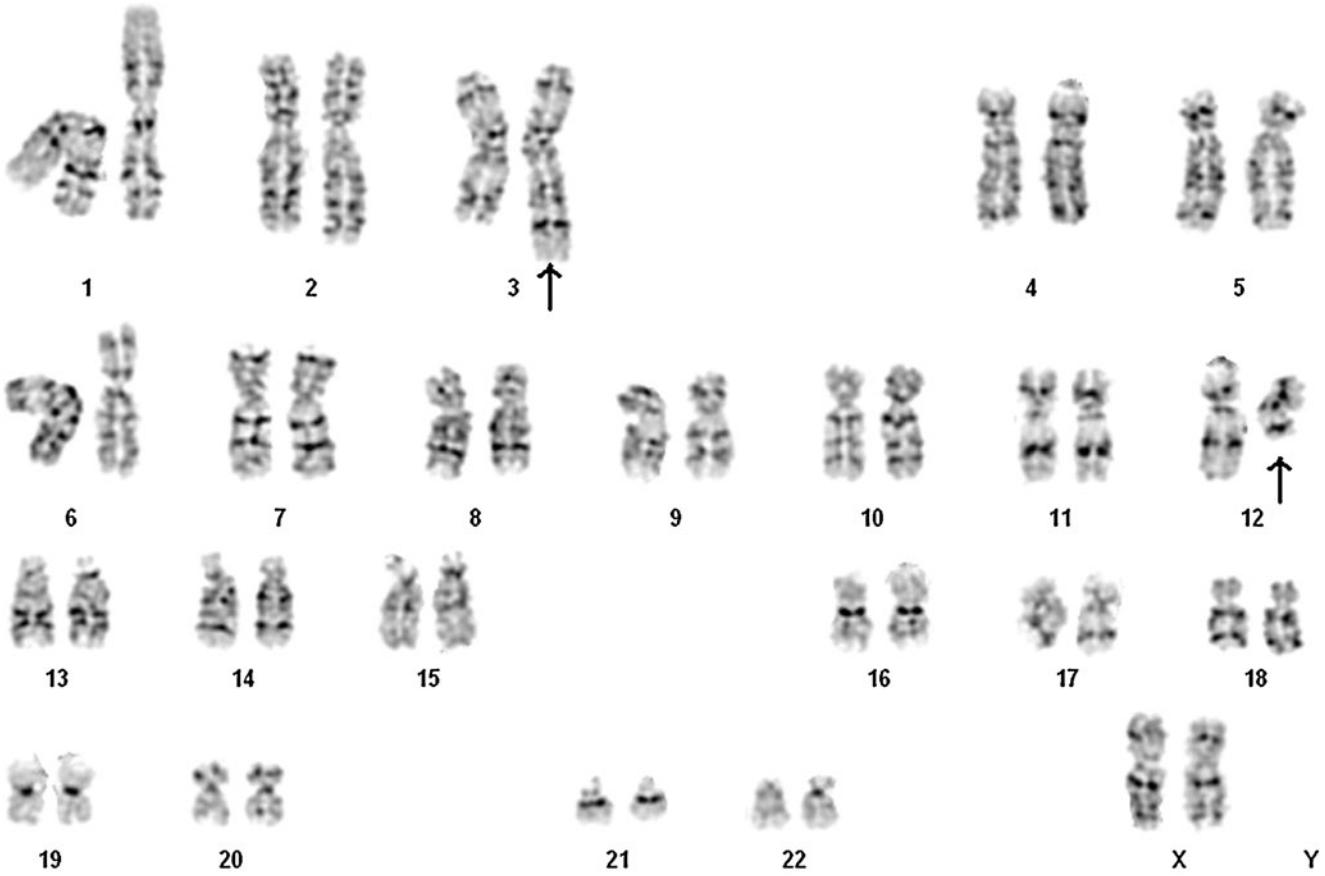

Fig. 10 Full karyotype from Case 3 showing a translocation involving the long arms of chromosomes 3 and 12 (*arrows*)

worrisome, especially if they are large or have certain features such as thickened fibrous septa [1]. Additionally, the presence of heterologous elements such as bone and cartilage can lead to diagnostic consideration of entities such as soft tissue chondroma, myositis ossificans, and extraskeletal osteochondroma. As in the three cases described above, fatty tumors in deep locations typically trigger further workup such as imaging and pathological sampling.

Even though simple lipomas and atypical lipomatous tumors are both well-differentiated lipomatous neoplasms, MRI can sometimes be helpful in distinguishing these lesions. Features such as thickened septa, nonadipose elements, prominent foci of high T2 signal and prominent areas of enhancement suggest atypical lipomatous tumor [7]. On the other hand, a discrete encapsulated homogeneous fatty mass on imaging would be consistent with a simple lipoma. Unfortunately, benign lipomas may also contain other mesenchymal elements such as blood vessels, fibrous septa or osseous metaplasia that can complicate imaging and mimic atypical lipomatous tumors. Galant et al. reported a case of osteolipoma that showed nodules/septa on T1-weighted images, but did not exhibit high

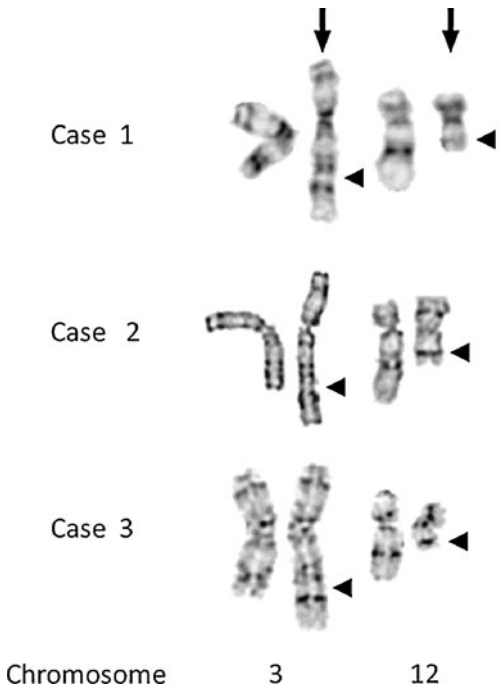

Fig. 11 Partial karyotypes from each patient demonstrating the presence of the recurring t(3;12)(q27;q13-15) in all three tumors. The breakpoints are indicated with *arrowheads*

signal intensity abnormalities on FS-T2/STIR. The paper subsequently noted that the presence of linear or nodular foci of hyperintensities on FS-T2/STIR sequences constitute a more specific sign than septa or nodules detected on T1 for the detection of atypical lipomatous tumors [8].

The radiological interpretations in Cases 1 and 2 were also complicated by the presence of calcifications, which raised the possibility of a chondroid neoplasm such as soft tissue chondroma. Cartilaginous neoplasms exhibit a characteristic ring-and-arc pattern of calcification that may coalesce to a radiopaque flocculent pattern [9]. The serpiginous appearance of T2 and post-gadolinium signal in Case 1 also led to consideration of a vascular process. Since the radiological differential in these three cases was somewhat nonspecific and included both benign and malignant entities, pathological sampling was necessary for definitive diagnosis.

The pathological findings in all three cases were similar and included mature adipose tissue with variable amounts of cartilage and bone. The most important morphological features in discriminating atypical lipomatous tumor from benign lipoma is the presence of atypical hyperchromatic stromal cells usually seen in fibrous septa or vessel walls of the former [1]. Although all cases lacked cytological atypia, the deep location of the lesions coupled with the presence of heterologous elements raised concern regarding atypical lipomatous tumor. Another diagnostic consideration included extraskeletal osteochondroma given the presence of chondroid and osseous elements. Extraskeletal osteochondromas are rare benign cartilaginous neoplasms with a predilection for the hands and feet [10, 11]. Fresh tissue sent for cytogenetic analysis revealed the presence of the recurring t(3;12)(q27;q13-15) in all three tumors, supporting the diagnosis of osteolipoma (Fig. 11) and arguing against entities such as atypical lipomatous tumor and extraskeletal osteochondroma.

Almost 75% of lipomas have chromosomal abnormalities, and two thirds of those aberrations involve 12q13-15. The most common rearrangement is t(3;12)(q27-28;q13-q15), but other reported partner chromosomes include 1p36,1p32-34, 2p22-24, 2q35-37 and 5q33 [1]. Other common cytogenetic aberrations include interstitial deletions of chromosome 13 and translocations involving 6p [12]. Atypical lipomatous tumors, in comparison, are characterized by giant marker and ring chromosomes that contain amplified sequences of 12q13-15 [13]. There are only limited reports of karotypic or molecular findings of lipomatous tumors with osseous elements. Petit et al. reported the karotype of a parosteal lipoma [14]. Chromosomal analysis showed the following result: 46,XX,t(3;12)(q28;q14). Matsui et al. described an intrapatellar tendon lipoma with an HMGA2-LPP fusion gene transcript [15]. The HMGA2 (HMGIC) gene encodes for a member of the high mobility group of proteins and is located on 12q15 [1]. To our knowledge this is the first report of cytogenetic findings in osteolipoma. The cytogenetic and molecular findings in our three cases support their relation to other lipomas of soft tissue.

The pathogenesis of osteolipoma remains unknown, although two main theories have been proposed. The first suggests that these tumors arise from multipotent mesenchymal cells [4]. However, the favored hypothesis is one of secondary ossification from repetitive trauma [16]. Our cytogenetic findings support the latter theory since the translocations in our three cases of osteolipoma are consistent with the karyotypic features of simple lipoma.

In conclusion, we reported the clinical, radiological, histological, and cytogenetic findings of three cases of osteolipoma. While routine karyotyping is not necessary for all deep fatty lesions, it may be helpful in larger tumors with worrisome radiological or morphological features. Cytogenetic analysis of our three cases provides evidence that osteolipoma is a variant of lipoma.

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Conflict of interest The authors declare that they have no conflict of interest.

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