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Case report

Tenosynovial giant cell tumor of the distal tibiofibular joint ☆,☆☆

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ABSTRACT

Tenosynovial giant cell tumors are extremely rare tumors with highly nonspecific symptoms. This benign but aggressive disease has a slow course of progression; however, it can ultimately lead to irreversible damage to a joint. Here we describe a case of a 45-year-old female with a diagnosis of tenosynovial giant cell tumors of the distal tibiofibular joint, the second case described in the literature for such location. Appropriate imaging studies and ultimately histologic studies are necessary for the correct diagnosis. Some locations are particularly unusual for these tumors making a high level of suspicion as well as treatment by an oncology orthopedic surgery specialist at a high-volume center paramount.

Introduction

Tenosynovial giant cell tumors (TGCT) were fist described in 1941 by Jaffe and include a group of tumors present usually in relationship with synovium, bursas or tendon sheaths [1]. In 2013 the World Health Organization re-named this disease from what was formerly being called extra-articular giant cell tumor of tendon sheath and nodular tenosynovitis to localized TGCT, while what was initially called intra-articular pigmented villonodular synovitis was-renamed diffuse TGCT and includes the diffuse-type giant cell tumors [2]. This disease affects most commonly adults between the third and fourth decade of life but has been known to affect the pediatric population as well [3,4]. Additionally, TGCT demonstrates a slight predominance for females (60%) [3]. TGCT is in the vast majority of the cases a monoarticular disease although multijoint affectation has been reported; moreover, as previously mentioned it can present as a localized nodule or diffusely affecting a joint [5,6]. The prevalence of TGCT is thought to be of 1.8 cases per million for the diffuse form and 9.2 per million for the localized form [7]. The localized form of this disease affects more commonly the hands and digits, followed by foot and ankle, while the diffuse form involves mainly the knee, followed in frequency by hip, ankle, and elbow [2,8]. Symptoms are nonspecific which along the rarity of this disease can cause a significant delay in the diagnosis of these patients [9]. Because this is a slow progressing disease time from initial symptoms to the final histologic diagnosis can vary from a year to 3 years [10]. Patients

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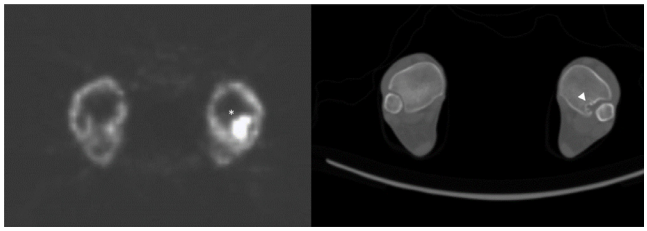

Fig. 1 – Positron emission tomography with computed tomography. Axial images demonstrating uptake at the level of the distal tibiofibular joint (*) with a standard uptake value of 7.9 as well as scalloping of the distal lateral tibia (arrowhead).

can present with pain, swelling and limitation of the affected joint as well as repeated episodes of hemarthrosis over time [9,11].

Here we describe a case of TGCT of the distal tibiofibular joint, an extremely rare location, managed by surgical resection. To the best of our knowledge this is the second localized case in such location to be described in literature.

Case report

A 45-year-old female with history of costochondritis, fibrocystic breasts, hypercholesterolemia, and gastroesophageal reflux disease, was referred to our orthopedic oncology clinic for further evaluation and management of a left ankle le-

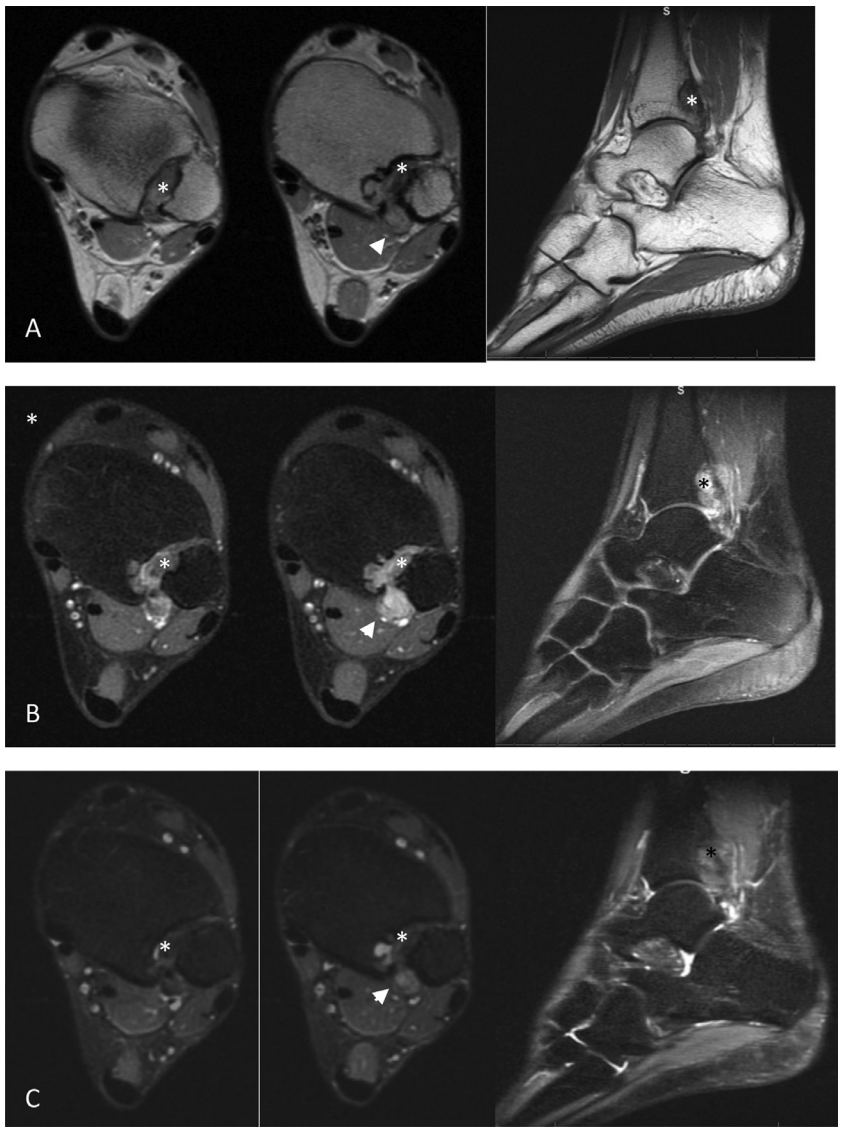

Fig. 2 – Magnetic resonance imaging study from August 2020 depicting the lesion in the distal tibiofibular joint (*), the distal lateral scalloping and posterior invasion into the soft tissues (arrowhead). (A) proton density sequency of 2 axial cuts view and 1 sagittal, (B) T1 fat suppressed with Gadolinium sequence, 2 axial cuts and 1 sagittal view, (C) short tau inversion recovery sequence, 2 axial cuts and 1 sagittal cut.

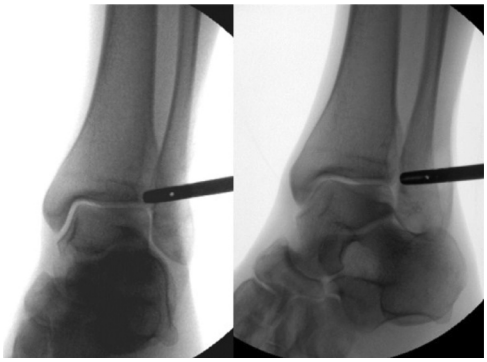

Fig. 3 – Fluoroscopic images used for guidance during the biopsy mini-open procedure. A pituitary instrument is observed within the distal tibiofibular joint.

sion found on recent imaging studies. During the initial visit, the patient reported left ankle pain which was new and had been present for 2 months. Patient stated the pain was moderated and controlled by nonsteroidal anti-inflammatories. Due to her pain, she was unable to exercise and required the use of a cane for assistance with ambulation. In addition, patient reported recent fatigue. She denied night sweats, chills, fever, unintentional weight loss, and loss of appetite. On physical examination, no palpable mass, tenderness, erythema, or swelling over the left ankle were noted. Range of motion and sensation in the ankle were within normal limits.

Prior to initial consultation, the patient obtained several diagnostic imaging studies due to a new mass noted on her breast. A positron emission tomography with computed tomography scan was obtained (July 2020) and revealed a lesion in the distal tibiofibular joint with fluorodeoxyglucose uptake and a maximum standardized uptake value of 7.9 (Fig. 1). A decision was made to obtain a contrasted magnetic resonance imaging (MRI) study. The MRI of the left ankle with and without Gadolinium contrast obtained in August 2020 demonstrated an enhancing 2.2 × 1.8 × 3.5 cm soft tissue mass at the syndesmosis space corresponding to the area of hyper-metabolic activity on the positron emission tomography with computed tomography scan (Fig. 2). Small foci of T1/T2 hypo-intense signal within the mass, a possible reflection of mineralization, was also reported. In addition, the MRI reported an area of cortical scalloping over the distal lateral tibia suggesting a chronic nonaggressive process with no abnormal marrow signal or other evidence of osseous infiltration, however overall characteristics of the mass were indeterminate and tissue sampling was recommended to exclude malignancy.

It was decided to proceed with an open biopsy of the left ankle mass under fluoroscopic guidance (Fig. 3). A 3 cm incision was made over the distal posterior aspect of the left lateral malleolus. Dissection was carried down to bone with a cautery. The fibular tendon and muscle were retracted medially and the posterior aspect of the tibiofibular joint visualized. A mass with yellowish and brown components was then observed, and samples were obtained for frozen and permanent pathology analysis (Fig. 4). Pathology report revealed a diagnosis of giant cell tumor of tendon sheath.

Patient was taken to the operating room 3 weeks later for left ankle tumor resection under fluoroscopic guidance. A 4 cm incision was done over the prior incision over the distal posterior aspect of the left malleolus. Deep dissection was carried down bluntly. The fibularis tendons were retracted distally and the posterior aspect of the tibiofibular joint was accessed. The TGCT was identified, marginally resected, and sent to pathology for analysis. Pathology report revealed mass to be synovial tissue with nodular hyperplasia with pigment deposition consistent with TGCT (Fig. 5).

Patient is currently 3 months post tumor resection with completely resolution of her ankle symptoms. Patient was recommended physical therapy and will continue surveillance studies with a new contrasted MRI in 6 months.

Discussion

TGCT are a group of benign tumors and although the disease tends to be slow growing it can potentially damage a joint and severely affect the quality of life of these patients [9,10]. The disease usually presents in young adults with highly nonspecific symptoms which leads to the diagnosis oftentimes being delayed for years. The etiology of this disease is not known though the mechanism by which it damages the joints has been identified [12,13]. There is an uncontrollable proliferation of the synovium (villonodular proliferation), hemosiderin deposits which causes the pigmentation seen in our mass (Fig. 4), the tumor cells attract an inflammatory infiltrate with mononuclear and multinuclear osteoclast-giant cells that along with the repetitive episodes of hemarthrosis are thought to be responsible for the joint damage [14,15].

On radiographs this disease can present as a joint effusion as well as bone erosion; with rare but described calcifications within the tumor [16,17]. The bone lesions present a sclerotic margin and are usually present in both sides of the joint [16]. As with most tumors the preferred imaging study is an MRI with and without contrast. There TGCT is depicted as a localized or diffuse mass with heterogeneous low signal intensity on T1 and T2-sequences that enhances with Gadolinium. Blooming effect is also usually observed due to the magnetic effect the iron within the hemosiderin deposits causes [18]. Some areas with low hemosiderin concentration can also display a high intensity on T1 and T2 sequences, but the classical image is the one of a mass low in T1 and T2 sequences [18]. More recently PET-CT scans have also been used to study TGCT and also to assess treatment effect when a systemic modality of treatment is chosen [19]. TGCT lesions present with significant uptake and can have a mean standardized uptake value of 8.7 behaving as hypermetabolic tumors, a characteristic that can mislead radiologists towards a malignant diagnosis such as sarcoma or metastatic disease [20,21].

On histopathology analysis TGCT present as a combination in variable proportions of small histiocytes, mononuclear cells with eccentrical nuclei, eosinophilic cytoplasm, and a peripheral rim of hemosiderin, osteoclasts-like giant cells, xanthomatous (foamy) macrophages, lymphocytes, and plasma

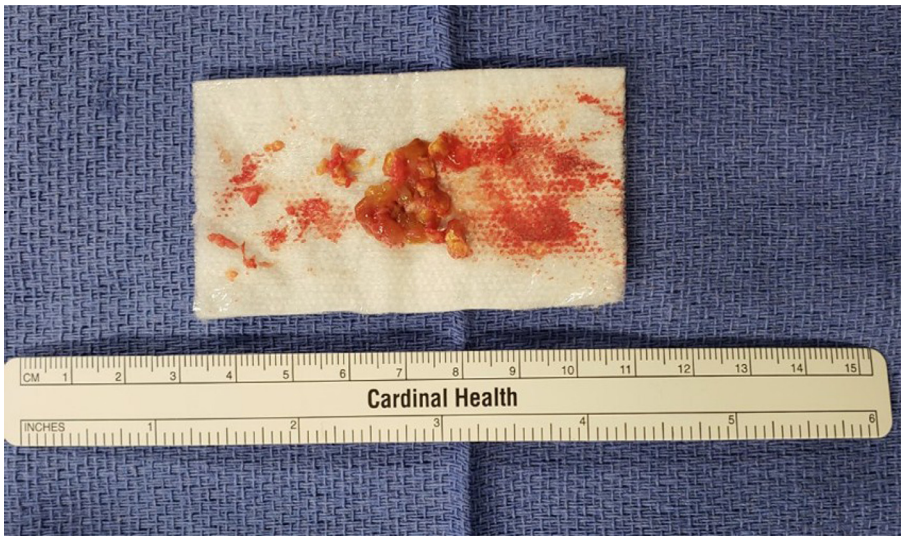

Fig. 4 – Gross image of the sample obtained for pathology analysis during the biopsy. A mass with yellowish and brown areas is seen. (Color version of figure is available online.)

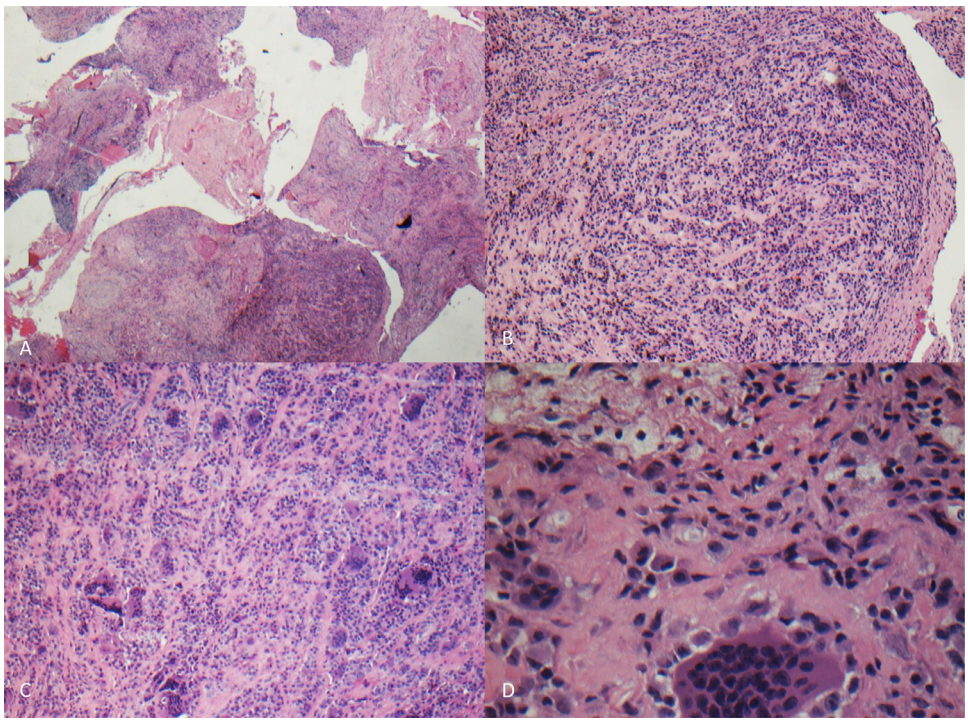

Fig. 5 – Histopathological analysis of the left ankle mass resection. (A) low power view of the mass depicting sheets of cells of infiltrative nature and a dense stroma (H&E, 10x), (B) Dense small mononuclear cell stroma (H&E, 10x), (C) Mononuclear cell stroma and osteoclast-like multinucleated giant cells (H&E, 20x), (D) Giant cells in more detail, histocytes and foam cells (H&E, 20x).

cells [22]. Due to this common facade of an inflammatory infiltrate, there was an initial thought that there was an inflammatory component to the nature of this disease, leading some to claim it was an inflammatory process such as rheumatoid arthritis, but a clonal mutation was identified which allowed to confirm the tumoral nature of this lesion [23,24]. A specific translocation involving chromosomes 1 and 2, causing the overexpression of colony-stimulating factor 1 (CSF1) was identified in 2006 as critical for development of this disease [24]. The augmented CSF1 expression is only found in 2%-16% of the cells, the remaining cells being the nonspecific inflammatory infiltrate previously described. These inflammatory cells are attracted due to a receptor that responds to the overexpressed factor (CSF1R) [24]. Currently available treatment

options target this receptor to address TGCT, when resection is not indicated [25].

Treatment for TGCT is predominantly surgical, with excision of the tumor. Depending on the location and the extent of disease, the procedure may be done open or arthroscopically. The rate of recurrence for this disease is high, 14%-40%, which causes patients to undergo several surgical procedures, future joint replacements, decreased range of motion and low quality of life [26,27]. Radiation therapy has been advocated as an option to decrease recurrence in diffuse TGCT however is not free of complications such as joint stiffness, osteoarthritis, osteonecrosis, and malignant transformation or secondary radiation induced sarcomas [28].

Conclusion

TGCT are benign but aggressive soft tissue tumors with highly nonspecific symptoms at presentation. Some locations such as the distal tibiofibular joint are particularly unusual and a high level of suspicion as well as the correct imaging studies are paramount for the correct diagnosis of this rare disease as it could be confused with a degenerative cyst. These tumors although slow growing have the potential to irreversibly damage a joint, making appropriate diagnosis and treatment by an oncology orthopedic surgery specialist at a high-volume center of the utmost importance.

Patient Consent

Per the local Institutional Review Board consent was exempt due to this being the case of research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimen with the information being recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

REFERENCES

[1] Jaffe HL, Lichtenstein L, Sutro CJ. Pigmented villonodular synovitis, bursitis and tenosynovitis. Arch Pathol 1941;31:731–65.

[2] De Saint Aubain Somerhausen N, van de Rijn M. Tenosynovial giant celltumour. In: Fletcher CDM, Bridge JA, Hogendoorn PCW, Mertens F, editors. WHO classification of tumours of soft-tissue and bone. Lyon: IARC; 2013. p. 100–3.

[3] Burton TM, Ye X, Parker ED, Bancroft T, Healey J. Burden of illness associated with tenosynovial giant cell tumors. Clin Ther 2018;40(4):593–602 e1. doi:10.1016/j.clinthera.2018.03.001.

[4] Mastboom MJL, Verspoor FGM, Uittenbogaard D, Schaap GR, Jutte PC, Schreuder H, et al. Tenosynovial giant cell tumors in children: a similar entity compared with adults. Clin Orthop Relat Res 2018;476(9):1803–12. doi:10.1007/s11999.0000000000000102.

[5] Tyler WK, Vidal AF, Williams RJ, Healey JH. Pigmented villonodular synovitis. J Am Acad Orthop Surg 2006;14:376–85.

[6] Botez P, Sirbu PD, Grierosu C, Mihailescu D, Savin L, Scarlat MM. Adult multifocal pigmented villonodular synovitis–clinical review. Int Orthop 2013;37(4):729–33. doi:10.1007/s00264-013-1789-5.

[7] Myers BW, Masi AT. Pigmented villonodular synovitis and tenosynovitis: a clinical epidemiologic study of 166 cases and literature review. Medicine (Baltimore) 1980;59:223–38.

[8] Mastboom MJL, Verspoor FGM, Verschoor AJ, Uittenbogaard D, Nemeth B, Mastboom WJB, et al. Higher incidence rates than previously known in tenosynovial giant cell tumors. Acta Orthop 2017;88(6):688–94.

[9] van der Heijden L, Gibbons CL, Hassan AB, Kroep JR, Gelderblom H, van Rijswijk CS, et al. A multidisciplinary approach to giant cell tumors of tendon sheath and synovium–a critical appraisal of literature and treatment proposal. J Surg Oncol 2013;107:433–45.

[10] Gouin F, Noailles T. Localized and diffuse forms of tenosynovial giant cell tumor (formerly giant cell tumor of the tendon sheath and pigmented villonodular synovitis). Orthop Traumatol Surg Res 2017;103(1S):S91–7. doi:10.1016/j.otsr.2016.11.002.

[11] Verspoor FG, Zee AA, Hannink G, van der Geest IC, Veth RP, Schreuder HW. Long-term follow-up results of primary and recurrent pigmented villonodular synovitis. Rheumatology (Oxford) 2014;53(11):2063–70. doi:10.1093/rheumatology/keu230.

[12] Singh R, Grewal DS, Chakravarti RN. Experimental production of pigmented villonodular synovitis in the knee and ankle joints of rhesus monkeys. J Pathol 1969;98(2):137–42.

[13] Hirohata K. Light microscopic and electron microscopic studies of individual cells in pigmented villonodular synovitis and bursitis (Jaffe) Kobe. J Med Sci 1968;14(4):251–79.

[14] Convery FR, Lyon R, Lavernia C. Pigmented villonodular synovi-tis. In: Klippel JH, Dieppe PA, editors. Rheumatology. London:Mosby; 1998. p. 1–3.

[15] Ota T, Urakawa H, Kozawa E, Ikuta K, Hamada S, Tsukushi S, et al. Expression of colony-stimulating factor 1 is associated with occurrence of osteochondral change in pigmented villonodular synovitis. Tumour Biol 2015;36(7):5361–7. doi:10.1007/s13277-015-3197-5.

[16] Llauger J, Palmer J, Roson N, Cremades R, Bagué S. Pigmented villonodular synovitis and giant cell tumors of the tendon sheath: radiologic and pathologic features. AJR Am J Roentgenol 1999;172:1087–91.

[17] Lindenbaum BL, Hunt T. An unusual presentation of pigmented villonodular synovitis. Clin Orthop Relat Res 1977;122:263–7.

[18] Spritzer CE, Dalinka MK, Kressel HY. Magnetic resonance imaging of pigmented villonodular synovitis: report of two cases. Skeletal Radiol 1987;16:316–19.

[19] Giustini N, Bernthal NM, Bukata SV, Singh AS. Tenosynovial giant cell tumor: case report of a patient effectively treated with pexidartinib (PLX3397) and review of the literature. Clin Sarcoma Res 2018;8:14. doi:10.1186/s13569-018-0101-2.

[20] Broski SM, Murdoch NM, Skinner JA, Wenger DE. Pigmented villonodular synovitis: potential pitfall on oncologic 18F-FDG PET/CT. Clin Nucl Med 2016;41(1):e24–31. doi:10.1097/RLU.0000000000000893.

[21] Takeuchi A, Yamamoto N, Hayashi K, Miwa S, Takahira M, Fukui K, et al. Tenosynovial giant cell tumors in unusual locations detected by positron emission tomography imaging confused with malignant tumors: report of two cases. BMC Musculoskelet Disord 2016;17:180 Published 2016 Apr 26. doi:10.1186/s12891-016-1050-7.

[22] Somerhausen NS, Fletcher CD. Diffuse-type giant cell tumor: clinicopathologic and immunohistochemical analysis of 50 cases with extraarticular disease. Am J Surg Pathol 2000;24:479–92.
[23] Vogrincic GS, O'Connell JX, Gilks CB. Giant cell tumor of tendon sheath is a polyclonal cellular proliferation. Hum Pathol 1997;28:815–19.
[24] West RB, Rubin BP, Miller MA, Subramanian S, Kaygusuz G, Montgomery K, et al. A landscape effect in tenosynovial giant-cell tumor from activation of CSF1 expression by a translocation in a minority of tumor cells. Proc Natl Acad Sci USA 2006;103:690–5.
[25] Brahmi M, Vinceneux A, Cassier PA. Current systemic treatment options for tenosynovial giant cell tumor/pigmented villonodular synovitis: targeting the CSF1/CSF1R Axis. Curr Treat Options Oncol 2016;17:10.
[26] Staals EL, Ferrari S, Donati DM, Palmerini E. Diffuse-type tenosynovial giant cell tumour: current treatment concepts and future perspectives. Eur J Cancer 2016;63:34–40.
[27] van der Heijden L, Mastboom MJ, Dijkstra PD, van de Sande MA. Functional outcome and quality of life after the surgical treatment for diffuse-type giant-cell tumour around the knee: a retrospective analysis of 30 patients. Bone Joint J 2014;96-B(8):1111–18. doi:10.1302/0301-620X.96B8.
[28] Mollon B, Lee A, Busse JW, Griffin AM, Ferguson PC, Wunder JS, et al. The effect of surgical synovectomy and radiotherapy on the rate of recurrence of pigmented villonodular synovitis of the knee: An individual patient meta-analysis. Bone Joint J 2015;97-b:550–7.