ORIGINAL ARTICLE

DOI: 10.4274/eamr.galenos.2020.22931
Eur Arch Med Res 2022;38(1):14-18

The Giant Cell Tumor of Tendon Sheath: Risk Factors for Recurrence

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Abstract

Objective: Giant cell tumors of tendon sheath (GCTTS) are the most common soft tissue tumors of the hand after ganglion cysts. Some other areas such as the foot, ankle, knee and thigh can also be involved. The recurrence rates up to 44% have been reported. This study evaluated the clinical results of GCTTS patients who underwent marginal resection and investigate any clinical or histopathological features that might be associated with recurrence.

Methods: Thirty patients who underwent surgical excision between 2011 and 2015 were analyzed retrospectively. Clinical, pathological and radiological examination results were collected from the patient files. The variables including tumor localization, tumor subtype, bone erosion and the presence of mitotic figures were analyzed for a possible association with recurrence.

Results: Amongst 30 patients who were treated surgically due to GCTTS, twenty-one patients were female (70%) and 9 were male (30%). The mean age was 40 [standard deviation (SD): ±14.4, range: 18-68 years]. The average follow-up period was 51 months (SD: ±29.2, range: 16-177 months). Histopathologically, 23 cases were identified as nodular type, 7 as diffuse type. In 8 patients, postoperative recurrence was observed. The recurrence rate was significantly higher in patients with preoperative bone erosion (p=0.015), while other variables including histopathological type, presence of mitotic figures and tumor localization did not significantly affect the recurrence rate. None of the patients experienced a malignant transformation.

Conclusion: Bone erosion at the time of presentation was found to be a risk factor for recurrence in GCTTSs. The presence of mitotic figures, histopathological type and tumor localization was not associated with recurrence.

Keywords: Giant cell tumor of tendon sheath, recurrence, risk factor, histopathology

INTRODUCTION

The giant cell tumor of tendon sheath (GCTTS) is a benign synovial tissue tumor, which is most commonly seen in hands, while they can also be encountered in other parts of the body such as foot, ankle, elbow, knee, hip and occasionally in spine. GCTTS is the most common solid soft tissue mass of the hand, and the second most common benign lesion of the hand after ganglion cyst (1). Total excision of the lesion is the generally preferred approach (2).

GCTTS is morphologically classified as nodular and diffuse types. The nodular type is usually located in hands while the diffuse type is usually located around large joints. In contrast to more localized and encapsulated nodular type, the diffuse type has multicentric lesions without encapsulation. The recurrence is more common in diffuse type (3).

Long-term stress on the bone may cause bone erosion and tumor recurrence has been reported at rates ranging from 7% to 44% (4-7). Recurrences usually occur within the first two years after surgery. This study aimed to analyze GCTTS case series operated in our clinic and investigate any clinical or pathological features that might be associated with increased recurrence.

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Received: 10.10.2019
Accepted: 14.10.2020

Cite this article as: Kara M, Hız M, Karaismailoğlu B. The Giant Cell Tumor of Tendon Sheath: Risk Factors for Recurrence. Eur Arch Med Res 2022;38(1):14-18

METHODS

After obtaining the approval of Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Local Ethical Committee (year: 2016, no: 83045809), all GCTTS patients who were treated surgically by marginal excision between 2011 and 2015 were included and investigated retrospectively. A total of 31 patients were available and the patient files were reviewed for clinical, radiological [direct radiography and magnetic resonance imaging (MRI) and pathological examinations]. The patients with missing file information or lost to follow-up were excluded. Only one patient was excluded due to loss of follow-up. The tumors were removed with marginal excision which was also confirmed by pathological examination. The patients were followed up by clinical examination and direct radiography during routine follow-ups. Direct radiographs were obtained per 3 months during the first year and per 6 months during the second year. After that, the clinical follow up and direct radiography evaluation was performed with one-year intervals. The patients were examined with MRI if any recurrence was suspected clinically (swelling, pain, warmth, erythema, deformity, etc.) or radiologically (soft tissue mass, cortical erosion, etc.) during follow-ups.

Bone erosion, tumor localization (only for lesions of the hand, as proximal and distal according to proximal interphalangeal joint), histopathological type and the presence of mitotic figures were investigated for any possible association with the recurrence. The size of the lesions was measured during pathological examination macroscopically.

Statistical Analysis

Descriptive statistics were employed using measures of the mean and standard deviation (SD). Categorical variables were analyzed using Fisher's Exact test. Bonferroni correction was used to calculate the actual p-value. The difference was considered significant when the p-value was less than 0.016. The analysis was performed using SPSS version 20 (SPSS, Chicago, IL).

RESULTS

In 30 patients who were treated surgically due to GCTTS, twenty-one patients were female (70%) and 9 were male (30%). The mean age was 40 (SD: ±14.4, range: 18-68 years) (Figure 1). The mean follow-up period was 51 months (SD: ±29.2, range: 16-177 months). Twenty-one lesions were seen in the upper extremity (70%) and 9 in the lower extremity (30%). (Table 1) The lesions in the hand were mostly located on the volar side (n=16, 84.2%) rather than the dorsal side (n=3, 15.8%).

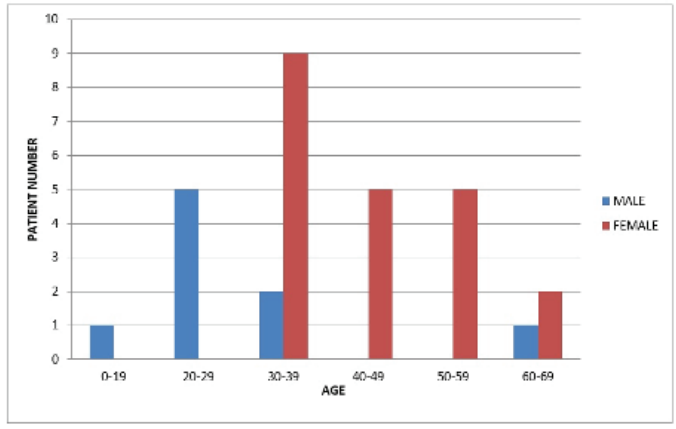

Figure 1. Distribution of the lesions according to age and gender

Table 1. Localization of the lesions		
Localization	**Number**	**Percent**
Hand	19	63.3
Foot	5	16.6
Ankle	3	10
Wrist	1	3.3
Knee	1	3.3
Elbow	1	3.3
Total	30	100

The histopathological type of tumor was 23 (76.6%) nodular (type 1) and 3 (23.3%) diffuse (type 2) GCTTS. In 19 hand cases, 18 were nodular type and one case was diffuse type GCTTS. The average lesion size (largest diameter) was 1.6 cm (SD: ±0.8, range; 0.6-4). The largest lesion was approximately 4x2.5x1.5 cm located on the left knee and was nodular type lesion (Figure 2). The average lesion size for recurrent lesions was 1.8 cm (SD: ±0.9, range; 0.8-3.4) and 1.5 cm (SD: ±0.7, range; 0.6-4) for non-recurrent lesions (p=0.35). None of the patients had an invasion of the neurovascular structures and no neurovascular damage was encountered. The pathological examination verified that all lesions were removed as marginal resection.

Recurrence was developed in 8 of the patients (26.6%). Four of the patients with recurrence were re-operated. The other 4 patients were not re-operated since they did not give their consent. Four of the recurrences were seen in the upper extremity (all of them in the fingers) and 4 in the lower extremity (3 in toes, one in the dorsum of the foot). Seven of the patients with recurrence were female (87.5%) and one patient was male (12.5%). Six of recurrent lesions were pathologically diagnosed as nodular type GCTTS and the other 2 were diffuse type GCTTS. The histopathological type of tumor was not found as a risk factor for recurrence (p=0.33) (Table 2). The number of mitotic figures was investigated to

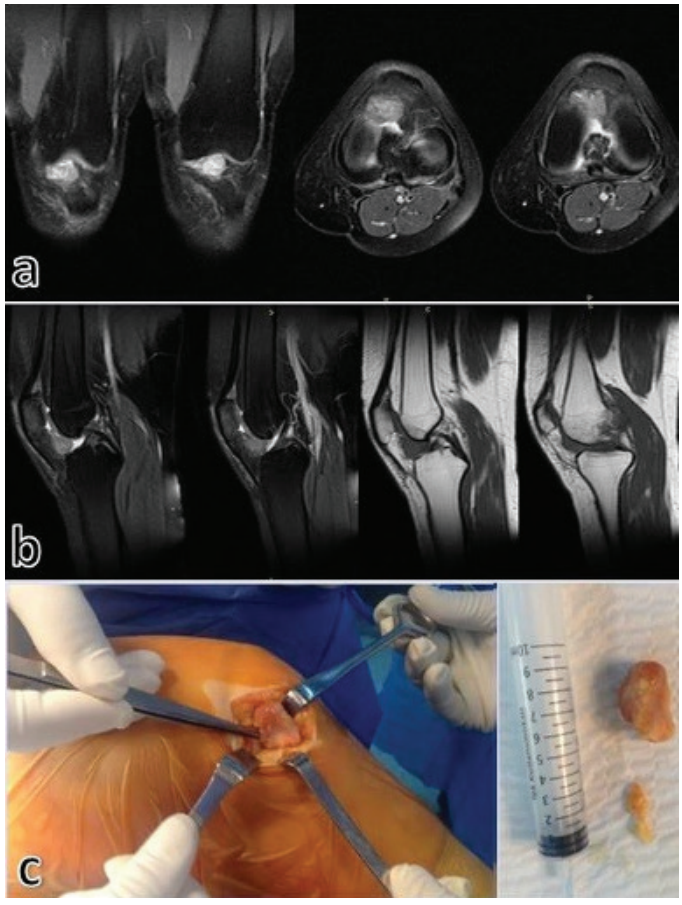

Figure 2. GCTTS of the left knee. (a) View on the coronal and axial sections of the MRI T2-weighted sequences, heterogeneous slightly high signal intensity of the tumor. (b) View on the sagittal sections of the MRI T2 fat-suppressed (moderate signal) &T1-weighted (low signal) sequences. (c) Perioperative image of excisional biopsy of the lesion and macroscopic views of the mass and it's pedicle (size: 4x2.5x1.5 cm) (the patient provided written informed consent for print and electronic publication of the figures)
GCTTS: Giant cell tumors of tendon sheath, MRI: Magnetic resonance imaging

evaluate their possible effect on recurrence development. Mitotic figures were detected in 7 of 8 patients who developed recurrence. Eleven of 22 patients without recurrence also had mitotic figures and the difference was not statistically significant (p=0.06) (Table 2). There was also no significant correlation between the localization of the hand lesions and recurrence rates (1 recurrence in the distal region (distal interphalangeal region and distal phalanx) and 3 recurrences in the proximal region) (p=0.82) (Table 2).

Bone erosion was detected in 3 of the cases (10%) preoperatively. Two of these cases were in the foot and one was in the hand. All patients with bone erosion developed recurrence. Bone erosion was found as a risk factor for recurrence (p=0.015) (Table 2). When a post hoc power analysis was performed using alpha 0.05, the power of the study was found to be 0.67. None of the patients had malignant transformation. No other complication was seen in the patients.

Table 2. Results of statistical analysis for possible risk factor variables

Variables	Patients without recurrence (%)	Patients with recurrence (%)	Risk ratio	p value
Bone erosion				
Yes	0 (0)	3 (100)	5.4	0.015*
No	22 (81)	5 (19)		
Mitotic figures				
Yes	11 (61)	7 (39)	4.66	0.06
No	11 (91.7)	1 (8.3)		
Tumor type				
Type 1 (nodular)	17 (74)	6 (26)	0.91	0.89
Type 2 (diffuse)	5 (71)	2 (29)		
Tumor localization (hand)				
Distal	3 (75)	1 (25)	0.75	0.82
Proximal	12 (80)	3 (20)		
*p<0.016 (Bonferroni correction)				

DISCUSSION

The treatment of GCTTS can represent a challenge for orthopedic surgeons due to the possibility of bone erosion and recurrent lesions. We analyzed the recurrence rate in our patient series and investigated the possible risk factors for recurrence. The overall recurrence rate was found as 26.6%. GCTTS with the presence of bone erosion was found related to increased risk of recurrence, while the presence of mitotic figures, histopathological type and tumor localization was not associated with recurrence.

GCTTSs are most frequently encountered in hands but they can also be seen in wrist, foot, ankle, elbow, knee, hip and rarely in spine. In a study of Ushijima et al. (8) which was published in 1986, out of 207 GCTTS patients; 158 lesions were on the fingers of the hand (76.3%), 25 lesions were on the toes (12%), 8 lesions were in the knee joint (3.8%), 4 lesions were in the wrist (1.9%) and 1 lesion was in the elbow. There were 30 patients in our series and the lesions of 19 patients were in hand (63,3%), 4 lesions in the toe (13,3%), 4 lesions in the foot and ankle (13,3%), 1 lesion in knee (3.3%) and 1 lesion in elbow (3.3%).

GCTTSs are more common in the volar face of the hand compared to the dorsal face and can interfere with grab and grip functions of the hand. In a study of 84 patients, published by Lautenbach et al. (9) 60 lesions were detected on the volar face (71%) and 24 lesions were detected on the dorsal surface of the hand (29%). In

our study, among 19 patients with lesions on their hand, 16 were volar (84.2%) and 3 were dorsal sided (15.8%) consistent with the literature.

There are two histopathological types of GCTTSs; type 1 (nodular) and type 2 (diffuse) (10). Nodular type is more common than diffuse type. Diffuse type is usually seen in the lower extremities, while nodular type GCTTS is usually seen on the hand (2). In Al-Qattan's (10) series of 43 cases, only 2 cases of diffuse type GCTTS were detected. In a study with 18 GCTTS cases published by Ikeda et al. (11); 10 cases were reported as nodular type and 8 as diffuse type GCTTS. In our study, 23 cases were identified as nodular type (76.66%) and 7 as diffuse type (23.33%). Among 19 cases with GCTTS in hand, 18 were classified as nodular type and one as diffuse type GCTTS.

Although GCTTSs are benign, they have high recurrence potentials. Recurrence rates has been reported in the literature from 7% to 44% (6). In our study, recurrence was detected in 8 patients (26.6%). In a study by Reilly et al. (12), 70 patients with GCTTS were followed and recurrence was detected in 19 (27%) of the patients and tumor localization was found to be a probable factor affecting recurrence. Most of the recurrences (57.6%) were seen in patients with lesions on the distal interphalangeal joint (12). They claimed that adequate excision is more difficult distally due to the limited space, the proximity to neurovascular structures, and limited soft tissue envelope leading to higher recurrence rates. In our study, 4 cases of recurrence were seen in the hand. There was no significant correlation between the localization of the hand lesions (proximal vs. distal) and recurrence rates (p=0.82). The recurrence rate of hand lesions in our study (21%) was slightly higher to current studies by Koutserimpas et al. (7) who found 11.1% recurrence rate among 36 patients, Jalgaonkar et al. (6) who found 9% recurrence rate among 46 patients and Williams et al. (13) who found 12.6% recurrence rate among 213 patients.

In a study with 43 cases by Al-Qattan (10), recurrence rates were higher in diffuse type GCTTS than in nodular type. Recurrence was observed in 5 patients out of 13 patients with diffuse type lesions (38%). It has been reported that no recurrence has been detected in any of the 30 cases with the nodular type lesions (10). In a recent study by Shi et al. (14), diffuse form was found related with recurrence. However, Reilly et al. (12) couldn't show a relation with the histopathology of the tumor and recurrence rate. In our study, recurrence was detected in 6 of 23 patients with nodular lesions (26%) and in 2 (28.5%) of the 7 cases with diffuse type. According to these findings, no significant relation was found between histopathological type and recurrence rates (p=0.33).

Although there are some publications in the literature reported that the increased number of mitotic figures is related to recurrence (15), there is not enough evidence. Rao and Vigorita (16) found a higher recurrence rate for tumors with increased cellularity and mitotic activity on histological examination. A high mitotic rate was thought to be indicative of local recurrence. Kotwal et al. (17) recommended radiotherapy in the presence of mitotic figures to overcome recurrences. However, Al-Qattan (10) reported that neither cellularity nor mitoses could be considered significant prognostic histological factors for recurrence. In their 71 patient series, Monaghan et al. (18) concluded that mitotic figures do not predict the clinical behavior of the tumor. In our study, no significant association was found between the presence of mitotic figures and recurrence (p=0.06). However, p value was close to significance, so the difference can become significant in patient series with a higher number of patients.

In GCTTSs, bone erosion can be observed because of long-term pressure by the lesion and these erosion can be detected in direct radiographs. In a study by Moore et al. (19), bone erosion was detected in 9% of 115 patients. Fyfe and MacFarlane (20) reported 36% bone erosion in their patient series of 51 cases. In our study, bone erosion was detected in 3 of 30 cases (10%) with a similar rate to the literature. Jalgaonkar et al. (6) reported that recurrence was detected more frequently in cases with bone erosion. In our study, recurrence was detected in all 3 patients with bone erosion and it was found as a risk factor similar to the literature. GCTTSs are benign tumors but rarely, they can also represent malignant transformation (21). In our study, the malignant transformation was not observed in any case.

Study Limitations

The most important limitation of this study was the small number of patients. However, even most recent studies on GCTTS include similar patient numbers since it is a relatively rare lesion (6,7,22,23). Larger multicenter studies will give more reliable results. The retrospective design of this study was another limiting factor.

CONCLUSION

Preoperative bone erosion is an important risk factor for recurrence in GCTTS and patients with preoperative bone erosion should be followed closely. The presence of mitotic figures, histopathological type and tumor localization didn't significantly increased the recurrence rate.

Ethics

Ethics Committee Approval: Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Local Ethical Committee (year: 2016, no: 83045809).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.H., Concept: M.H., Design: M.H., M.K., Data Collection or Processing: M.K., B.K., Analysis or Interpretation: M.K., B.K., Literature Search: M.K., B.K., Writing: M.H., M.K., B.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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