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Outcomes of Surgical Treatment for Localized Tenosynovial Giant-Cell Tumor of the Foot and Ankle: A Case Series

Edoardo Ipponi*
Department of Orthopedics and Trauma surgery, University of Pisa, Italy

Alfio Damiano Ruinato
Department of Orthopedics and Trauma surgery, University of Pisa, Italy

Leonardo Lombardi
Department of Orthopedics and Trauma surgery, University of Pisa, Italy

Martina Cordoni
Department of Orthopedics and Trauma surgery, University of Pisa, Italy

Silvia De Franco
Department of Orthopedics and Trauma surgery, University of Pisa, Italy

Antonio D'Arienzo
Department of Orthopedics and Trauma surgery, University of Pisa, Italy

Lorenzo Andreani
Department of Orthopedics and Trauma surgery, University of Pisa, Italy

Abstract. ***Background:*** *Giant cell tumor of the tendon sheath* (GCTTS), also termed *Tenosynovial giant cell tumor* (TGCT), is a locally aggressive tumor which originates from tendon sheaths or bursas. Around 3–5% of these tumors arise from foot and ankle. Localized lesions in this area are often manifested as firm masses or nodules with slow but continuous progression through months and years. Pain associated with weight-bearing, as well as limitations in joint motions, may be reported, depending on tumor's location. Surgery is the treatment of choice for the definitive removal of GCTTSs with the aim to eradicate the neoplasm and restore the lower limb's functionality.

Methods: Thirteen cases suffering from GCTTS of the foot and ankle underwent surgical resection at our institution between 2017 and 2022. For each case we recorded pre-operative and post-operative symptoms, as well as their pre-operative and post-operative functional status according to both MSTS and AOFAS scores. Eventual complications and local recurrences were reported.

Results: Each patient experienced an at least mild pain before surgical treatment. The mean pre-operative MSTS and AOFAS scores were 22.8 and 70.7, respectively. The mean tumor size was 17.7 mm. Each patient received a resection with wide margins. Two cases (15.4%) had local recurrences. None had major complications at their latest follow-up. After the surgery, the mean post-operative MSTS and AOFAS scores increased to 28.3 and 92.2, respectively.

Conclusion: Resection with wide margins for foot and ankle GCTTS is effective in restoring the patients' lower limb functionality and is associated with reasonable local recurrence rates.

Keywords: Tenosynovial giant cell tumor, giant cell tumor of the tendon sheath, foot, ankle, resection, functionality, AOFAS

* Corresponding author: Edoardo Ipponi, Department of Orthopedics and Trauma surgery; University of Pisa Via Paradisa 2, 56124, Pisa, Italy. Tel: +39 3386381712. E-mail: edward.ippo@gmail.com

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Lokalizuoto tenosinovinio gigantinių ląstelių naviko pėdoje ar kulkšnyje chirurginio gydymo baigtys: atvejų aprašymas

Santrauka. ***Kontekstas:*** Gigantinių ląstelių sausgyslių apvalkalo navikas (trumpinys GCTTS), kuris taip pat vadinamas tenosinoviniu gigantinių ląstelių naviku (trumpinys TGCT), yra lokalus agresyvus navikas, visų pirma pasireiškiantis sausgyslės apvalkale arba bursoje. Maždaug 3–5 % šių navikų atsiranda pėdoje arba kulkšnyje. Lokalūs šios srities pažeidimai dažnai pasireiškia susidarančia kieta mase arba gumbeliais, kurių lėtas, tačiau nuolatinis progresavimas gali trukti mėnesius ar net metus. Pacientų galimi nusiskundimai – skausmas, atsiradęs nešant svorį, ir sąnarių judesių ribotumas; tai priklauso nuo naviko vietos. GCTTS užtikrintai pašalinti būtina operacija. Tokiu būdu sunaikinama neoplazma ir atkuriamas apatinės galūnės funkcionalumas.

Metodai: Mūsų institucijoje nuo 2017 iki 2022 metų buvo nustatyta 13 GCTTS atvejų pėdoje ar kulkšnyje, kai prireikė chirurginės rezekcijos. Kiekvienu atveju registravome priešoperacinius ir pooperacinius simptomus. Taip pat fiksavome priešoperacinį ir pooperacinį funkcinį statusą pagal tiek MSTS, tiek ir AOFAS skalių vertinimus. Pateikėme ataskaitą apie vėlesnes komplikacijas ir vietinį išplitimą.

Rezultatai: Prieš chirurginį gydymą kiekvienas pacientas patyrė bent jau nestiprų skausmą. Vidutiniai priešoperaciniai MSTS ir AOFAS skalių vertinimai buvo atitinkamai 22,8 ir 70,7. Vidutinis naviko dydis – 17,7 mm. Kiekvienam pacientui buvo atlikta rezekcija su didelėmis pakraščio zonomis. Dviem atvejais (15,4 %) navikai vėl susiformavo. Nė vienam pacientui vėlesnio stebėjimo laikotarpiu nepasireiškė jokių sudėtingesnių komplikacijų. Atlikus operaciją, vidutiniai pooperaciniai MSTS ir AOFAS skalių balai išaugo atitinkamai iki 28,3 ir 92,2.

Išvada: Rezekcija su didelėmis pakraščio zonomis pėdos ar kulkšnies GCTTS atveju efektyviai padeda atkurti pacientų apatinių galūnių funkcionalumą ir yra susijusi su priimtinai nežymiu naviko išplitimo procentu.

Raktažodžiai: tenosinovinis gigantinių ląstelių navikas, gigantinių ląstelių sausgyslių apvalkalo navikas, pėda, kulkšnis, rezekcija, funkcionalumas, AOFAS ir MSTS skalės

Introduction

Giant cell tumor of the tendon sheath (GCTTS), also termed Tendonsynovial giant cell tumor (TGCT), is a slow-growing, benign but locally aggressive tumor that originates from tendon sheaths or bursas [1]. Although it can occur at any age, its incidence – that globally amounts to 30.3 per million person per year [2] – has a peak between the third and the fifth decade of age and is slightly higher in the female gender [3]. Macroscopically, these tumors generally appear as nodular circumscribed masses, often connected to the synovial panicle by a peduncle. Their color can range from dark-red to light brown or yellow [4].

Microscopically, they may present with a wide range of appearances. Various combinations of mononuclear cells with polyhedral and epithelioid appearance, multinucleated giant cells and foam cells can show alongside areas of hemosiderin deposition within a lobular or diffuse architecture [4]. While most cells within the tumor mass do not show neoplastic characteristics, a minority can have peculiar chromosomal abnormalities. The most common is a t(1;2) translocation which fuses the colony-stimulating factor-1 (CSF-1) gene on chromosome 1 and collagen type-VI promoter gene on chromosome 2. This mutation leads to the overexpression of CSF-1, which activates and attracts swarms of non-neoplastic inflammatory cells within the tissue [4-7].

Although GCTTS mainly occurs in the hand and in the extremities of the upper limb, around 3–5% of these tumors arise from foot and ankle [1, 8]. Localized lesions in this area often present as firm masses or nodules with slow but continuous volumetric progression through months and years. Pain associated with weight-bearing, as well as limitations in joint motions, may be reported depending on tumor location [8-10].

Despite the recent introduction of CSF1R inhibitors [11], surgery remains the treatment of choice for the definitive eradication of GCTTSs, in particular for their localized forms. The aim of a correct surgical treatment for localized lesions is to perform the complete removal of the neoplastic mass, in order to prevent local recurrences. In fact, although in most of the cases clinical and functional post-operative outcomes come to be satisfactory within months and years after surgery, these lesions are inevitably burdened by a certain risk of local recurrence. Literature reports global recurrence rates of 20–28%, although the overall incidence is lower for cases suffering from localized lesions [12,13]. In this paper we report our experience with surgery for localized GCTTS of foot and ankle, evaluating the impact of the treatment on patients' lives in terms of both functional and oncological outcomes.

Materials and Methods

This single-center retrospective study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Informed consent was obtained from all individual participants included in the study. Our study consisted of a review of all the patients who were diagnosed and treated surgically for localized Tenosynovial Giant-Cell Tumor of the foot and ankle in our institution between January 2017 and January 2022.

For each patient we collected data regarding their age, gender and symptoms alongside with the date in which GCTTS was diagnosed. The date and type of surgeries performed were recorded for everyone. Pre-operative and post-operative functional status of our patients were assessed with both the American Orthopedic Foot and Ankle Score (AOFAS) and the Musculokeletal Tumor Society Score (MSTS), respectively, at the moment of their hospitalization before surgery and at the moment of their latest follow-up. For each patient, pre-operative MRIs were taken and used to correctly locate masses, orientate diagnosis, aid surgical planning and estimate tumor size.

Exeresis was performed with wide macroscopical margins of resection. Each surgical specimen underwent histological examination by a pathologist to confirm the diagnosis of localized Tenosynovial Giant-Cell Tumor. None of our cases received local adjuvant therapy during surgical intervention nor targeted therapies before or after surgery.

Post-operative follow-up consisted of several office visits, clinical evaluations and post-operative MRIs. Cases were routinely visited 1, 3 and 9 months after surgery, while subsequent visits were scheduled depending on the needs of every single individual. MSTS and AOFAS scores were calculated according to the combination of data observed and reported by the patients.

Each complication with grade II or higher according to the Clavien–Dindo Classification was recorded.

Statistics. Statistical analysis was performed using Stata SE 13 (StataCorp LLC, College Station, TX). Statistical significance was set at 0.05 for all endpoints.

Results

Thirteen cases of Giant cell tumor of the tendon sheath (GCTTS) localized in the ankle or foot underwent surgical resection in our institution between January 2017 and January 2022. They were 10 females and 3 males, with an average age at surgery of 36.7. The mean tumors' larger diameter was 34.5 mm. Seven lesions were localized in the ankle region, four occurred in the forefoot, whereas the remaining two lesions involved the midfoot.

At their hospitalization, eight cases complained of at least mild pain in association with localized swelling. Swelling alone was reported by 4 cases. In the remaining patient (case 6), pain was the main symptom and was not associated with any palpable nodularity.

Patients' mean pre-operative MSTS score and AOFAS score were 22.8 (12–30) and 70.7 (33–97) respectively. A summary of patients' pre-operative overall conditions is reported in Table 1.

Table 1. Summary of pre-operative clinical conditions in our population.

N	GENDER	AGE (y)	SITE	SIZE (mm)	PAIN	SWELL.	MSTS (/30)	AOFAS (/100)
1	Female	38	Ankle (anterior)	35	+	+	28	79
2	Female	58	Ankle (anterior)	55	+	+	23	64
3	Female	36	Ankle (anterior)	40	+	+	23	95
4	Male	37	Ankle (antero-medial)	45	+	+	21	55
5	Female	36	Ankle (lateral)	25	-	+	28	85
6	Female	20	Ankle (medial)	15	+	-	12	59
7	Female	13	Ankle (postero-medial)	35	-	+	29	90
8	Male	39	Forefoot (dorsal)	50	+	+	26	71
9	Female	50	Forefoot (dorsal)	20	+	+	15	34
10	Female	58	Forefoot (dorsal)	30	-	+	26	97
11	Female	46	Forefoot (plantar)	40	+	+	14	33
12	Female	8	Midfoot (dorsal)	30	-	+	30	95
13	Male	38	Midfoot (plantar)	30	+	+	22	62

Swell = Swelling (y) = Years

All our cases underwent complete excision of their neoplasm with wide margins (Figure 1).

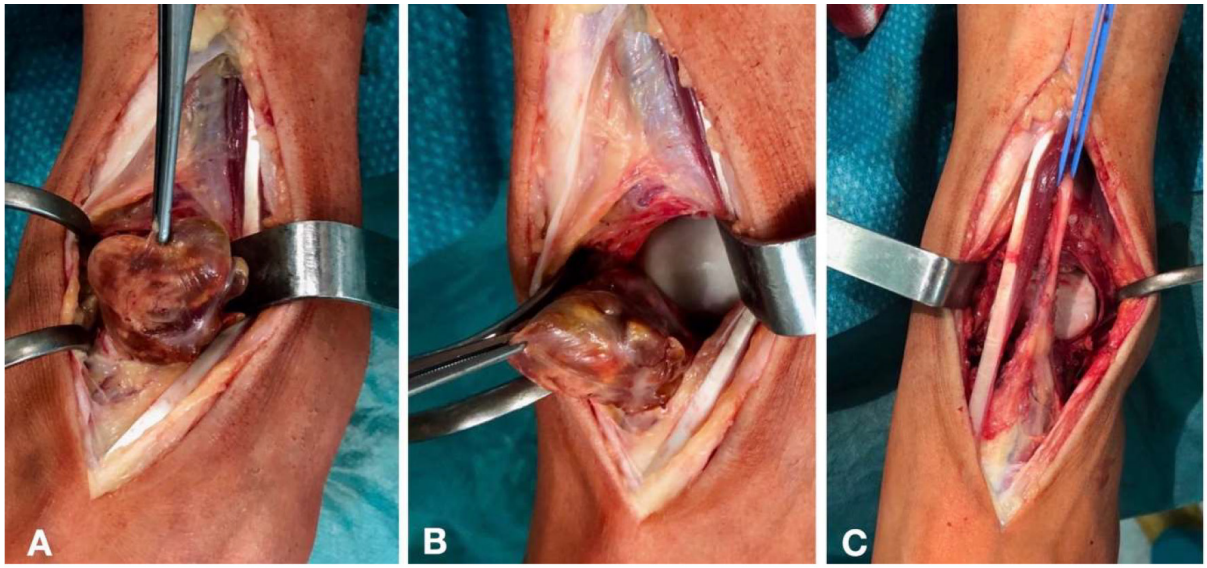

Figure 1. Intra-operative images of tumor resection, carried out through the identification of the mass (**A**), its mobilization (**B**) and consequential removal from the surgical field (**C**).

Excision did not require the sacrifice of tendons, major vessels, nerves nor the complete resection of the main ligamentous structures of foot and ankle. None of our cases had major intra-operative complications.

In each case the diagnosis of GCTTS was confirmed by histological evaluations on surgical specimens. The mean post-operative follow-up of our population was 35.1 (13–69) months. None of our cases suffered from major post-operative complications. Only case 6 suffered from mild-to-moderate post-operative pain and had a delay in her wound closure, which still succeeded without the necessity of further surgical treatments.

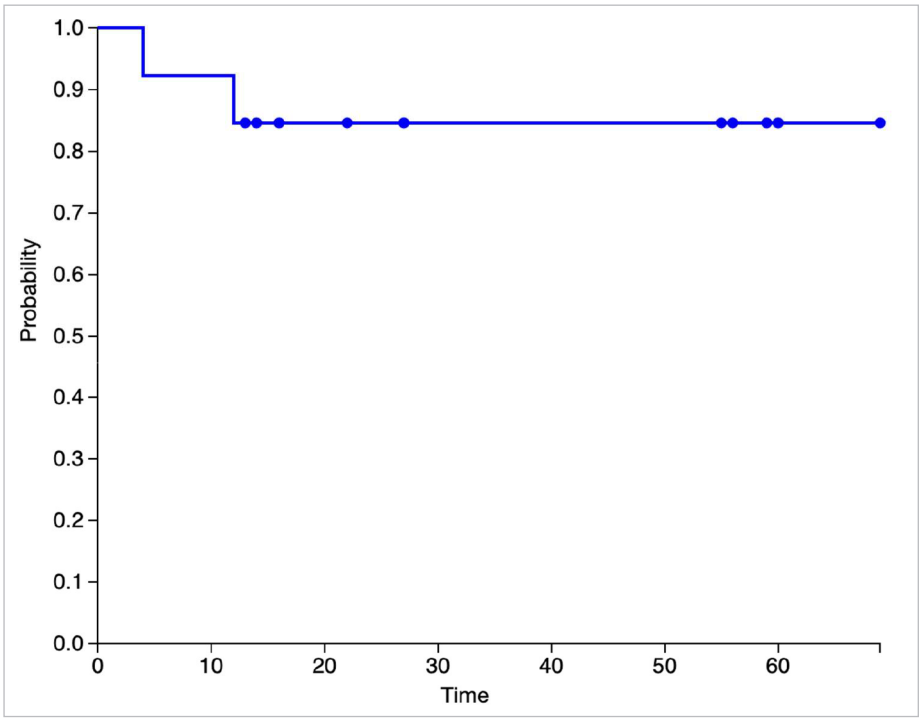

Figure 2. Kaplan–Meier recurrence-free survival curve of our cohort

None of our cases had a reduction of their MSTS or AOFAS scores after surgery, and at least one of the two scores got better in each patient. Our patients' mean post-operative MSTS score was 28.3 (17–30), with a mean increment of 5.4 (0–15) compared to the pre-operative evaluations. The one-tailed Student's t-test demonstrated a statistically significant difference between pre-operative and post-operative scores (p=0.005). The mean AOFAS scores also improved by 21.5 (0–52) after surgery, reaching an average of 92.2 (66–100). AOFAS scores were significantly higher after surgery, as testified by the one-tailed Student's t-test (p=0.002).

Eleven of our 13 cases (84.6%) were continuously disease-free at their latest follow-up. The remaining 2 cases (15.4%), both suffering from GCTTSs of the dorsal forefoot, had a local recurrence. The secondary lesions were diagnosed within 4 and 12 months after surgery, respectively (Figure 2).

Both are now alive with disease (AWD), as they refused further operations and are now under serial clinical follow-up.

An overview of our patients' clinical and oncological outcomes is portrayed in Table 2.

Discussion

Giant cell tumors of the tendon sheath (GCTTSs) are benign soft tissue lesions with a remarked local aggressiveness and tendency to progressive growth. Their mass effect and the pressure exerted on the surrounding soft tissues can lead to the onset of symptoms such as pain and swelling, especially in narrow anatomical segments such as the ankle and foot [1, 4, 8-10]. Previous literature established pain as the most frequent and main symptom in patients suffering from foot and ankle GCTTSs, followed by localized swelling [1, 3]. Our casuistry confirms the prominence of soreness in foot and ankle GCTTSs' clinical picture, as 69% or our patients were complaining of at least moderate pain at the moment of their hospitalization. However, although pain had high pre-operative prevalence, swelling was the most common symptom among our cases, as it had been reported by all but one of them (92%). These symptoms can have a negative impact on patients' quality of life and limit some of their activities of daily living. This was confirmed by the relatively low functional scores obtained

Table 2. Post-operative picture of our case series.

N	SITE	SIZE (mm)	PAIN	SWELL.	MSTS (/30)	AOFAS (/100)	L.R.	COMPL.	FU (M)
1	Ankle (anterior)	35	-	-	30	95	no	no	59
2	Ankle (anterior)	55	-	-	28	90	no	no	14
3	Ankle (anterior)	40	-	-	30	100	no	no	27
4	Ankle (antero-medial)	45	-	-	30	100	no	no	55
5	Ankle (lateral)	25	-	-	30	95	no	no	13
6	Ankle (medial)	15	+/-	-	26	66	no	yes	16
7	Ankle (postero-medial)	35	-	-	30	100	no	no	60
8	Forefoot (dorsal)	50	-	-	30	95	no	no	69
9	Forefoot (dorsal)	20	-	-	17	84	yes (4M)	no	26
10	Forefoot (dorsal)	30	-	-	30	97	yes (12M)	no	13
11	Forefoot (plantar)	40	-	-	29	85	no	no	22
12	Midfoot (dorsal)	30	-	-	30	100	no	no	56
13	Midfoot (plantar)	30	-	-	28	92	no	no	27

Swell = Swelling L.R. = Local Recurrence COMPL = Complications
FU = FollowUp (M) = Months

by our patients before surgery. A mean MSTS value of 22.8 and a mean AOFAS score of 70.7 highlighted the significant impairment caused by the disease.

To this date an adequate surgical excision, performed with the aims to eradicate the tumor and restore patients' functionality, still represents the gold standard for the treatment of localized GCTTSs [4]. During the intervention, surgeons are called to pursue a good tumor clearance, necessary to minimize the risk of local recurrence, and simultaneously respect the nearby soft tissues that would play a pivotal role in patients' rehabilitation and long-term functionality [14].

Although literature agrees that localized forms of GCTTS, compared to diffuse lesions, are burdened by a lower risk of post-operative local recurrence, it still represents one of the main concerns when treating these lesions [3, 9-13, 15]. In 2017 Fraser et al. [4] published a literature review evaluating the prognosis of 131 cases of GCTTS, 71 of which were localized in the ankle and 80 in the foot. The cumulative incidence of local recurrence in the analyzed populations was 19.7% for ankle lesions and 12.5% for foot lesions. In our cohort the recurrence rate was 15.4%. Peculiarly, in our cohort the forefoot was the site associated with the higher risk of local recurrence (50%). This tendency matches the ones reported by some studies on short sized populations like the ones by Brien et al. [16], Ghert et al. [17] and Korim et al. [10], while studies on larger cohorts such as the ones by Gibbons et al. [9] and Zhang et al. [18] reported incidences lower than 10% for forefoot GCTTSs. Our recurrence rates, obtained on cases treated with wide resections, are reasonable and in line with what had already been reported in literature.

While the risk of local recurrence has been largely evaluated and described by the vast majority of the case series on the topic [4], only few of them provided an accurate outlook on functional outcomes. In 2014, Korim et al. [10] evaluated the post-operative functionality of 30 cases of GCTTSs of the foot and ankle, 22 of whom had localized lesions. These patients had a mean AOFAS score of 78, suggesting the effectiveness of surgical treatment. Similar results have been reported by Çevik et al [19] in 2019, whose 9 cases of localized lesions had a mean AOFAS score of 80. Compared to these two studies, our cohort had even better functional outcomes, as our patients' mean post-operative

AOFAS score was as high as 92. This outcome confirms the promising results of previous studies in terms of foot and ankle functionality, but also in terms of lower limbs' performances, since the mean post-operative MSTS score of 28.3. Furthermore, unlike previous papers, the design of our study allowed the proper comparison between patients' pre-operative and post-operative clinical conditions. Comparing cases' presentation before and after surgery, the increasement of both MSTS scores (from 22.8 to 28.3) and AOFAS scores (from 70.7 to 92.2) resulted to be significantly higher according to one-tailed Student's t-tests ($p=0.005$ for MSTS and $p=0.002$ for AOFAS). This provides further evidence that a proper and accurate surgical resection can be effective in the treatment of foot and ankle GCTTSs.

We acknowledge our study had some limitations. The rarity of these tumors did not allow us to operate on wider populations, which partially limited the statistical significance of some of the data associations we wanted to investigate at the beginning of our research. Another limitation is represented by the retrospective nature of our study, which did not allow a perfect standardization of the post-operative follow-up procedures for each patient.

Our functional results, although obtained on a small cohort, do not find matchings in literature, in part because of the rarity of the neoplasm and the consequential paucity of studies on this topic. The significant increasement of both AOFAS and MSTS scores after surgery, alongside with the low post-operative complication rates and the reasonable risk of local recurrence, testifies the effectiveness of surgical resection for the treatment of GCTTSs of foot and ankle.

Conclusion

Tendonsynovial giant cell tumors of foot and ankle are locally aggressive lesions that can lead to severe pain and limit patients' functional performances, thereby undermining their quality of life. An accurate resection, performed with wide margins, can be effective in restoring patients' functionality in respect of reasonable complication risks and local recurrence rates.

Authors' Contributions

Conceptualization: EI, LA. **Methodology:** EI, ADR. **Formal Analysis and Investigation:** ADR, LL, MC. **Writing of the article:** EI, SDF. **Supervision:** LA, ADA.

Declarations

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Conflicts of Interest. The authors declare they have no conflict of interest to disclose.
Data availability. The data that support the findings of this study are available from the corresponding author upon reasonable request.

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