Clinics of Oncology

Inguinoscrotal Sarcomas, a Deep Look into Multidisciplinary Treatment: Outcome Analysis of 28 Cases Treated by Surgical Approach

González-Abós S[1]*, Codina C[1], Solans M[1], Majercakova K[2], Sebio A[3], Gracia I[4], Fernández M[5], Moral A[1], and González JA[1]

[1]Department of General and Digestive Surgery, Hospital de la Santa Creu i Sant Pau, Spain

[2]Department of Oncological Radiotherapy, Hospital de la Santa Creu i Sant Pau, Spain

[3]Department of Oncology, Hospital de la Santa Creu i Sant Pau, Spain

[4]Department of Orthopedics Surgery, Hospital de la Santa Creu i Sant Pau, Spain

[5]Department of Plastics and Reconstructive Surgery, Hospital de la Santa Creu i Sant Pau, Spain

*Corresponding author:

Sandraa González-Abós,
Department of General and Digestive Surgery,
Hospital de la Santa Creu i Sant Pau, Spain,
E-mail: sgonzaleza@santpau.cat

Citation:

González-Abós S, Inguinoscrotal Sarcomas, a Deep Look into Multidisciplinary Treatment: Outcome Analysis of 28 Cases Treated by Surgical Approach. Clin Onco. 2023; 6(21): 1-6

1. Abstract

1.1. Background: Inguinoscrotal sarcomas are extremely rare tumors. The current standard therapeutic approach has been radical inguinal orchiectomy with wide local resection of surrounding soft tissues. Nevertheless, there is no consensus on the description of prognostic factors, most authors consider low-grade tumor and complete excision as two significant factors associated with a favorable outcome.

1.2. Methods: A retrospective analysis was performed. A total of 28 patients underwent surgical treatment of inguinoscrotal sarcoma between 2005 and 2020.

1.3. Results: mean age was 53 years. Median follow-up was 46 months [27-69]. Recurrence occurred in 15/28 (42.8%) patients, a total of 8 patients experienced only local recurrence (28.5%), four patients developed only distant metastatic disease (14.3%) and three patients experienced both, local and distant failure (10%). Overall survival rates were 100%, 88% and 67.3% at one, three and five years respectively.

1.4. Conclusion: The unexpected discovery of a sarcoma in the inguinal region often poses a surgical dilemma when considering options for complete resection. The gold standard of treatment is complete surgical resection. In patients with locally advanced disease; en-bloc resection of major critical structures, including vascular and muscular tissue excision followed by vascular and/or free flap reconstruction should be considered as a therapeutic option in limb salvage.

2. Introduction

Inguinoscrotal sarcomas are extremely rare tumors, constituting 2% of all soft tissue sarcomas and 1% to 2% of malignant tumors of the genitourinary tract [1] with a low incidence rate (0.3-0.5 cases per million) [2]. In adults, more than 75% of these lesions arise from the spermatic cord [2]. According to Lewis et al. inguinoscrotal sarcomas have demographic similarities with sarcomas of retroperitoneal origin [3]. Due to the low incidence of these tumors, little information is available. There is no consensus on the description of prognostic factors, but most authors consider low-grade tumor and complete excision as two significant factors associated with a favorable outcome [4]

The current standard therapeutic approach has been radical inguinal orchiectomy with wide local resection of surrounding soft tissues [2], suggesting that wide re-resection in patients with previous positive margins is associated with a reduction in recurrence risk improving local control [5]. When an aggressive surgery is needed to obtain negative surgical margins, a multidisciplinary approach must be done including tissue and vascular reconstruction [6]. However, as drainage of the spermatic cord includes the ipsi-

lateral pelvic, ilioinguinal, and paraaortic nodes, elective treatment of these areas either with surgery or radiation therapy has also been advocated [2]. Nevertheless, the use of lymphadenectomy or adjuvant radiotherapy or both remains controversial [7]. In order to decrease the risk of local recurrence, radiotherapy in pre- or postoperative setting is feasible. Nevertheless, only few studies regarding to radiotherapy were published [8]. This treatment should be indicated in big voluminous lesions, high grade tumors, R1-R2 resections or in local recurrences. Interpolating information from extremity sarcomas studies, in preoperative radiotherapy the irradiated volume in smaller and the dose is 45-50 Gy. However, the patients have higher risk of wound healing complications [9, 10]. Further, in postoperative radiotherapy is the treatment field more extended and the dose is higher according to histological margins (50-70 Gy).

According to surgical complications, the use of adjuvant or neoadjuvant radiotherapy seems to enlarge the risk of wound dehiscense leading to a high number of complications. In those patients is mandatory to obtain a good local soft tissue reconstruction. Due to that, the confection of local or free flaps should be done in patients with large resections (>10 cm), treated with radiotherapy and patients with vessel resection and reconstruction; in order to assure a correct soft tissue cover. In those patients, microquirurgical free flaps can be the best surgical option to avoid complications.

Therefore, the risk of fibrosis is more frequent [10]. Though, with Intensity-Modulated Radiotherapy (IMRT), when better sparing of organs at risk is possible, no high-grade toxicity is reported, and the most frequent acute toxicity is only dermatitis. Although, more studies are necessary to achieve more information about impact and ideal sequence of radiotherapy [11].

The low clinical suspicion associated with the rarity of these tumors results in late diagnosis. The typical presentation is a unilateral inguinal swelling or scrotal mass, which may or may not be painful and is occasionally accompanied by a hydrocele. Usually, when the inguinal mass is small, it is suspected to be an inguinal hernia or lipoma and surgery is performed without previous radiological test or biopsy.

Preoperative distinction between malignant paratesticular tumors and other benign inguinoscrotal conditions is mandatory to avoid potential incomplete resection.

In most of the clinical cases described in the literature, these tumors are diagnosed after the histo-pathological analysis, leading to an incomplete surgical procedure and worse oncological results. In this study, we describe our experience in surgical treatment of inguinoscrotal sarcomas, postoperative course and survival.

3. Materials and Methods

3.1. Patient Sample

A retrospective analysis of clinico-pathological data was performed. A total of 28 patients who underwent surgical treatment of inguinoscrotal sarcoma between 2005 and 2020 were included. Patients were identified from a database all the sarcomas treated in our institution (National sarcoma referral center in Spain, treating surgically over 200 sarcomas per year). The histopathologic analysis was reviewed and only patients affected of primary inguinoscrotal sarcomas were selected. No patient was lost to follow-up.

The data abstracted included age, side of the tumor, date of surgery, surgical technic, histopathologic subtype, general tumor characteristics (grade and stage), site and date of recurrence, additional treatment and follow-up.

The indication for surgical resection was established by a multidisciplinary sarcoma committee following the center protocol and was based on patient baseline characteristics and radiological findings. MRI and CT scan were performed before surgery; PET scan or body-MRI were performed in patients with suspected distant dissemination.

Primary treatment consisted of radical excision of the primary tumor or second-look surgery with margin revision and ampliation. The implementation of adjuvant treatment was discussed in a multidisciplinary sarcoma committee; five patients underwent neoadjuvant treatment due to a large primary tumor at diagnosis. Four were treated with chemotherapy and a fifth patients received multimodal treatment with chemotherapy and radiotherapy

3.2. Tumor Grading

The tumor grade was assigned according to the Hajdu grading system (12)(6) based on histopathological type, cellularity, stromal content, necrosis, maturation and mitotic activity, classifying patients as high grade versus low or moderate grade.

3.3. Follow-up and Study Endpoints

All patients were routinely follow-up by CT scans or MRI of the surgical area every three months in the first postoperative year and at 6 months intervals after. Disease recurrence was defined as first clinical or radiological finding of local or distance disease after primary tumor resection. Death was attributed to sarcoma if there was uncontrolled recurrent disease at the time of death.

3.4. Statistical Analysis

Distributions were summarized using frequencies, medians and range. Overall survival rates were estimated using the Kaplan-Meier method and the log-rank test. Given the low number of events no multivariate analysis was performed. Any $p<0.05$ was considered statistically significant. All analyses were performed using the Statistical Package for Social Sciences (SPSS 21).

4. Results

A total of 28 patients were included, 9 women and 19 men, and mean age was 53 years old at the diagnosis of primary tumor. Twenty-one (75%) patients presented with clinical symptoms associated with the disease, and one presented with paraneoplastic thrombotic syndrome and pulmonary thromboembolism. The majority was referred to the hospital due to the appearance of an

inguinal tumor suspected to be an inguinal hernia, lipoma or inguinal mass without diagnosis (Table 1). Six (21%) patients were previously diagnosed with lipoma and one (3.5%) was suspected to have an incarcerated inguinal hernia. In two patients was diagnosed as incidental radiological findings.

Three patients had metastases at the time of primary tumor diagnosis and three were locally advanced tumors. Most frequent histologies were liposarcoma with 7 patients (25%) and leiomyosarcoma with 5 patients (17.8%). All anatomopathological diagnoses are described in table 2.

Table 1: Patients baseline characteristics

Patients baseline characteristics	Value
Median age, yo	53
Male, sex, n (%)	19 (68)
ASA**	
I	3
II	15
III	11
IV	0
Clinical manifestations	
Clinical symptoms, n (%)	21 (75)
Inguinal tumour	22
Suspicion of lipoma	6
Suspicion of incarcerated hernia	1
Others	13
Pulmonary thromboembolism	1
Incidental radiological findings	3 (11)
Incidental anathomopatological findings	4 (14)
Disseminated disease at diagnosis, n(%)	3 (11)

**ASA: preoperative classification of American Society of Anesthesiology

Table 2: Anatomopathological results

Pathological data	Value
Pathological analysis, n (%)	
Liposarcoma	7 (25)
Leyomiosarcoma	5 (17.9)
Dermatofibrosarcoma	4 (14.3)
Solitary fibrous tumour	2 (7.1)
Synovial sarcoma	2 (7.1)
Rhabdomyosarcoma	2 (7.1)
Spindle-cell sarcoma	2 (7.1)
Edwing sarcoma	1
Other	3
Tumour grade	
I - II	16 (57)
III	12 (43)

Twelve patients (42,8%) underwent surgery in another center and were referred to our institution for further treatment. Eight of these patients were suitable for wide re-resection because of incomplete prior surgery (positive margins) and in one was indicated by the multidisciplinary committee for observation due to low grade tumor and aggressiveness in the pathological analysis and the presence of marginal resection. Of the 16 patients (57.1%) operated in our center at the first time, 3 required second-look surgery for wide re-resection, one of them with an initial misdiagnosis of adenopathy, confirming the presence of malignant cells after anathomotological analysis.

The surgical procedure was wide excision in 22 patients (78,6%) including 12 (42.8%) patients who underwent surgical resection of the primary tumor and 10 (35.7%) who underwent surgical wide re-resection. Five patients (17.7%) required immediate surgical reconstruction with a microvascularized free flap and two (7.1%) underwent comun femoral vein reconstruction; this patient was not postoperative complications. Three patients did not immediate soft tissue reconstruction, with free flaps, required re-intervention for wound debridement due to postsurgical seroma infection. These patients needed a microsurgery free flap reconstruction in a second time.

All surgical procedures were performed in a similar way, performing an extent resection in order to obtain negatives margins; there was no variance depending on histological subtype due to reduced surgical area. Only in patients with vascular involvement, vascular reconstructive surgery was done. Multidisciplinary approach was performed including 4 surgical teams (General surgery, Orthopaedics surgery, Plastic surgery, Urology and Vascular Surgery). In most cases of primary surgery, only one surgical team was needed. In cases of wide re-resection or local recurrence a combined surgery was done including General surgeons, Plastic surgeons and vascular surgeons were required in those patients who underwent a reconstructive procedure.

Five patients (17.8%) received neoadjuvant therapy; four patients received chemotherapy and one a combination of radiotherapy and chemotherapy. Fifteen patients were treated with adjuvant therapy. Seven were treated with radiotherapy, 6 with chemotherapy and 2 with a combination of both.

Median follow-up was 46 months [27-69]. Recurrence occurred in 15/28 (42.8%) patients, a total of 8 patients experienced only local recurrence (28.5%), four patients developed only distant metastatic disease (14.3%) and three patients experienced both, local and distant failure (10%). Nine out of 28 patients (32%) died of the disease. Disease-free survival was 78.1%, 67.3%, and 39.1% at one year, three, and five years respectively. Median free-survival was 55 months [45-64]. Local recurrence-free survival was 92%, 79.4%, and 57.5% at one year, three, and five years respectively. There were no differences in local recurrence in patients who received adjuvant radiotherapy, although it seems in graphical

analysis (Graphic 1) that the recurrence event was later in patients treated with radiotherapy than those without (144 months vs 58 months respectively p 0.46).

Overall survival rates were 100%, 88% and 67.3% at one, three and five years respectively (Graphic 2). Median overall survival was 103 months.

Surgical treatment of recurrence was performed in 11 patients, including 16 surgical procedures due to second relapses in of some patients. Over those procedures, 5 lead to high complexity surgery including sigmoidectomy in one patient, duodenopancreatectomy in another patient and plastic surgery of soft tissues in three patients including flap confection in one patient and vascular reconstruction in two patients.

In our cohort, tumor grade 3 was associated with significant worse overall survival (OS) (96 months vs 47 months p 0.04) and disease-free survival (DFS) (55 months vs 88 months p 0,02) (Graphic 3). The liposarcoma histology subgroup had better surveillance, but without reaching statistical significance.

No differences in survival or relapse were found between patients with positive margins who underwent margin wide re-resection in a second surgery and patients with negative margins who underwent radical excision as primary surgery OS 89% vs 86% p 0.57; DFS 58% vs 52% p 0.60). No differences were found in survival between patients with radical excision and those who required a reconstructive surgery.
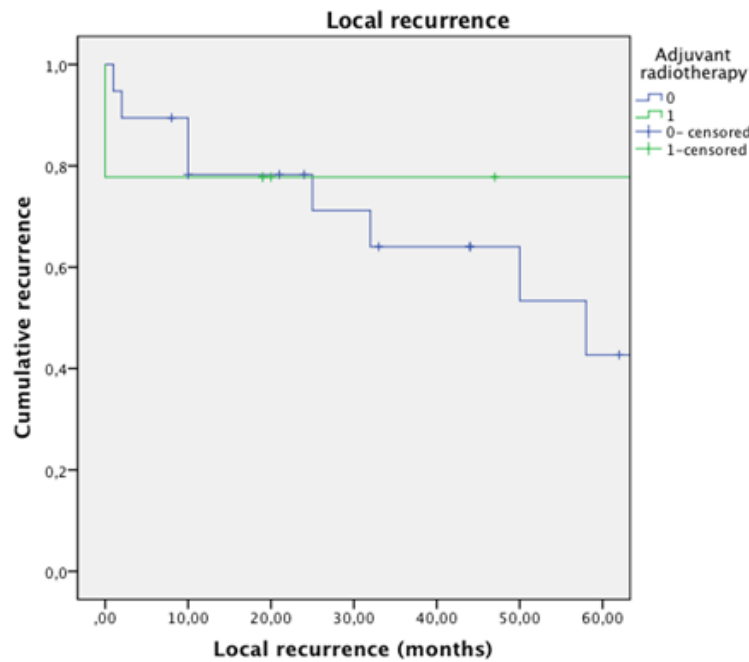
Graphic 1: Relation between local recurrence and adjuvant radiotherapy treatment in patients afected of inguinoscrotal sarcoma.
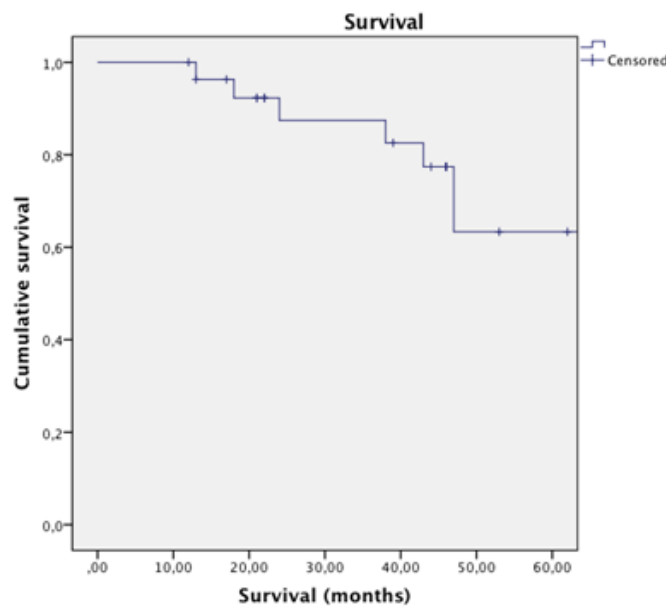
Graphic 2: Overall survival after surgical resection of patients diagnosed with inguinoscrotal sarcoma.
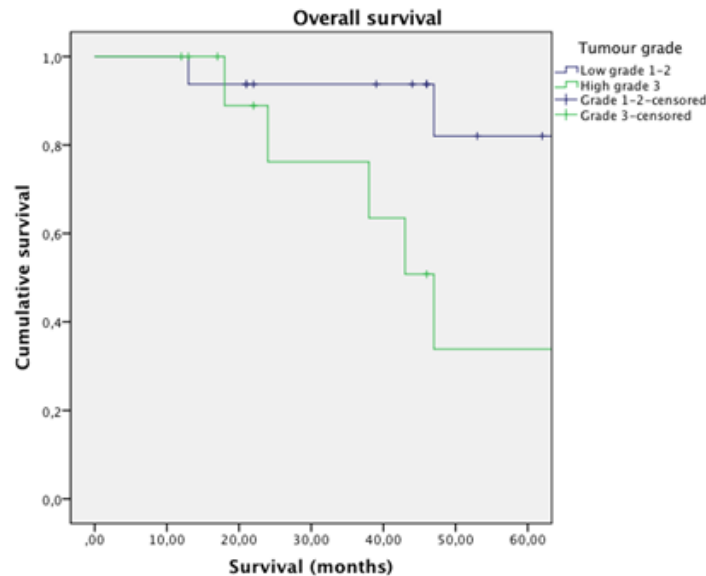
Graphic 3: Overall survival after surgical resection depending on tumour grade.

5. Discussion

Inguinoscrotal sarcomas are rare malignancies of the inguinal and paratesticular region. Just few publications are available, and they consist predominantly on case reports. Several cohorts describe few patients over decades; a single-center study over a 18-year period collected 7 inguinoscrotal sarcomas [13] only, an Italian multi-center study over a 19-year period included fewer than ten patients [14], a single-center study over a 20-year period Froehner et al described one of the largest series including 35 patients and Chowdhry et al described recently a retrospective including 24 patients [9].

The unexpected discovery of a sarcoma in the scrotum or inguinal region often poses a surgical dilemma when considering options for complete resection. The common presentation as lipoma or inguinal hernia highlights the difficulties in treating and investigating these tumors, leading to initial misdiagnosis. Most patients in this series (12 of 28) were initially explored and treated in another centers before referral to our department for further treatment. We found that the most common histology was liposarcoma, followed by leiomyosarcoma (25%) as described in the literature [2]. However, in this study we found a lower percentage of liposarcoma than in most of the previous series. We believe that imaging test should be done before surgery to avoid misdiagnosis, in some cases inguinoscrotal tumor is an extension of retroperitoneal sarcoma [15].

No concluding data about prognostic and risk factors in inguinal tumors is available. Rodríguez et al. analyzed the SEER cancer registry in the United States, collecting a huge cohort of 362 patients. They conclude that undifferentiated tumor grade, distant stage, positive lymph nodes, and histiocytoma or leiomyosarcoma cell histology were all independent predictors of poor disease-specific survival [2].

The gold standard of treatment for patients with localized soft tissue sarcoma is complete surgical resection with negative margins (R0). There is no consensus on second look surgery in patients with marginal surgery, though it is recommended in those with positive surgical margins (R1). Some authors reported that positive surgical margins significantly increased the risk of local recurrence [16], in addition to increasing the risk of distant metastases and disease related death. Due to reduced surgical site in inguinal sarcomas, surgical technique is similar regardless the histological phenotype.

In patients with locally advanced disease; en-bloc resection of major critical structures, including vascular and muscular tissue excision followed by vascular and/or free flap reconstruction should be considered as a therapeutic option in limb salvage [3]. Multidisciplinary approach including plastic surgery, orthopedic surgery and vascular surgery must be done. Although no differences in survival was found in this group of patients, local recurrence seems to be lower after aggressive resections [3]. In those patients, with pre or postsurgical radiotherapy, immediate and complete soft tissue local reconstruction with free flaps, present a low number of local complications such as wound dehiscence or infection.

To our knowledge, our study has one of the largest and most homogeneous cohort of patients with inguinoscrotal sarcoma, since it is based on the experience of a single center and dedicated multidisciplinary team. Our findings, although not significant, are consistent with those previously published.

In our cohort, tumor differentiation has a significant impact in overall survival, well-differentiated tumors (G1-G2) had higher specific survival compared to those with undifferentiated tumor grades (p0.04). Our series presents a high rate of undifferentiated tumors (42%), compared with previous series published in the literature, eventhough we describe similar survival rate. Chowdhry

et al. described overall survival of 71% and 64% at three and five-years respectively. In our serie, survival rate found were 100%, 88% and 67.3% at one, three and five years respectively. We also found differences regarding recurrence-free survival when comparing tumor grade differentiation (p< 0.02). Although not significant, we found differences in survival in liposarcoma compared to other anatomopathological diagnoses. No difference in OS and recurrence-free survival was found in marginal status analysis, probably due to low number of patients. Furthermore, no advantage in cancer specific survival was found in patients who received adjuvant treatment.

When analyzing marginal status, we did not find differences in survival and recurrence-free survival, probably due to the low number of events (83 months vs 84 months). We found a non-significant association between adjuvant therapy and a decrease of specific cancer survival, probably due to bias selection; usually patients with the worst prognosis were those who received adjuvant therapies.

In conclusion, our series contributes to increase the knowledge in this rare entity highlighting once more.

References

1. Russo P, Brady MS, Conlon K, Hajdu SI, Fair WR, Herr HW, et al. Adult urological sarcoma. J Urol. 1992; 147(4).

2. Rodríguez D, Barrisford GW, Sanchez A, Preston MA, Kreydin EI, Olumi AF. Primary spermatic cord tumors: Disease characteristics, prognostic factors, and treatment outcomes. Urol Oncol Semin Orig Investig. 2014; 32(1): 52.e19-52.e25.

3. Emori M, Hamada K, Omori S, Joyama S, Tomita Y, Hashimoto N, et al. Surgery with vascular reconstruction for soft-tissue sarcomas in the inguinal region: Oncologic and functional outcomes. Ann Vasc Surg [Internet]. 2012; 26(5): 636-42.

4. Froehner M, Koch R, Lossnitzer A, Schober RR, Schuler M, Wirth MP. Adult inguinoscrotal sarcomas: Outcome analysis of 21 cases, systematic review of the literature and meta-analysis. World Journal of Urology. Springer Verlag. 2014; 32: 445-51.

5. Murray KS, Vertosick EA, Spaliviero M, Mashni JW, Sjoberg DD, Alektiar KM, et al. Importance of wide re-resection in adult spermatic cord sarcomas: Report on oncologic outcomes at a single institution. J Surg Oncol. 2018; 117(7): 1464-8.

6. Catton CN, Cummings BJ, Fornasier V, O'Sullivan B, Quirt I, Warr D. Adult paratesticular sarcomas: A review of 21 cases. J Urol [Internet]. 1991; 146(2): 342-5.

7. Rodríguez D, Olumi AF. Management of spermatic cord tumors: A rare urologic malignancy. Ther Adv Urol. 2012; 4(6): 325-34.

8. Cerda T, Martin, Truc G, Créhange G, Maingon P. Faisabilité et efficacité de la radiothérapie avec modulation d'intensité dans la prise en charge des sarcomes du cordon spermatique. Cancer/Radiotherapie [Internet]. 2017; 21(1): 16-20.

9. Chowdhry VK, Kane JM, Wang K, Joyce D, Grand'maison A, Mann GN. Testicular, Spermatic Cord, and Scrotal Soft Tissue Sarcomas: Treatment Outcomes and Patterns of Failure. Sarcoma. 2021; 2021.

10. Pisters PW, O'Sullivan B MR. No Title Evidence-based recommendations for local therapy for soft tissue sarcomas. J Clin Oncol. 2007.

11. Gerrand CH, Rankin K. Preoperative versus postoperative radiotherapy in soft-tissue sarcoma of the limbs: A randomised trial. Class Pap Orthop. 2014; 359: 485-6.

12. Hajdu SI. Pathology of soft tissue tumors. 1979.

13. Rhu J, Cho CW, Lee KW, Park H, Park JB, Choi Y La, et al. Comparison of retroperitoneal liposarcoma extending into the inguinal canal and inguinoscrotal liposarcoma. Can J Surg. 2017; 60(6): 399-407.

14. Mondaini N, Palli D, Saieva C, Nesi G, Franchi A, Ponchietti R, et al. Clinical characteristics and overall survival in genitourinary sarcomas treated with curative intent: A multicenter study. Eur Urol. 2005; 47(4): 468-73.

15. Ananthprabhu K, et al. International Journal of Biomedical and Advance Research 2015, 6: 75-77 and Tajima Y, et al. J Neurol. 2005; 252: 1416-7.

16. Stojadinovic A, Leung DHY, Hoos A, Jaques DP, Lewis JJ, Brennan MF. Analysis of the prognostic significance of microscopic margins in 2,084 localized primary adult soft tissue sarcomas. Ann Surg. 2002; 235(3): 424-34.