International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2019): 7.583

Retroperitoneal Liposarcoma: Clinicopathologic and Outcome Analysis

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Abstract: ***Introduction: Retroperitoneal liposarcoma (RPL), a rare adipose tissue malignant tumor, grows to a huge size before beinga clinically observed problem, its treatment options still under investigation. Tumor recurrence after resection and tumor growth management remain as anobstacle. Aim: The aim of this study is to correlatethe frequency and clinicopathological variablesof retroperitoneal liposarcoma to patients outcome. Materials and Methods: Retrospective analysis of surgical specimens of seven patientsand their clinical, surgical, treatment options and follow-up data were collected from medical documents. The specimens submitted toa private histopathology laboratory in Benghazi during the period from January 2018 to September 2019. Statistical analysis performed using IBM SPSS Statistics for Windows, version 22.Kaplan-Meier method used for survival analysis. Results: The patients` mean age was 63±9.7 years, nearly no gender predilection. Complete tumor resection wasperformed for all cases with adjoiningorgan resection in three cases.The mean tumors diameter was19.4±6.8 cm with clear resection margins.Histopathological examination showedwell differentiatedRPL (4 cases), dedifferentiated RPL (2 cases) and pleomorphic RPL (1 case) with grade I in 4 cases and grade II in (3 cases). There was no metastasis; (5 cases) were classified as stage I and (2 cases) as stage II. The mean follow-up period was 18±10.5 months and the median survival time 18 months (95%CI: 7.7-28). The better survival result was achieved in cases where only surgical resection of the tumorwas preformed (p-value: 0.008). The better survival result was also seen in cases with grade I (p-value of 0.01). Conclusion: Low grade tumor and complete tumor resection with negative margin were associated with better over-all survival result in RPL.***

Keywords: Low grade sarcoma, Retroperitoneal liposarcoma, tumour grade

1. Introduction

Liposarcomas are malignant tumors of adipocytic mesenchymal origin (1) arises anywhere in the body but commonlyseen in the extremities and in retroperitoneum (1, 2). Retroperitoneal liposarcoma (RPL) is common histologic type of the rare retroperitoneal sarcomatous tumour (3, 4) that occurs in all ages but the usual presentation appears between 5th and 6th decades; the tumor develops slowly in retroperitoneum, reaches a huge size, and compresses the abdominal organs, as a result. In many cases, it could affect the function of the compressed organ (4). The main cause of RP liposarcoma is still unclear but some studies indicate its association with increased age, exposure to toxic chemicals and previous radiotherapy (5). Most retroperitoneal liposarcomas rarely metastasize, and its fatal course is related to local aggressiveness (6-9). Recently, so many researches focus on how to prevent the tumour and avoid the recurreance (4,10).

In this study, we discuss the clinical and histopathological factors that determine the treatment options and affect the patient survival.

2. Materials and Methods

A retrospective study of seven patientswho underwent surgical resection of primary and recurrent RPL. The specimens submitted to a private histopathology laboratory in Benghazi, Libya during the period from 2018 to September 2019.The clinical data were collected from the surgical departments where the surgeries were performed.

The excised tumor masses were grossly examined, the tumor size was defined by its maximum diameter, and categorized into ≤15 cm and >15 cm. Margins of the tumor were evaluated grossly then microscopically. Ifthere was no tumor within 1 mm from the edge of the inked specimen, then the surgical margins were considered free (10,11).

The received specimens were fixed in 10% formalin, routinely processed and paraffin-embedded blocks were prepared. Microtome was used to cut 4µm sectionsfrom theseblocks, mounted on slides and then stained using haematoxylin and eosin stain (H&E). Histological sections were examined, and tumors were classified according to World Health Organization (12,13) into well-differentiated, dedifferentiated, myxoid, round cell and, pleomorphic liposarcoma. All the tumor types were graded according to French Federation of Cancer Centers Sarcoma Group (FNCLCC) system(14).Tumor staging performed using TNM staging systemof the American JointCommittee on Cancer (AJCC)(15,16).The recurrence-free and overall survival weredefined as the time interval from the date of surgery to thedate of first recurrence or death by any cause. Based on oncologist advice, some patients received chemotherapy and or radiotherapy. The follow up duration 12-33 months starting from the date of diagnosis to the date of death or the last follow-up. The patients` outcome was categorized into patients who alive with no evidence of disease, alive with disease and died of disease.

3. Statistical Analysis

The study was descriptive, and the statistical analysis performed using IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, N.Y., USA). Continuous variables

expressed as mean ±SD, whereas categorical variables expressed as numbers and percentages. The survival analysis performed using Kaplan-Meier method with a significance level was set at $P< 0.05$.

4. Result

Seven patients suffering from retroperitoneal masses which were diagnosed as liposarcoma were included in this study.The mean age was 63±9.7 years, the median age was 62 years (age range: 47-77). Three cases were males while four were females. Complete tumor resection restricted of the mass was performed in four cases (57%), complete tumor resection with splenectomy was done for one case(14.4%), complete tumor resection with multiple organ resection was done for two cases (28.6%) i.e. spleno-pancreatectomy was performed for one case and gastro-spleno-pancreatectomy was done for anothercase. The mean maximum diameterof the resected tumors was19.4±6.8 cm, the median tumor size 18 cm (range: 12-33). A representative gross picture of the tumor mass was shown in figure 1.

Histopathological analysis of the resected tumors showed, well differentiated RPL (figure 2A and B), dedifferentiated RPL (figure 2C and D) and pleomorphicRPL (figure 2E). A representative clear area adjacent to spleen was demonstrated in figure 2F.The percentage of each subtype was shown in figure 3A

The tumor grade demonstrated in figure 3B. The well-differentiated RPLs were grade I and dedifferentiated and pleomorphic subtypes were grade II. There was no distance metastasis in all cases. Five cases were stage I and two cases were stage II as shown in figure 4. The surgical margins were clear in all cases. Local recurrence of the tumor occurs in four cases. Two patients received radiotherapy and chemotherapy. The mean follow-up period was 18±10.5 months, the median follow-up time18 months (range: 2-33).The survival analysis aftersurgicalintervention and treatment was significant (p-value: 0.008) and revealed that surgical resection of the tumor is the foundation for treating RPL as displayed in figure 5, and the survival analysis depending on tumor grade showed that grade 1 revealed significantly better result than grade 2 (p-value: 0.01) as displayed in figure 6. The median survival time 18 month (95%CI: 7.7-28).

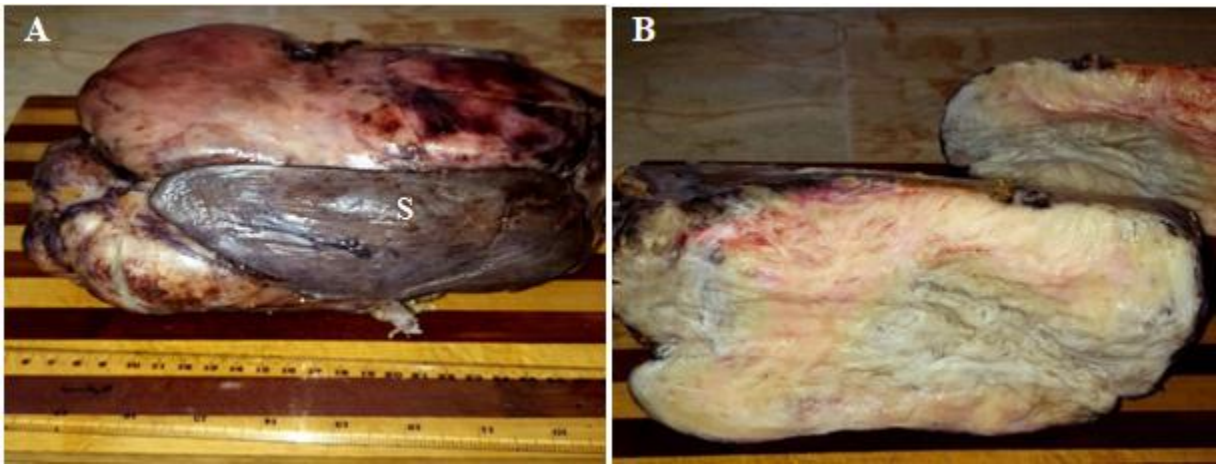
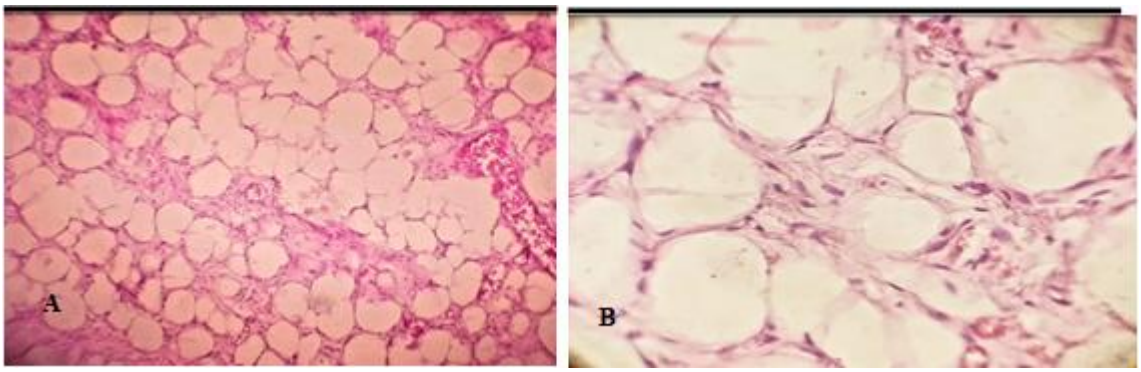


Figure 1: Shows the gross features of RPL. (A) Large irregular lobulated tumor mass, measures 22x10x8 cm in diameter, with hemorrhagic surface and attached to spleen, S. (B) Cut section showed solid yellow mass with foci of hemorrhage.



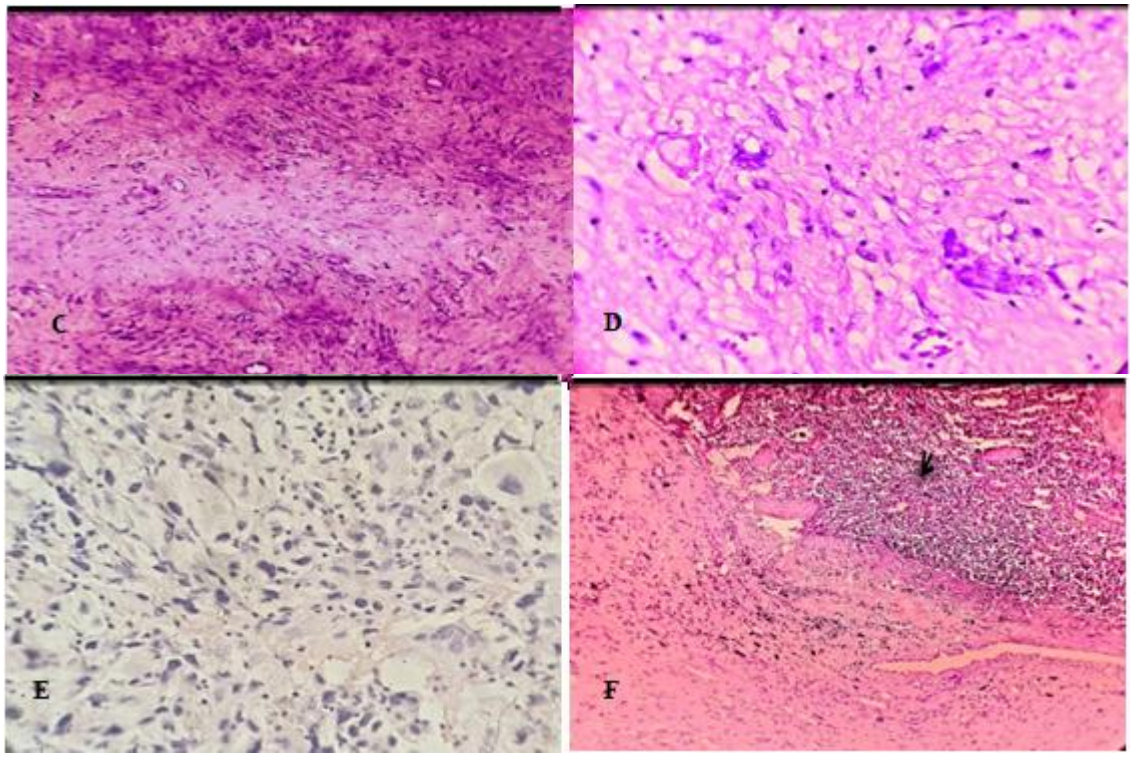


Figure 2: Shows the light microscopic appearance of RPL. (A) Well differentiated RPL relatively mature adipocytic proliferation, minimal variation in cell size, mild nuclear atypia and hyperchromasia(H&E, original magnifications ×100). (B) Well differentiated RPL high power view from A (H&E, original magnifications ×400). (C) Dedifferentiated RPL shows pleomorphic spindle cellular areas with varying amounts of eosinophilic cytoplasm. (H&E, original magnifications ×100). (D) Dedifferentiated RPL high power view from C (H&E, original magnifications ×400). (E) Pleomorphic RPL shows bizarre cells with enlarged round to bizarre nuclei (H&E, original magnifications ×400). (F) Liposarcoma cells adjacent to normal splenic tissue –arrow (H&E, original magnifications ×100).

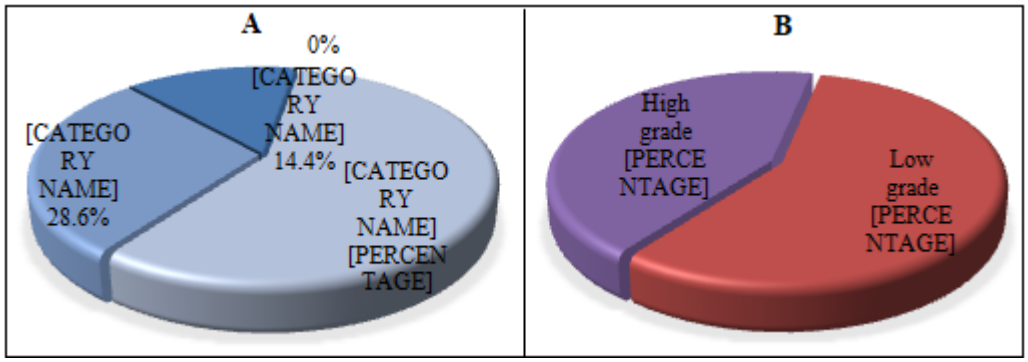


Figure 3: Histological subtypes and grade of liposarcoma. (A) 57% of the analyzed cases was well differentiated, 28.6% was dedifferentiated and 14.4% was pleomorphic. (B) 57% of analyzed cases was low grade whereas 43% was high grade

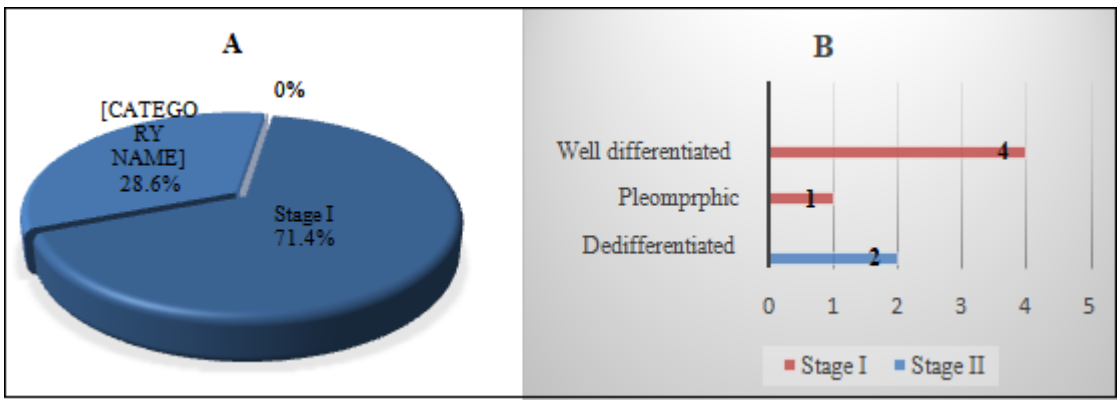


Figure 4: TNM stage. (A) Most of the cases were stage I and only 2 cases were stage II.(B) Well differentiated and pleomorphic liposarcoma were stage I and the dedifferentiated case was stage II

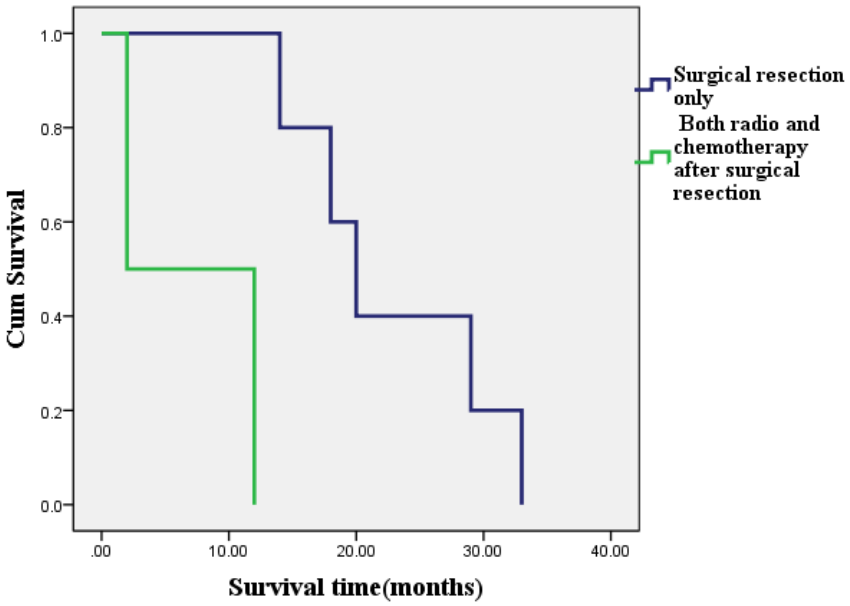


Figure 5: Plots of Kaplan-Meier estimates of survival of patients after surgical resection only and after receiving therapy(*P*-0.008).

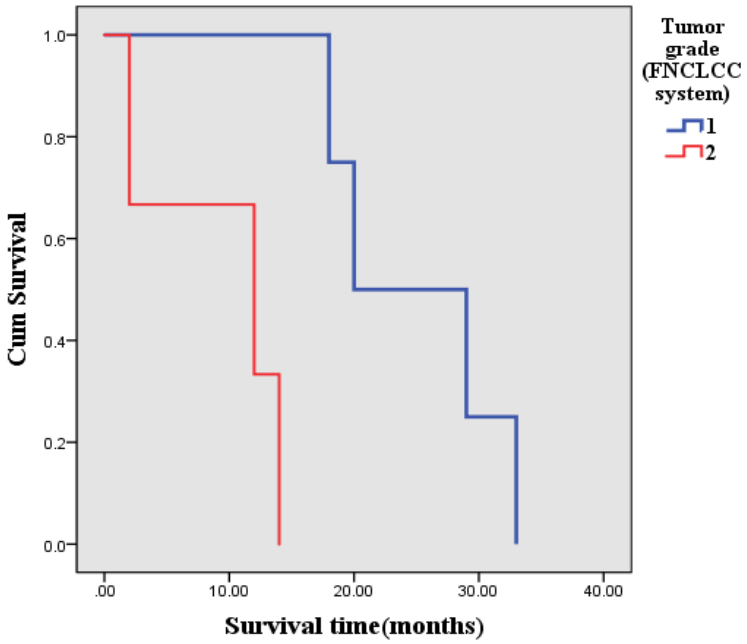


Figure 6: Plots of Kaplan-Meier estimates of survival of patients according to tumor grade (*P*-0.01).

5. Discussion

Retroperitoneal sarcoma is a rare soft tissue tumor, and liposarcoma is the commonest subtype of retroperitonealsarcoma. Due to its slowgrowth, retroperitoneal liposarcoma usually diagnosed when it becomes hugely large. The treatment and prognosis of RPL is still under investigation. So, in this study, seven patients were analyzed in a period of 21 months and the diagnosed was made in a private qualified histopathology laboratory. Then the results were compared to several studies thatanalyze the clinicopathological features of RPL. Fernández-Ruiz M *et al.*(13)analyzed ten cases in a period of eight-year, Tan MCB *et al.*(10) analyzed 399 cases in period of 28 years and Luo P *et al.*(11)examined61 cases in 11years duration. The comparison of these studies showed that the number of cases is differ from area to another, but in general it is an infrequent type of malignancy

In this study, there was almost no gender predilection and the mean age was 63±9.7 years and the median age was 62 years. Karadayi K *et al.*(17) showed same results, as he demonstrated equal male and female involvement, with median age of 61.5 years. Another study performed by Fernández-Ruiz M *et al.*(13) in which the mean age was 63.2±11 years, like the mean age in this work, but regards gender; males were 6 cases and females were 4 cases. In compared to a study by Patil S *et al.*(18)showed the mean age 60.4 ± 14.5years, males (48.1%) were lightly less than and females (51.9%).

The tumor size detected in the present study was 19.4±6.8 cm with median diameter 18cm (12-33). Similar median value was seen in a study by Luo P *et al.*(11) in which the median diameter was 19cm (range 4.3-50) but in contrast, in studies by Karadayi K *et al.*(17) and Fernández-Ruiz M *et al.*(13)the median tumor size was a bit larger (22cm) (range 15-50) and (23±10.8cm) (range 8-35) respectively, with median size 23.5cm. All these finding indicates that RPL, in general, is a large tumour and most of them more than 10cm at presentation (4).

As In previous studies (10, 13, 19), this study showed that, well differentiated and dedifferentiated RPL are of the common histologic subtypes followed by pleomorphic liposarcoma. Similar result was demonstrated by Fernández-Ruiz M *et al.*(13), whereas a study by Tan MCB *et al.*(10) showed that the dedifferentiated RPL and pleomorphic RPL were more than well differentiated RPL. In a study performed by Blay J-Y *et al.*(19) the well differentiated and dedifferentiated liposarcoma almost had equal percent (5.9% and 6.4% respectively).

In this study, According to FNCLCC system, the tumor grade was grade I in four cases, all were well differentiated RPL and grade II in three cases, dedifferentiated RPL, 2 cases, and pleomorphic RPL one case. The finding in Fernández-Ruiz M *et al.* paper (13) was nearly same, as he reported five cases as grade I, of which four cases were well differentiated RPL, and one round cell and five cases asgrade II, of which two cases were dedifferentiated RPL, one case pleomorphic RPL and two case well differentiated RPL. In many studies, the histologic grade was a useful prognostic factor, and help in expectingofdistant metastasis and disease-free period (20).

Various studies indicate that, even with complete resection of primary tumor, 25% of patients with soft tissue sarcoma showed distant metastasis (20). In contrast, in this study, none of the cases develop metastasis and the tumor stage was stage I for well differentiated and pleomorphic RPL, and stage II for dedifferentiated RPL cases. Fernández-Ruiz M *et al.*(13) showed the same staging results.

Surgery with complete tumor resection of localized RPL was the basic treatment (13) and good prognosis is based on complete tumor resection. However, more than 70% of cases showed local recurrence despite complete gross resection (7,8). Due to the missing of essential data, the use of radiation or chemotherapy in recurrent diseaseis still not established, therefore, the local recurrence isthemain cause of mortality related to RPL (20).

In this study, the surgical resection of tumor applied for all patients and accompanied by adjacent organ resections performed for three patients, in which the tumor was grossly expected to show infiltration to theses organs. Recurrence occurred in four cases, of which one cases were dedifferentiated RPL treated with surgery and adjuvant radiotherapy and chemotherapy. The other case of dedifferentiated RPL was primary, and the tumor resurgence occurred and treated with surgery and adjuvant radiotherapy and chemotherapy. In contrast to study by Fernández-Ruiz M *et al.* (13), all patients underwent complete surgical resection, negative microscopic margin was achieved in four cases andconcomitant resection of adjacent organs was in five cases.Four cases developed tumor recurrence in thelower abdomen location and one inupper abdomen. Two cases received chemotherapy and one case received radiotherapy, these cases were well differentiated RPL. A study accomplished by An JY *et al.* (21) revealed that complete surgical resection was associated with good prognosis.

The median follow-up time in this work was18 month (range: 2-33). The outcome of patients at the end of this period was as following, five cases alive without evidence of the disease, one case alive with disease, and one case deceased due to complication two months after operation. Comparing these findings with results in a study by Fernández-Ruiz M *et al.* (13) where the end of follow up period was between 1.2–125.4; three cases were died, other cases showed three-year overall survival 79%. Another study performed by Karadayi K *et al.*(17) involved eight cases of well differentiated RPL underwent complete surgical resection with adjacent organ resection in 25% of cases, after median follow-up of 21 months (range: 15-24), all cases were alive without recurrence apart from one case died.

6. Conclusion

As asporadic malignancy with slow course, RPL usually presented late with huge tumor size. Tumor stage and grade are important for the decision of the treatment options. The main treatment option is always the complete tumor resection whereas the tumorgrade is the most important prognostic factor. Tumor recurrence can occur even with complete tumor resection and the use of adjuvant therapy may improve survival rate. Small sample number nearly showed same results that were achieved when large number of cases were analyzed. The role of adjuvant therapy to control the disease and prevent recurrence has to be highlighted.

7. Limitation of the study

Since retroperitoneal liposarcoma is an infrequent tumor, it is hard to obtain the essential data that lead to the complete understanding of the tumor behavior to select treatment options andpredict prognostic factors.

8. Acknowledgment

We appreciate the support of Tiba histopathology pathology laboratory, Benghazi, Libya

9. Conflicting Interest

There is no conflict of interests regarding the publication of this paper.

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