ORIGINAL ARTICLE

MALIGNANT PHYLLODES TUMOUR OF THE BREAST

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Background: Malignant Phyllodes Tumour (MPT) is considered to be a rare disease of the breast. The most frequent clinical presentation of a MPT is a rapidly growing breast lump. **Methods:** Consecutive cases of MPT registered between Jan 1, 1995 and Dec 31, 2012 at the Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, were reviewed, to obtain information on age, tumour size, treatment given, disease-free survival, and overall survival. Disease-free survival was computed between the dates of surgery and recurrence, whereas, the overall survival time between the dates of diagnosis and last contact, both in months. **Results:** A total of 101 cases of Phyllodes tumour were recorded. These included: malignant tumours (42) benign (27), and borderline (32). Malignant Phyllodes tumours (42 cases) were studied further and 41 included for additional analysis. The mean age of the women in the study was 40.3±12.5 (22–72 years). Of the 33 patients who were disease-free after surgery, 15 had a recurrence, whereas, 18 did not have a recurrence. In those who had surgery alone versus those who received radiation treatment in addition to surgery, the median disease-free survival was 117 and 44.2 months, respectively. The mean overall survival time was 33.7 months. **Conclusion:** In this study, patients presented at a younger age than in other studies. Further exploration into molecular, biologic, geographic, and socioeconomic factors is needed to clearly understand the epidemiology of this disease in our population.

Keywords: Phyllodes tumour, age, recurrence, breast cancer, women, Pakistan

INTRODUCTION

Malignant Phyllodes Tumour (MPT) of the breast is a rare fibroepithelial disease of the breast.[1] The age at diagnosis is usually between 35 and 55 years. The median size of the tumour is 4 cm but it can grow rapidly to even larger sizes. Diagnosis is established by mammography and ultrasound guided core needle biopsy having a high sensitivity and specificity.[1,2] The essentials of diagnosis include the presence of both epithelial and stromal elements within the lesion. Surgical resection is the mainstay of management and treatment options include wide local excision or mastectomy to obtain histologically clear margins.[3] However, local recurrence can occur if the margins have not been adequately removed by more than 1 cm. The role of adjuvant chemotherapy, radiotherapy, and hormonal therapy has not yet been fully investigated. Because the disease is a rare one, the information available about it in Pakistan is also limited. An attempt was made to retrospectively review and report the cases seen at the Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH & RC)[4], Lahore, Pakistan.

PATIENTS AND METHODS

A list of all patients diagnosed with Phyllodes tumour of the breast at SKMCH & RC, between January 1, 1995 and December 31, 2012, was obtained. A total of 101 cases of Phyllodes tumour were recorded at the hospital. There included: 42 malignant tumours; 27 benign, and 32 borderline cases. Of the 42 malignant Phyllodes tumour patients (females), one presenting with a recurrence at the first visit and having a single visit to the hospital, was removed from the analysis. Forty-one MPT cases were studied further through file review, conducted between January and March 2013, to obtain information on age at presentation (years), tumour size (cm.), treatment received, disease-free survival (DFS), and overall survival (OS). Treatment received both at SKMCH & RC and other hospitals was categorised as surgery alone, surgery and radiation therapy, radiation therapy only, and surgery and chemotherapy. In 2 cases, the type of treatment received was not known. Surgery included lumpectomy, segmentectomy, simple mastectomy, and modified radical mastectomy. Disease-free survival was computed from the date of surgery till recurrence and overall survival time between the dates of diagnosis and last contact, both in months. Patients were classified as being lost to follow-up if they had missed their last scheduled appointment and a period of at least 4 months had lapsed since. Kaplan-Meier analysis was conducted to determine if there was any difference in survival between the treatment groups under review. Recurrence was the endpoint of interest. Those who did not reach the endpoint of interest were censored in the analysis. The Log Rank (Mantel Cox) test was used for overall comparisons. The test was considered to be significant at an alpha-level of 0.05. The Statistical Package for Social Sciences, version 19, was used to conduct the analysis.

RESULTS

The mean age of the 41 MPT cases was 40.3±12.5 years (22–72 years) with a median of 37 years. Tumour size was available in 24 cases: mean 9.2±5.6 Cm (2–21 Cm);

median 8.5 cm. Further, treatment received, disease-free survival, and overall survival were studied. Of these 41 patients in the study, 22 (53.7%) were lost to follow-up. There was no record of death of any of the patients in the files. One patient had an overall survival of 0.1 months and was removed from the overall survival study. The mean survival time (OS) of the 40 patients was 33.7±35.1 months (0.3–152.8 months), with a median of 24.2 months. The type of treatment these 41 patients received either at SKMCH & RC, outside the hospital, or both, included surgery and radiation therapy: 23 (56.1%), surgery alone: 14 (34.1%), radiation therapy alone: 1 (2.4%), a combination of surgery and chemotherapy: 1 (2.4%), and it was unknown in 2 cases (4.9%) as the treatment these patients received outside SKMCH & RC was not found in the records. Thirty-three patients were disease-free after receiving treatment and, in these patients, recurrence was documented in 10 (47.6%) of the 21 who had both surgery and radiation therapy and in 5 (45.5%) of the 11 who had surgery alone. Recurrence was not recorded in one who had a combination of surgery and chemotherapy and this patient was not included in the survival analysis. Kaplan-Meier analysis comparing the two groups consisting of those who had undergone surgery alone versus those who had also received radiation treatment along with surgery showed the median disease-free survival to be 117 and 44.2 months, and the 5-year cumulative probability of survival to be 65% and 38%, respectively. Figure-1 displays the curves based on the Kaplan-Meier analysis and Table-1 shows details related to survival analysis. At an alpha-level of 0.05, no statistically significant difference could be demonstrated between the two groups under consideration (p=0.55).

Figure-1: Disease-free survival by treatment

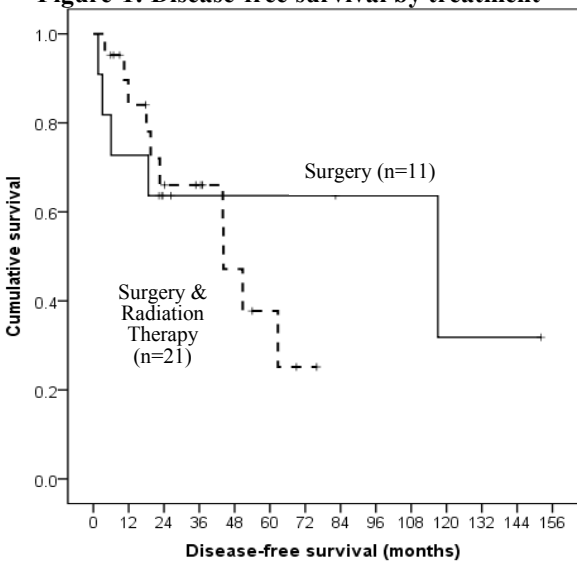

Table-1: Disease-free survival by treatment modality using the Kaplan-Meier method (N=32)

Treatment	Recurrence (Event)	Censored	5-year cumulative probability of survival	Median survival time (months) (95% CI)	Range (months)
Surgery (n=11)	5	6	65%	117.0 (0–260.3)	1.63–152.07
Surgery+Radiotherapy (n=21)	10	11	38%	44.2 (34.4–53.9)	3.90–75.87

DISCUSSION

Phyllodes tumour constitute only 0.3–0.9% of breast tumours.[5] Most Phyllodes tumours are benign, but 10 percent are malignant (cancerous).[6] At least 12.5% of patients with Phyllodes tumour have a history of fibroadenoma and 20% have a concurrent fibroadenoma.[7] Wide local excision with 2 Cm margin (minimum 1 Cm) is the treatment of choice.[3] MPT rarely metastasises to regional lymph nodes; therefore, lymph node dissection or sentinel lymph node biopsy is not recommended.[3] In about 20% of both benign and malignant cases, PT will recur locally.[5]

The reviews from Pakistan on Phyllodes tumour include some that discuss just the malignant type of Phyllodes tumour, while others discuss the whole spectrum ranging from benign to malignant. These reviews take into account 30 cases, including 15 benign, 8 borderline, and 7 malignant, from Karachi, in 6 years, with mean age at presentation of the 30 cases being 40 years and of those having malignant tumours being 45.6 years[8]; 35 cases including 23 benign, 5 borderline, and 7 malignant, in 6 years, with mean presenting age being 24 years, in a study from Jamshoro[9]; 22 patients in 4 years with 10 benign, 4 borderline, and 8 malignant, with mean presenting age being 31 years[2]; 7 cases from Quetta[10]; one case from Lahore in a seven month primigravida[11]; 3 cases from Peshawar diagnosed through mammography[12]; 42 cases, ≤25 years of age from Karachi, in a 16-year time period, with 14 each classified as benign, borderline, and malignant.[13]

The mean age at presentation of the MPT patients studied at SKMCH & RC was 40.3 years. However, another aforementioned study in Pakistan[8] has reported it to be around 46 years. The mean presenting age is lower in our study compared to what has been reported by Shireen *et al*[8] and, also, as stated for other types of breast cancers at SKMCH & RC, where it was around 46 years[14]. It is noteworthy that a study from India[15], on 37 women in a 17-year time period from 1982 to 1998, has also described the mean age to be 39±11 years (19–62 years). This is comparable to our study. Further, the mean age of 40 years, as reported in a study from the West[3], is similar to what has been reported in our study.

Of the eighteen women in our study who initially had a lumpectomy, 16 underwent segmentectomy, wide local excision, or mastectomy at a

subsequent stage. Recurrence was recorded in 15 of the 33 cases. Khurshid *et al*[13] have recorded that, in a review of 42 cases, lumpectomy was performed in 50% of benign, 78% of borderline, and 64% of malignant cases. It has also been reported by Khatoon *et al*[9], in a study of 35 cases, that lumpectomy was performed in 25.7% and mastectomy in 74.3% of the patients having 23 benign, 5 borderline, and 7 malignant cases. In this study, on follow-up, recurrence was seen in just one patient with benign disease who previously had a lumpectomy. In yet another study of 7 patients by Damani *et al*[8], breast conserving surgeries were performed in 4 and mastectomy in 3 cases, representing 57% and 43% of the cases, respectively. Soomro reported a follow-up of 12–40 months of 8 cases of MPT having mastectomy and receiving radiation therapy; in this group of patients, two patients died due to lung metastases, whereas 6 patients were tumour free when file review ended.[2] The follow-up period reported in that study was shorter than that reported as overall survival in our study. Pandey has reported the median follow-up to be 43 months (1–170 months).[15]

There were no statistically significant differences between the two treatment groups in our study. This may be because of a small sample size in each group. The wide confidence interval may be due to variation in the survival data.

CONCLUSION

Phyllodes tumour is a rare disease and prospective studies, with long term follow-up, could help improve its understanding with regard to its epidemiology and treatment outcomes.

ACKNOWLEDGEMENTS

The authors would like to thank the Registry Officers Raqib Faraz and Adna Yousaf for collecting the data, and Dr. Faisal Sultan and Dr. Aasim Yusuf for their support in the area of cancer registration.

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