A clinical study and treatment results of adrenocortical carcinoma patients presented in Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore

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Abstract
Adrenocortical carcinoma is a rare and aggressive malignancy with an incidence of 0.5-2 per million per year and its overall prognosis is very poor. This study was aimed to point out the factors associated with tumour recurrence and patient's survival after complete surgical resection of this aggressive malignancy. Patients admitted from January 2011 till December 2015 were retrospectively reviewed using case notes. In these five years 29 patients were admitted with adrenal tumour out of which 13 had adrenocortical carcinoma. On five year follow up, six (46.2%) patients developed recurrence. MEAN disease free survival was 31.0 ± 23.92 (2-63) months 53.8% while MEAN overall survival was 46.69 ± 22.81 (14-80) months 92.3%. Results concluded that hormonally active tumour on clinical presentation, positive surgical resection margins, positive nodal status and poorly differentiated tumour on histopathology are the factors associated with tumour recurrence and patient's survival.

Keywords: Adrenocortical carcinoma, Mitotane, Radical surgery.

Introduction
Adrenocortical carcinoma is a rare tumour and has an incidence of 0.5-2 per million per year.1 Adrenocortical carcinoma can occur at any age but bimodal distribution is more frequent. The neoplasm is more common in childhood (1-6 years old) and in 4-5th decade of life.2 Women have a higher incidence of this disease as compared to men by about 2:1.3

Adrenocortical carcinoma is a very aggressive malignancy and overall prognosis is rather poor. Studies have reported that five-year survival for adrenocortical carcinoma is good for stage I disease (82%) and as stage increases, five-year survival reduces to 13% for stage IV disease. Complete surgical resection of the tumour has good chances of cure but even after complete surgical resection leaving no residual tumour behind, chances of recurrence is as high as 75-85%.4

As for all other malignancies management and treatment of adrenocortical carcinoma also requires a multidisciplinary team approach mainly including a medical oncologist, an endocrine surgeon and endocrinologist. Although few medical management options also exist for this malignancy but surgical resection remains the main treatment option and provides the only chance of disease cure if tumour is completely resected without leaving any residual tissue.6 The surgical strategy for adrenocortical carcinoma confined to the adrenal gland with regional lymph node metastasis or with invasion of local organs is complete tumour excision. Radical open surgery excising perirenal fat, regional lymph nodes and if necessary adjacent organs (spleen, tail of pancreas and kidney) is often required to achieve clear resection margins.7

Adrenocortical carcinoma is a rare disease and no data is available from our part of world regarding management and outcome of this disease. So a retrospective study was conducted which reported the presentation and management of thirteen patients with adrenocortical carcinoma referred to our institute. Objective of this was aimed at analyzing the clinical outcome and treatment results of patients with adrenocortical carcinoma and to point out the factors associated with recurrence and survival after complete surgical resection.

Case Series
A retrospective search for adrenocortical tumours was conducted on patients presenting with adrenocortical tumour in Shaukat Khanum Memorial Cancer Hospital, Lahore from January 2011 till December 2015. All data was retrieved from case notes of the selected patients. Patients who had adrenocortical carcinoma on final histopathology were included in the study while patients with a benign tumour were excluded. Patient age, gender, clinical presentation, tumour size, TNM staging as per CT scan findings, surgical procedure, pathological TNM staging, histopathological findings, adjuvant therapy, tumour recurrence and patient survival were
There were 6 men (46.2%) and 7 women (53.8%). Five (38.5%) patients had age less than 40 years while 8 (61.5%) patients were more than 40 years. The mean age was 35.62 ± 17.02 (4-75) years. Hormonally active tumour was diagnosed in 5 (38.5%) patients while all the remaining presented with vague symptoms or abdominal mass. At diagnosis, 5 (38.5%) patients had tumour size less than 10 centimeters and 8 (61.5%) patients had tumour size more than 10 centimeters. The mean tumour size on CT scan was 14.68 ± 7.32 (5.60-33.4) centimeters. On final histopathology of specimen, mean tumour size were 16.26 ±8.0 (5.00-36.0) centimeters and weight was 1281 ±1015.52 (60.0-3470) grams. Twelve patients (92.3%) had T2 and one patient (7.7%) had T3 tumour on CT scan. On histopathology 9 (69.2%) patients had T2 disease and 4 (30.7%) patients had T3 disease. Out of thirteen two (15.4%) patients had lymph node positive disease. Four (30.7%) patients had positive resection margins while 9 (69.2%) patients had negative resection margins on histopathology. Seven (53.8%) patients received adjuvant treatment with Mitotane while 6 (46.2%) patients underwent surgical resection alone. On five year follow up, 6 (46.2%) patients out of thirteen developed recurrence. The mean disease free survival was 31.0 ± 23.92 (2-63) months (53.8%) while mean overall survival was 46.69±22.81 (14-80) months 92.3%.
Results showed that patients with hormonally active disease on clinical presentation, positive resection margins and poorly differentiated tumour on histopathology developed recurrence as reported in Table-1. Also, the survival status of the patients depends on these parameters with positive nodal status having border line significance as reported in Table-2.

Discussion
Adrenocortical carcinoma, a highly lethal malignancy, has a poor overall survival and only few available treatment options. This study uncovered several factors that are responsible for poor prognosis of the tumour, disease recurrence, disease free survival and overall survival of patients presenting with adrenocortical carcinoma. These factors include hormonal disturbance on clinical presentation, positive resection margins and poorly differentiated tumour on histopathology whereas lymph node positive disease had border line significance. When these results were compared with previously published studies, comparable results were found.

Complete surgical resection with negative resection margins is the only curative treatment option available for adrenocortical carcinoma. Even if the tumour is locally advanced, resection of the involved adjacent organs enbloc with the tumour offers the best chances of cure. However, if resection margins turn out to be positive than recurrence is certain while disease free survival and overall survival is also poor. When we compare our results with other international studies overall survival and disease free survival in our patients was far better than other international studies and it is most likely due to the fact that we operate on patients with stage II and III disease. Almost half of our patients underwent surgical resection along with adjuvant treatment with mitotane and other half underwent surgical resection alone. Our results concluded no additional benefits of using adjuvant treatment over surgical resection alone.

Our study has certain limitations. It was a retrospective series with a small sample size. A prospective study with large sample size is recommended. It will help us to understand clinical behaviour and outcome of patients with adrenocortical carcinoma which will improve management and treatment options for this challenging malignancy.

Conclusion
Hormonally active tumour on clinical presentation, positive resection margins, positive nodal status and poorly differentiated tumour on histopathology are factors associated with recurrence, disease free survival and overall survival. Complete surgical resection of the tumour without any residual disease behind is the only definite treatment for adrenocortical carcinoma. So we recommend that adrenocortical carcinoma should always be considered for surgical resection even if tumor is locally advanced.

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Reference