A case series of chromophobe renal cell carcinoma treated in a urology unit of Sri Lanka

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Introduction

Renal cancer accounts for 5% of all cancers in men and 3% of all cancers in women (1). Worldwide, renal cancer is the 13th most common malignancy, with approximately 338 000 new cases diagnosed each year (2). Renal cell carcinoma (RCC) accounts for 90% of all renal malignancies (3). Chromophobe renal cell carcinoma (CHR RCC) constitutes 5-7% of all renal cell carcinomas (4). It is commonest in the sixth decade of life and has a slight male preponderance. Most CHR RCC are diagnosed as an incidental finding of routine ultrasound scans. Macroscopically they are tan to brown-coloured and the intensity of brown colour is proportionate to the concentration of eosinophilic cells (4). Microscopically tumour cells are arranged in solid sheets with vascular septa in between. The cells are large and pale with reticular cytoplasm and prominent cell membranes. The eosinophilic variant has smaller cells with fine oxyphilic granularity.

Perinuclear halos and positive Hale's colloidal iron staining are traditionally described characteristics of CHR RCC that helps in histological diagnosis. Recently described immunohistochemical features include positivity for KIT, parvalbumin and kidney-specific cadherin (5). Vimentin is generally negative in CHR RCC. It has a good prognosis with a five-year survival rate of 75-100% (4,5,6). Tumour stage, sarcomatoid change, necrosis and small vessel invasion determine the prognosis. CHR RCC cannot be graded using the ISUP grading system because of its innate nuclear atypia (4). There are no studies published on CHR RCC in Sri Lanka and this case series was aimed at describing the clinicopathological characteristics and outcome of CHR RCC managed in a single urology unit of a Teaching Hospital in Sri Lanka.

Methods

This was a prospective cohort study conducted at the Urology Unit of Colombo South Teaching Hospital (CSTH) where a comprehensive cancer registry and a data base is maintained. Adult (≥ 18 years) patients who had treatment for histologically confirmed chromophobe renal cell carcinoma over a period of eight years (1 January 2012 to 31 December 2019) were followed up after appropriate treatment. The data related to clinical characteristics, treatment modality, outcome and early and long term complications were recorded prospectively. The duration of the follow-up was calculated from date of diagnosis to the date of death or last follow-up. The primary end points of this study were overall survival and cancer specific survival.

All patients with renal tumours had a CECT KUB if serum creatinine was below 150 $\mu\text{mol/l}$ to characterise the lesion. Depending on the renal nephrometry score (7), age, existing comorbidities, advice of oncologists and patient's wish, decisions were taken to perform partial or radical nephrectomy. Histopathological evaluation was done according to the World Health Organisation (WHO) and International Society of Urological Pathology (ISUP) classification, 2016 (8,9). Tumour staging was done using the TNM classification of the Union for International Cancer Control 2009 (10). Approval for the study was obtained from the Ethics Review Committee of the Institute.

Results

During the study period, there were 285 patients with histologically confirmed renal cell carcinoma (Table 1). Out of them eight (2.8%) were chromophobe RCC. Four of them were men resulting in a male to female ratio of 1:1. Mean age of patients with CHR RCC was

56.4 years (range 43-65 years). Average size of the tumour at the time of diagnosis was 5.9 cm (range 2.5 cm-14.5 cm).

Table 1. Histological subtypes of renal cell carcinoma

Histological type	Number (%)
Clear cell renal cell carcinoma	230 (80.7)
Papillary renal cell carcinoma	44 (15.4)
Chromophobe renal cell carcinoma	8 (2.8)
Multilocular cystic clear cell renal neoplasm of low malignant potential	3 (1.1)
Total	285 (100%)

In one patient the renal lesion was first detected in 2015 and the size was 4.8 cm but nothing had been done. When he presented to us two years later, it had become 5.5 cm and we were able to convince him to undergo surgery. Approximate growth rate is 4mm per year when this case is considered. Tumour was involving the left kidney in five patients. In another patient, renal lesion was detected after a routine ultrasound scan before coronary stenting (PCI) for non-STEMI. As the patient was high risk for renal surgery, she had undergone a core needle biopsy in another unit. It was reported as a clear cell RCC. When we performed the partial nephrectomy, it turned out to be a CHR RCC.

Two patients had renal vein involvement (25%) and one of them was extending to the IVC. Open surgery was performed in all eight patients. Radical nephrectomy was performed in four patients while the other four patients had partial nephrectomy. In five patients, tumour stage was T1. Rest of the patients had T3 disease where two of them had renal vein involvement and one had peri-renal fat involvement. None of the patients had metastases at the time of diagnosis. One patient had eosinophilic variant of the CHR RCC and another had two separate tumours in the same kidney confirming multifocality.

In our series, the mean follow-up period was 27 months (range 6-90 months). There were no deaths during the follow-up. No patients developed local recurrences or metastases during the follow-up period. Therefore, the overall five-year survival rate was 100%.

Discussion

According to the data published by National Cancer Control Programme of Sri Lanka, 187 cases of RCC have been reported in 2014 (11). But the cancer registry does not give any details regarding the different histological types of RCC. Hence even the number of cases of CHR RCC diagnosed in Sri Lanka is not known. There are only a handful of publications related to renal cancer in Sri Lanka and none on CHR RCC (12,13,14). This is the first publication on CHR RCC in Sri Lanka. The proportion of CHR RCC in the Urology Unit of Colombo South Teaching Hospital is 2.8% while the worldwide reported rate is 5-7% (4). Our rate is closer the rate of CHR RCC in Japan 2.8% (15). In Scandinavian countries it is around 5% (16). In neighbouring India, the rate of CHR RCC is about 6.4% of all renal cancer (17).

CHR RCC are generally asymptomatic; hence the tumours are large at presentation around 7 cm. In this series the average size of the tumours was 5.9 cm. This enabled us to do partial nephrectomy in half of our patients. Average age of our patients was (56.4 years) lower than the usually described average age of 60 years (4,5,6). This may be due to the age structure of the populations in the developed world where there is a higher proportion of elderly. Renal vein involvement in renal cell carcinoma is about 15% (18). The rate of renal vein involvement is 25% in this series but the number is too small to make any valid comparison. However even the publications involving large number of CHR RCC do not report details of renal vein involvement and true frequency is not yet established (5).

Sarcomatoid changes are seen only in 2-8% of CHR RCC which is much less than in clear cell RCC (4,5). It is a poor prognostic factor in CHR RCC, similar to other histological types of RCC (5,6). In our series we did not encounter any patients with sarcomatoid change though we had two patients with T3 stage which is another known poor prognostic factor (tumour size more than 7 cm). Microvascular invasion and microscopic necrosis are also known to be associated with poor prognosis in CHR RCC (5). Luckily the patients who had large tumours and also those with renal vein invasion in our study are still alive though the median follow-up time is only 28 months. The previously described Fuhrman grading system or the recent ISUP grading system do not reflect the aggressiveness of the CHR RCC and cannot be used for purposes of prognostication (4,5,19). The modified cellular grading systems described specifically for CHR RCC also have been found to be less reliable and are

not used by most pathologists (5,19). We had one patient with eosinophilic variant of CHR RCC but even that has no difference in prognosis compared to the classic variety.

Multifocality in CHR RCC is seen in about 3% cases and we had one patient out of the eight displaying multifocality (5,6). Bilateral tumours are even rarer and not seen in our series. About 2% of patients with CHR RCC has metastases at the time of diagnosis and another 2% develop metastases during the next five years after surgery indicating excellent prognosis after surgery (5). None of our patients had metastatic disease at presentation or during the follow-up, and none had local recurrences.

The small number of patients is the major limitation of this study. However, considering its rarity and the availability of follow-up data for several years the findings of this study would be of relevance to practising urological surgeons in planning treatment and in prognostication. Furthermore, it is the duty of the surgeons to record, audit and publish the outcome of their patients and it was in 1911, Ernest Amory Codman a founder member of American College of Surgeons and a pioneer in quality and safety of surgery said that those surgeons who do not do so are full of humbug and self-deception (20).

In conclusion, CHR RCC is a rare subtype of RCC and has a very good prognosis. Despite being large size at presentation nephron sparing surgery is possible in many. Compared to other subtypes of RCC, CHR RCC shows a good prognosis irrespective of advanced tumour stage.

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