

Bellini Duct Carcinoma: Series of Two Clinical Cases

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Abstract

Bellini Duct Carcinoma is a rare and aggressive type of Renal Cancer which shares histological and clinical features with Transitional cell carcinomas. We present the two single cases recorded in our hospital with a medical literature review. Although there are no exact guidelines to treat this disease, when is disseminated we normally used chemotherapy schemes based on platinum salt like in Urothelial cancer. The targeted therapy should be considered for the treatment of metastatic collecting duct carcinoma but a prospective evaluation is necessary in multicenter clinical trials.

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Introduction

Bellini Duct Carcinoma is known as a rare variant of renal cancer originating from the Collecting tubules, unlike all other renal tumors which originate from the proximal tubules.

The first series of collecting duct epithelial tumors was discussed by Manzilla-Jimenez in 1976 [1], Although Mason [2] had previously described this different type of renal tumor in 1955. Fleming and Lewi [3] defined the diagnostic criterion and established it as a different diagnostic entity originating from the renal medulla.

These sorts of tumors present an early dissemination and fatal clinical course in addition to histological characteristics similar to Urothelial tumoral types.

Chemotherapy schemes similar to those used for Urothelial tumors being employed, we present two cases of this disease arising at our Hospital for reviewing the currently-existing literature concerning this disease.

Case Series

We searched the database of Anatomico-Pathological Service and founded two cases of Bellini Duct Carcinoma which were reviewed.

Case Number 1

A 54 years old male patient with medical history of smoking and Ischemic heart disease underwent a Nephrectomy as a result of

a renal mass, being diagnosed with Bellini Duct Carcinoma. Two years later, he presents lung, bone and lymph node metastasis and a lung FNAB (fine-needle biopsy aspiratory) being performed, confirming the recurrence.

The patient started chemotherapy treatment as per Carboplatin (AUC 3) - Gemcitabine (1000 mg/m²) scheme because of moderate renal failure secondary to previous Nephrectomy. Two cycles were administered but he underwent a quick thoracic spread which required hospitalization due to uncontrolled pain.

The patient received a new chemotherapy scheme with Docetaxel 75 mg/m², undergoing exclusively one cycle. Thereafter he showed a suddenly deterioration of his overall condition and death occurred three months following the relapse due to respiratory complications and two years after the diagnostic of renal cancer.

Case Number 2

A 49 years old male with no prior medical history except of Grade 1 Obesity who came to the Emergency department due to symptoms of breathlessness and fever

Hypoxemic respiratory failure and a chest Rx (**Figure 1**) compatible with Bilateral pneumonia being objectified, as a result of which he was admitted to Internal Medicine with empiric antibiotic coverage for severe Community-Acquired Pneumonia and oxygen therapy.

The patient did not progress satisfactorily, the hypoxemia continuing and showing no Improvement in the chest X-ray as a result of which the decision was made to run a CT TAP (Thoracic-abdominal-pelvic scan) (**Figures 2-4**), showing lesion compatible with right kidney Tumor infiltrating renal parenchyma with retroperitoneal, preaortic and retrocaval metastatic lymph nodes compressing and infiltrating the inferior cava with thrombosis of right renal vein.

Also showing lung metastasis with wedge-shaped airspace consolidations and peripheral distribution in relation to pulmonary infarcts

A right renal mass Macro biopsy was performed, showing a histological diagnostic compatible with Collecting duct Carcinoma (**Figure 5**).

The patient was placed under care in Oncology with diagnosis of Stage IV Renal Carcinoma -Variant Bellini Duct Carcinoma. The physical examination revealing the presence of hypoxemia and palpation of a painless renal mass at the level of the right flank. Analytically, renal insufficiency of a pre-renal profile was highlighted. Medical treatment was adjusted and anticoagulation was begun.

We offered a palliative Chemotherapy –based treatment with Carboplatin (AUC 5) – Gemcitabine (1000 mg/m²) days 1, 8, 15, undergoing a total of 3 cycles with subsequent improvement of renal function and minor response as per RECIST criteria (response evaluation criteria in solid tumors) in thoracic scan reevaluation, as a result of which changed over to Cisplatin (75 mg/m²) – Gemcitabine (1200 mg/m²) days 1 and 8, having completed a further two cycles of treatment.

The patient's overall condition worsened with asthenia and pain, a CAT scan having revealed pulmonary and lymph node progression, as a result of which scheme was changed to Paclitaxel 80 mg/m² weekly, having completed a total of 6 cycles.



Figure 1 Hypoxemic respiratory failure and a chest Rx.

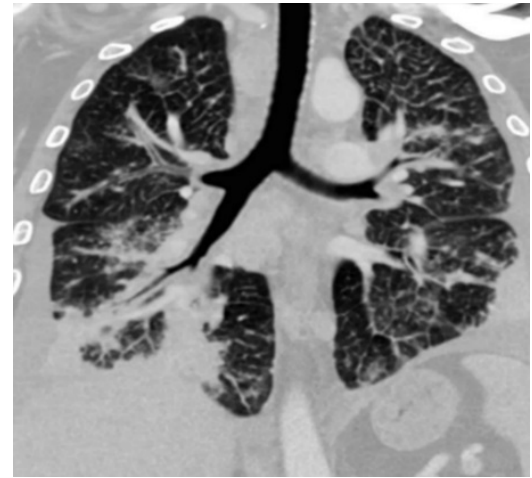


Figure 2 Thoracic-abdominal-pelvic scan.



Figure 3 Axial view: Hypo dense central mass of ill-defined edges. Presents a pattern of infiltrative growth with pyelocalyceal, medullar and cortical affection. Delayed nephrogram. As this is a tumor of the Bellini ducts and they are located in the renal medulla, the origin of the tumor is the medulla. When the tumor is small, the medullar epicenter of the lesion is evident.

The patient went to a Private Hospital for a second opinion where a supraclavicular Adenopathy FNAB ((fine-needle biopsy aspiratory) was performed for conducting a 50-gene sequencing panel study in search of a possible response to biological therapies. No genetic alterations were found which would predict a specific response to any drug, but due to the presence of some polymorphisms in c-kit (tyrosine kinasa receptor) and KDR (kinase insert domain receptor); it was suggested to assess treatment with Sorafenib, Pazopanib and Sunitinib.

The patient's condition worsened at 7 months of the diagnosis starting Palliative Care control with an optimal symptom management but he died a month later.

Discussion

The most frequent histological type of renal Carcinoma is Clear-

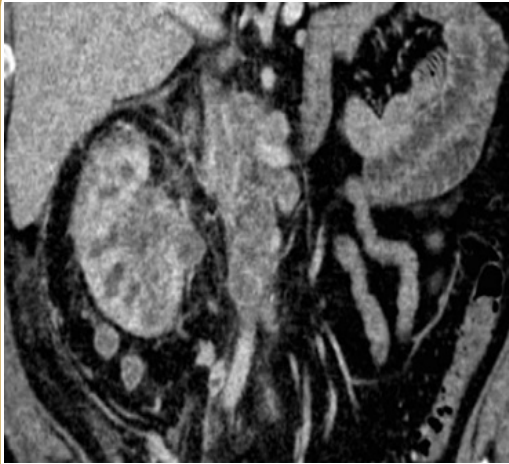


Figure 4 Adenopathic conglomerate in theoretical site of inferior vena cava. The inferior vena cava is not identified. Preaortic, retrocaval and interaortocaval adenopathies compressing stenosing and probably infiltrating inferior vena cava, right renal vein thrombosis and entrapment.

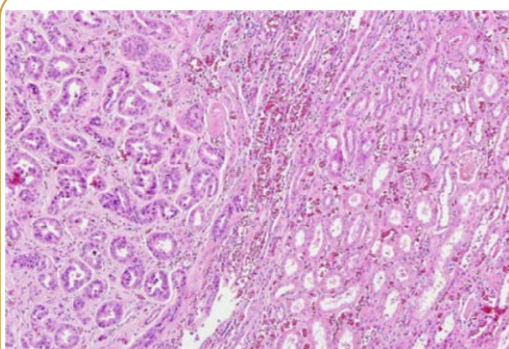


Figure 5 Fragment of renal medulla with groups of cells with eosinophilic cytoplasm and large nuclei with prominent nucleoli suggestive of renal cell Carcinoma with immunohistochemical positive for CK34 (Cytokeratin 34), CK7 (Cytokeratin 7) and Vimentin.

cell, comprising 75% of all renal Carcinomas. Bellini Duct Carcinoma is a rare subtype of renal Carcinoma (<1%) with a poor prognosis. This tumor shares morphological and cytogenetic characteristics with urothelial cancers.

From the immunohistochemical standpoint, they are positive for Vimentin, E-cadherin and Cytokeratins. [4,5]

The amplification of HER2 gen (human epidermic grow factor 2) has been reported in a large number of cases in these tumors, being associated with a poorer prognosis.

Some 270 cases have been reported in the literature to date. More predominant in younger and male patients than any other renal tumors and are characterized by early dissemination and aggressive course.

The most frequent metastatic sites are the lymph nodes, lungs, bone with blastic lesions more frequent than lithic lesions and the liver.

The clinical presentation most commonly involves abdominal pain, mass at level of flanks as well as hematuria.

There are currently no clinical guides setting out a definite treatment for this disease. Nephrectomy is not recommended in patients with ganglionic affection or distant metastasis with an expected survival less than a year given the major perioperative risk involved [6].

Unlike other types of non-clear-cell renal cell carcinoma, it seems to respond better to cytotoxic chemotherapy. Due to its similarities with Urothelial carcinomas, active chemotherapy regimens of choice in urothelial carcinomas are used to treat this sort of renal cancer.

There are found some responses rates to the conventional MVAC scheme (methotrexate, Vinblastine, Doxorubicin and Cisplatin) [7].

A French multicenter prospective Phase II study including 23 patients with metastatic disease and concludes that the standard first-line chemotherapy regimen must be platinum-based on achieving a tumor response in six patients with an average overall ten-month survival rate with a combination of Gemcitabine and Cisplatin or Carboplatin if renal insufficiency was involved [8,9].

After conducting a review of the literature, the McMaster University group recommends this scheme as standard due to the results achieved [10].

Adding Bevacizumab to the platinum-based combination followed by maintenance Bevacizumab increased progress-free survival and overall survival in a small cohort of five patients, and in this study one clinical case of complete remission of pulmonary metastasis it was found [11,12].

The French Collaborative Group is planning to conduct a multicenter phase II study for evaluating the efficacy of this triple combination.

The efficacy of the target treatments in renal Cancer has not been evaluated in these tumors in clinical trials, although isolated cases with modest response to both Tyrosine kinase inhibitors and m-TOR kinase inhibitors have been reported [8,13,14]. Targeted therapy should be considered for the treatment of metastatic collecting duct carcinoma and its prospective evaluation is encouraged.

As in our second patient, genetic sequencing being done in search of alterations which we can use as pharmacological targets could be evaluated.

We believe the cases presented to be of interest as a result of it being helpful to report cases based on one's own experiences to improve the management of infrequent diseases.

In the first of these two cases, the survival was longer as a result of a non-metastatic disease, which is less common in this entity and being able to perform a nephrectomy. With the recurrence, the patient worsened quite rapidly without it having been possible to administer hardly any cytotoxic treatments at all.

As regards the second case, the metastatic presentation was treated by way of a platinum-based scheme, it not having been possible - given the past history of embolism - to use Bevacizumab, which has been shown to have benefits in small series of cases in the literature. The patient's survival was as

anticipated, having maintained good quality of life during the chemotherapy treatment.

Conclusion

Collecting duct carcinoma is a rare and aggressive sort of renal cancer that shares some characteristics with urothelial cancers.

By now the treatment for of early stage disease is nephrectomy but for metastatic disease is necessary chemotherapy treatment schemes like urothelial cancers based on platinum salt. Targeted therapy has been shown to be effective and could be a promise for the treatment of these patients but new clinical trials are necessary to confirm this data.

References

- 1 Mancilla-Jimenez R, Stanley RJ (1976) Papillary renal cell carcinoma. A clinical, radiologic and Pathologic study of 34 cases. *Cancer* 38: 2469-2480.
- 2 Mason P (1955) In: Kobernick S (translator) *Tumeurs humaines: human tumors, histology, diagnosis and technique*. (2ndedn) Detroit: Wayne State University Press.
- 3 Fleming S, LewiHJ (1986) Collecting duct carcinoma of the kidney. *Histopathology* 10: 1131-1141
- 4 Natsume O, Ozono S (1997) Bellini duct carcinoma: a case report. *JPN J Clin Oncol* 27: 107-110.
- 5 Kafé H, Verbavatz JM, Cochand-Priollet B (2004) Collecting duct carcinoma: an entity to be redefined? *Virchow's Arch* 445: 637-640.
- 6 Méjean A, Roupret M, Larousserie F (2003) Is there a place for radical nephrectomy in the presence of metastatic collecting duct (Bellini) carcinoma? *J Urol* 169: 1287-1290.
- 7 Matthew I, Millosky, Alyssa R (2002) Active Chemotherapy for Collecting Duct Carcinoma of the Kidney: A case report and Review of the Literature. *Cancer* 94: 1.
- 8 Rui-ning Zhao, Li-hong Nie, Rui gong (2013) Active targeted therapy for metastatic collecting duct carcinoma of the kidney: a case report and review of the literature. In *Urol Nephrol* 45: 1017-1021.
- 9 Oudard S, Banu E (2007) Prospective multicenter phase II study of gemcitabina plus platinum salt for metastatic collecting duct carcinoma: results of GETUG (Groupe d'Etudes des Tumeurs Urogenitales)study. *JUrol* 177: 1698-1702
- 10 Dason S, Allard C, Sheridan-Jonah A (2013) Management of renal collecting duct carcinoma: a systematic review and the Mc Master experience. *Curr Oncol* 20: e223-232
- 11 Barrascout E, Beuselinck B, Ayllon J (2012) Complete remission of pulmonary metastases of Bellini duct carcinoma with cisplatin, gemcitabine and bevacizumab. *Am J Case Rep* 13: 1-2.
- 12 Pécuchet N, Bigot F, Gachet J (2013) Triple combination of bevacizumab, gemcitabina and platinum salt in metastatic collecting duct carcinoma. *Annals of Oncology* 24: 2963-2967.
- 13 Ansari J, Fatima A (2009) Sorafenib induces therapeutic response in a patient with metastatic collecting duct carcinoma of kidney. *Onkologie* 32: 44-46
- 14 Zhao R, Li-hong Nie (2013) Active targeted therapy for metastatic collectin duct carcinoma of the kidney: a case report and review of the literature. *Int urol Nephrol* 45:1017-1021.