Case report

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Osseous metaplasia in a case of papillary renal cell carcinoma

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Introduction

Osseous metaplasia (OM) is a rare phenomenon seen with certain malignancies and inflammatory conditions, which is different from amorphous calcification. The identification of mature matrix and cellular components of bone in the background of another condition such as malignancy defines OM. A significant proportion of renal cell carcinomas (RCC) (10.3%) has calcific foci within the tumour (1). However, the frequency of OM in RCC is yet to be determined. Out of the histological subtypes of RCC, Clear cell (ccRCC) and Chromophobe (chRCC) types are better known for OM while only five cases of papillary RCC (pRCC) have been reported in the English language literature. Here we report a case of pRCC with distinct OM amidst significant sarcomatoid differentiation (30%), which is an extremely rare combination, reported only once before (2).

Case report

A 42 years old female with haematuria was found to have a mass lesion in the left kidney. She was diagnosed with carcinoma of the breast two years ago, which was managed with right mastectomy, radiotherapy and chemotherapy. She was a mother of two children and was a non-smoker. Apart from the evidence of right mastectomy and irradiation of the chest wall her physical examination was unremarkable.

A computerized tomographic urogram (CTU) demonstrated a heterogeneously enhancing mass lesion in the left renal hilum measuring 2.4 cm × 2.8 cm with a radiopaque area in the north-eastern corner of the tumour close to the capsule, suggestive of calcification (Figure 1). The nephrometric (RENAL) score of the tumour was 10. Her right kidney was contracted measuring 9.6 cm. Her pre-operative serum creatinine was 96 µmol/L. Left open partial nephrectomy was done.

Figure 1. CT images of the tumour (A) – a coronal section showing the central location of the tumour and encapsulation. The right kidney is contracted. (B) – a sagittal section of the tumour showing the suspected area of osseous metaplasia (arrow).

Macroscopically the tumour was well encapsulated and the area to be recognized as OM later was identifiable macroscopically (Figure 2). Microscopically the tumour composed of complex papillary structures lined by polygonal cells with abundant eosinophilic cytoplasm and stratified large vesicular nuclei containing prominent nucleoli (Figure 3A). Foamy macrophages were seen within the papillae. There was well-formed bone matrix with marrow elements comprising of nucleated red blood cells and megakaryocytes (Figure 3B). In addition, there

were tumour giant cells and haemosiderin-laden macrophages. About 30% of the tumour was showing sarcomatoid morphology (Figure 3C). A final diagnosis of papillary type 2 renal cell carcinoma (pT_{1a}) with significant sarcomatoid differentiation and osseous metaplasia was made (ISUP grade IV). She had no evidence of metastatic disease in the lungs or bone on CT evaluation. She was followed up by the oncologist and had no evidence of disease progression after 6 months.

Figure 2. Macroscopy of the tumour (A) – The outer surface of tumour showing the undisturbed capsule after partial nephrectomy (B) – Cut sections showing a well encapsulated, yellow to brown colour, firm tumour with few cystic areas (white arrow). The area of osseous metaplasia which was confirmed microscopically can be identified in the north-eastern corner of the tumour (black arrow).

Figure 3. Microscopic examination of the tumour (A) – Papillae lined by polygonal cells with abundant eosinophilic cytoplasm, stratified, large vesicular nuclei, prominent nucleoli consistent with type 2 pRCC (H&E, 400x). (B) – Foci of osseous metaplasia (arrows) (H&E, 100x). (C) – An area of sarcomatoid differentiation (H&E, 400x).

Discussion

The identification of histological variants and combinations of pathological subtypes are common with RCC. On many occasions, the identification of these variant pathologies like sarcomatoid differentiation indicate poor prognosis. OM is a rare phenomenon found to be coexisting with many histological subtypes and variants. Yet, the clinical relevance of finding OM in RCC is not properly understood, as the outcome of RCCs bearing OM was not found to be different from that of the primary histological subtype. In fact, OM is sometimes considered a marker of good prognosis because the majority of cases of OM were found in early stage RCCs without local invasion or dissemination similar to the index case (3).

Out of the main histological types of RCC, ccRCC and chRCC are the two types commonly associated with OM. In a review by Maioli et al in 2017, 11 cases of ccRCC and 4 cases of chRCC were found to have OM. In the same review, only two cases of pRCC were found to have OM (4). Since then three new cases of pRCC with OM have been reported (2, 5, 6), making the total number of cases six, after the addition of the case of this report. Therefore, OM in pRCC is extremely rare. In addition, chondroid differentiation (6) and bone marrow differentiation are two recognized associates of OM in cases of RCC (7, 8).

Many cellular and molecular mechanisms are identified which can be responsible for the process of post-traumatic heterotopic OM (9, 10). However, a little is known about the pathophysiology of intra-tumoral OM. Some authors have suggested OM in malignant tumours to be a process secondary to ischaemia, haemorrhage, necrosis and fibrosis all of which creates a hostile tissue environment. The index case received systemic chemotherapy for breast carcinoma before. A possible explanation to this occurrence could be the tumour necrosis and subsequent ossification due to the effect of chemo-therapeutic agents at a sub-clinical stage of the disease. This observation also strengthens the hypothesis of requiring a hostile tissue environment for the development of OM.

Conclusion

Osseous metaplasia can co-exist with all three main histological types of RCC. The clinical implications of OM in a RCC of any histological subtype is unclear as only a limited number of cases are reported.

References

1. Daniel WW Jr, Hartman GW, Written DM, Farrow GM, Kelalis PP. Calcified renal masses: A review of ten year experience at the Mayo clinic. *Radiology* 1972; 103: 503-8.
2. Zhang H, Majeed NK, Sharifi R, Guzman G. A Case of Sarcomatoid Renal Cell Carcinoma with Osseous Metaplasia and Papillary Renal Cell Carcinoma Metastasis. *Clin Pathol*. 2019; 12: 2632010X19848005. Published 2019 May 13. doi:10.1177/2632010X19848005
3. Sostre G, Johnson JF 3rd, Cho M. Ossifying renal cell carcinoma. *Pediatr Radiol* 1998; 28: 458-60.
4. Maioli H, Sharma M, Crane GM, Wu G, Miyamoto H. Renal cell carcinoma with osseous metaplasia: A case report and literature review. *Integr Cancer Sci Therap* 2017; 4: 1-4.
5. Sharma N, Kothari V, Meh V. Papillary Renal Cell Carcinoma with Extensive Osseous Metaplasia: A Case Report. *Annals of Pathology and Laboratory Medicine*, Vol. 5, Issue 10, October, 2018.
6. Ahmed A. Chondroid and osseous metaplasia in an incidental type II papillary renal cell carcinoma with extensive solid areas: an unraveled molecular character. *Pan Afr Med J*. 2018; 31: 26. Published 2018 Sep 13. doi:10.11604/pamj.2018.31.26.16137
7. Cribbs RK, Ishaq M, Arnold M, O'Brien J, Lamb J, Frankel WL. Renal cell carcinoma with massive osseous metaplasia and bone marrow elements. *Ann Diagn Pathol*. 1999; 3(5): 294-99. doi:10.1016/s1092-9134(99)80025-2
8. Ozkanli S, Yildirim A, Zemheri E, Keskin SK, Basok EK. Osseous metaplasia and bone marrow elements in a case of renal cell carcinoma. *Case Rep Urol*. 2012; 2012: 649257. doi:10.1155/2012/649257
9. Shi ST, de Gorter DJJ, Hoogaars WMH, 't Hoen PAC, ten Dijke P. Overactive bone morphogenetic protein signaling in heterotopic ossification and Duchenne muscular dystrophy. *Cell Mol Life Sci* 2013; 70: 407-23.
10. Ramirez DM, Ramirez MR, Reginato AM, Medici D (2014) Molecular and cellular mechanisms of heterotopic ossification. *Histol Histopathol* 29: 1281-5.