

CASE REPORTS

Open Access



Concomitant clear cell renal cell carcinoma with osseous metaplasia and papillary thyroid microcarcinoma: a case report with literature review

Saman S. Fakhraddin^{1,2}, Deedar K. Qader^{2,3}, Abdulwahid M. Salih^{1,2}, Ari M. Abdullah^{2,3}, Hiwa O. Baba^{2,4}, Soran H. Tahir^{1,2}, Aras J. Qaradakh^{2,5}, Dilan S. Hiwa¹ and Fahmi H. Kakamad^{1,2,4*}

Abstract

Backgrounds Although calcifications have been observed in various renal masses, osseous metaplasia has very rarely been reported. Here, we present a case of concomitant clear cell renal cell carcinoma with osseous metaplasia and papillary thyroid microcarcinoma.

Case presentation A 52-year-old male was being investigated for having post-prandial gaseous abdominal distention. Computed tomography of the abdomen showed a heterogeneous mass lesion measuring 27 × 24 mm at the upper/mid pole of the right kidney. It also revealed two small (10 and 11 mm) benign bone islands in the body of the D4 and L4 vertebrae. The patient underwent a metastatic workup by computed tomography, which revealed a 93 × 35 mm mass in the left thyroid lobe with coarse calcification. A partial nephrectomy was planned for the renal mass, but the site of the mass deemed this impossible. Six months after the operation, the patient underwent total thyroidectomy. Histopathology of both tissue samples revealed concomitant clear cell renal cell carcinoma with heterotopic bone formation and papillary thyroid microcarcinoma.

Conclusion Although rare, osseous metaplasia in renal cell carcinoma can occur and may indicate an early-stage carcinoma with a favorable prognosis.

Keywords Renal cell carcinoma, Heterotopic bone formation, Osseous metaplasia, Papillary thyroid microcancer, Bone islands

1 Backgrounds

Renal cell carcinoma (RCC) is considered one of the most common cancers in the world, constituting 4% of new cancer incidences [1]. It is the 7th most frequently diagnosed carcinoma among western nations [2]. Based on the cellular origin, cancers arising from the kidneys are mainly RCCs that arise from the renal cortex, transitional cell carcinoma originating from the mucosal surfaces of the renal collecting tubules, calyces, and pelvis, or oncocytomas, collecting duct tumors, and renal sarcomas from other parenchymal epithelia [3]. Heterotopic bone formation (osseous metaplasia) is an uncommon clinical

*Correspondence:

Fahmi H. Kakamad
fahmi.hussein@univsul.edu.iq

¹ College of Medicine, University of Sulaimani, Madam Mitterrand Street, Doctors City, Building 11, Apartment 50, Sulaimani, Kurdistan 46000, Iraq

² Smart Health Tower, Madam Mitterrand Street, Sulaimani, Kurdistan, Iraq

³ Sulaimani Teaching Hospital, Sulaimani, Kurdistan, Iraq

⁴ Kscien Organization, Hamdi Str, Azadi Mall, Sulaimani, Kurdistan, Iraq

⁵ Shorsh Teaching Hospital, Sulaimani, Kurdistan, Iraq

entity; it is the presence of mature and immature bone in tissues where bone is not normally found [2]. It has been seen in endometrial lesions and various benign and malignant tumors ranging from spinal meningiomas to ductal carcinomas of the breast and different polyps [4–6]. Although calcifications have been observed in various renal masses, osseous metaplasia has very rarely been reported in the literature [7].

Here, we present a case with an incidental finding of concomitant clear cell RCC (ccRCC) with osseous metaplasia and papillary thyroid microcarcinoma.

2 Case presentation

2.1 Patient information

A 52-year-old male was being investigated for having post-prandial gaseous abdominal distention. His condition was not associated with difficult urination, dysuria, hematuria, frequent urination, or weight loss. He did not have any chronic medical ailments. He had undergone an open appendectomy three years before. The patient did not have a positive family history of renal masses. He had no history of smoking, alcohol intake, or recreational drug abuse.

2.2 Clinical findings

Upon examination, he was an overweight male with a BMI of 29.6 kg/m². Apart from a grid-iron incision for his appendectomy, the abdominal examination was normal.

2.3 Clinical diagnostic approach

The patient was found to have a right renal mass on abdominal ultrasound and was referred to our urology department. Computed tomography (CT) of the abdomen showed a heterogeneous mass lesion measuring 27 × 24 mm at the upper/mid pole of the right kidney, anteromedially near the renal pelvis and adjacent to the renal vessels, but with no invasion to these vessels, calyces, or into inferior vena cava (Fig. 1). The examined sections on the CT scan also revealed two small (10 and 11 mm) benign bone islands in the body of the D4 and L4 vertebrae. He was normal upon general urine examination and renal function test.

The patient underwent a metastatic workup, including a chest CT, which was normal. The CT scan of the thyroid gland revealed a 93 × 35 mm mass in the left lobe with coarse calcification. Due to the obesity of patient and the lack of complications, the neck mass was not observed during his initial visit. Thyroid stimulating hormone level appeared normal, but T3 level was low (0.987 nmol/L). Parathyroid hormone was also checked and turned out to be high (115 pg/ml) but with a normal serum calcium level. He then underwent FNA aspiration

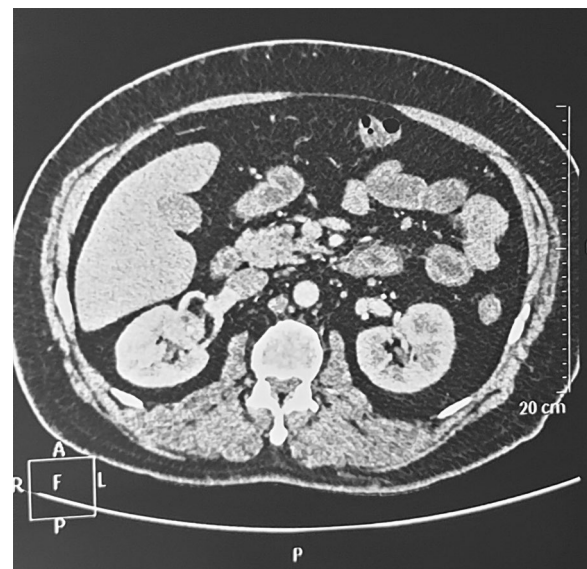


Fig. 1 Axial section of abdominal CT scan showing a heterogeneous mass at the upper/mid pole adjacent to the hilar vessels

for his thyroid mass which showed a benign follicular nodule (Bethesda II).

2.4 Therapeutic intervention

The patient was prepared for an open partial/simple nephrectomy. During the operation, the mass was noticed to be very close to the renal pedicle and was surrounded by two segmental arteries branching from the main renal artery. (We then decided to perform a simple nephrectomy). We bisected the kidney in the operation room to see a macroscopically round, well-encapsulated, brown-colored mass with small, yellow-colored, relatively more friable areas. The mass had a rubberier and harder feeling than the rest of the kidney and had an area of fat surrounding it (Fig. 2). The right kidney with the upper ureter was sent for histopathological examination.

On sectioning, a 2.1 cm well-defined, heterogeneous, firm, lobulated, brown, and hemorrhagic nodule was identified within the hilar fat away from the hilar resection margin by 0.5 cm. The examined sections revealed ccRCC with WHO/ISUP grade II and FUHRMAN grade II, which had focal areas of necrosis. On a higher power magnification, it showed mature lamellated bone trabeculae with osteoblastic rimming and non-hematopoietic bone marrow composed of mature adipocytes (Figs. 3 and 4).

2.5 Follow-up and outcome

The postoperative period was uneventful, and the patient got discharged on the second postoperative day. The patient was put on periodic surveillance. After six

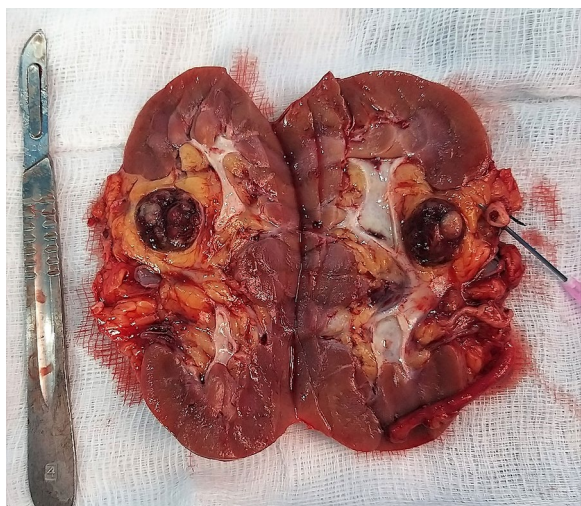


Fig. 2 A photograph of the bisected kidney showing the brown, hemorrhagic nodule surrounded by a layer of fat

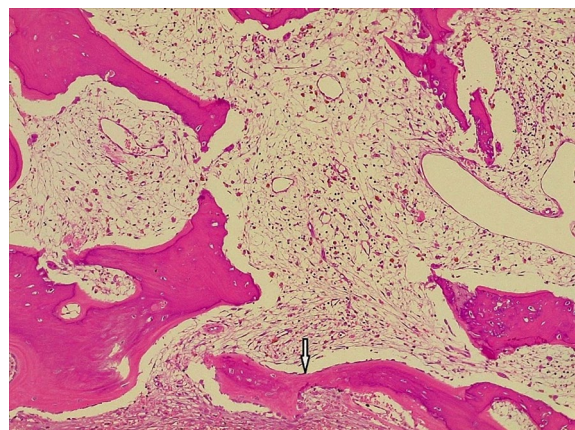


Fig. 4 Higher power magnification shows mature lamellated bone trabeculae with osteoblastic rimming (white arrow) with the non-hematopoietic bone marrow that is composed of mature adipocytes



Fig. 3 Microscopic examination of H and E, stained sections showed compact nests of cells with clear cytoplasm and distinct cell borders (dark arrow) with foci of mature bony trabeculae (yellow arrow) and a non-hematopoietic bone marrow (dark star)

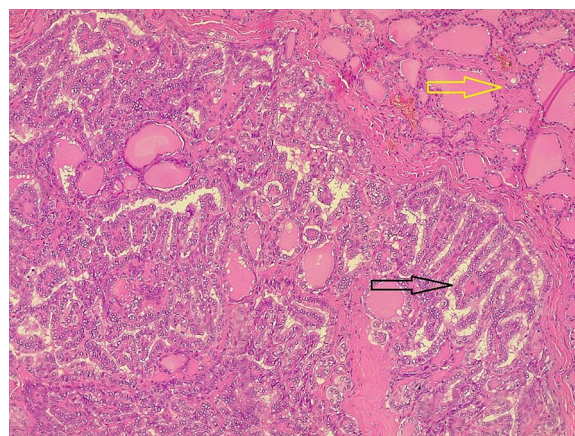


Fig. 5 Section shows benign thyroid tissue (yellow arrow) containing a cellular nodule with papillary structures (black arrow) with nuclear features of papillary thyroid carcinoma like clearing and overlapping

months (although still biochemically euthyroid), he was having bouts of palpitation, heat intolerance, and constipation. There was a multinodular enlargement of the thyroid gland, with no stridor or difficulty in swallowing. After a multidisciplinary team meeting, the decision was made to do total thyroidectomy for the patient. The histopathological examination revealed a small (0.5 cm) papillary microcarcinoma of the thyroid gland (conventional type) (Fig. 5). Until the submission of this paper, one year after his nephrectomy and six months after his total thyroidectomy, the patient is on regular follow-up and is generally in good condition.

3 Discussion

Renal Cell Carcinoma has a multitude of subtypes, but the most common subtype is ccRCC, which accounts for (70–80%) of all RCCs and arises from the proximal tubule of the nephron [8]. Osseous metaplasia in RCC is a very rare incident. To our knowledge, only about 30 cases have been reported in the English literature, of which less than half have been documented in the clear cell subtype. This is the first case of osseous metaplasia in ccRCC to be reported to have a concomitant papillary microcarcinoma of the thyroid gland and multiple small bone islands.

With no regard to the tumor or polyp site it develops in, the mechanism of osseous metaplasia development

is a topic of significant debate, and no clear pathophysiology has been pointed out yet [2]. Some earlier reports have hypothesized a causal relationship between hypovascularity in some renal tumors and the higher probability of heterotopic bone formation in them, such as a causal relation between ischemic degeneration and calcification [7, 8]. A heterotopic bone formation may also occur due to inflammation or necrosis in the tumor or surrounding tissues [9]. And more recent reports have shown a possible correlation between osseous metaplasia and Bone Morphogenetic Protein 2 (BMP2), which is a member of the TGFB superfamily and plays an integral role in the formation of new bone. The mechanism is that BMP2 is secreted by the tumor cells, which in turn affects the pluripotential stem cells and transforms them into osteoblast cells [10, 11]. There is an additional explanation for osseous metaplasia; it has been reported that a hormone called parathyroid hormone-related peptide may also contribute to heterotopic bone formation [2, 12].

Bone islands or enostosis have been historically considered benign lesions that can be seen anywhere in the skeleton. They are thought to be congenital or result from failed resorption during endochondral ossification [13].

Renal cell carcinoma usually affects adults aged between 55 and 60 years old, with more male predominance [2]. Besides the male sex, its risk factors can also include obesity, smoking, and hypertension [14]. On the other hand, thyroid cancer is a more female-oriented condition, and its risk factors can include exposure to radiation, reduced iodine intake, and family history [15]. The kidneys and the thyroid gland are two deeply inter-related organs, with dysfunctions in one of them significantly impacting the other [16]. A systematic review in 2022 by Bellini et al. that included 18 studies and 776 patients investigated the bidirectional relationship between these two cancers, with only 6 patients being associated with synchronous occurrence. They identified family history and obesity as common shared risk factors, and genetic susceptibility as a strong contributor to both cancers. They found that after a thyroid cancer, men were more likely to develop renal cancer [17]. According to a study by Van Fossen et al., female patients with thyroid cancer were nearly two times more likely to develop a subsequent renal carcinoma, and the risk was 4.5-folds in men. On the other hand, female patients with renal cancer were 1.5 times more likely to develop a subsequent thyroid cancer, and the risk was 4.5-folds in men [18]. Hence, the male sex is seen as a risk factor for the association of these cancers. Even though exposure to radiation is a well-known risk factor for cancer development in general and particularly for thyroid cancers, Bellini et al. did not find any association between radiotherapy

and the development of renal and thyroid cancers [17]. Our case did not have a history of radiation exposure.

Regarding RCC of any type with osseous metaplasia, patients of various ages have been reported, of whom the majority were older than 50 years. The youngest case was reported by Bloom et al., who had multilocular cystic RCC with osseous metaplasia and was 25 years old [19]. While O'Connor presented the oldest patient, who was 97 years old and had tubulocystic RCC with bone metaplasia [20]. The current case was male and 51 years old.

Inside the renal tumor, osseous metaplasia by ossification gives an appearance similar to that of calcification on radiological imaging. Hence, it can be challenging to distinguish between calcification and heterotopic bone formation based on radiology alone [21]. Due to the extensive calcifications observed in CT scans, the differential diagnosis may include RCC, metastatic carcinoma, adrenal neoplasm, soft tissue sarcoma, and mature cystic teratoma [2]. Ultimately, the definitive diagnosis relies on histopathological examination and immunohistochemical stains [12]. We did not anticipate the presence of heterotopic bone formation prior to surgery and histopathological examination, and the operation was planned to be a partial nephrectomy, but the site of the mass deemed this impossible.

Although the overall survival of patients with ccRCC is worse compared to other subtypes, the prognostic value regarding the presence of osseous metaplasia is unclear due to the scarcity of reported cases [1]. However, it has been generally seen as a good prognostic sign in a renal tumor because the majority of the cases have been found at an early stage of the disease without local invasion or distant metastasis [1, 9, 12, 22]. Hence, indicating a favorable prognosis. Our study is in agreement with the aforementioned opinion. On the other hand, some reports contradict this and suggest that osseous metaplasia is associated with high-grade tumors and a poor prognosis [9, 23].

It is very important to classify the type of RCC present in a patient as the subtype has a significant effect on treatment and prognosis [2]. Because of the exceedingly rare nature of the condition and controversial clinical implications, patients like the current case need to be put under continuous postoperative periodic surveillance [9].

4 Conclusion

This report showcases a unique case of concomitant ccRCC with heterotopic bone formation and papillary thyroid microcarcinoma, representing different pathological conditions rarely occurring simultaneously. Our findings support the idea that osseous metaplasia in an RCC indicates an early-stage carcinoma with a favorable prognosis.

Acknowledgements

None to be declared.

Author contributions

The surgeons SF and DQ performed the operation and contributed to final approval of the manuscript. Major contribution of the idea and final approval of the manuscript were done by AS. DH and FK contributed to writing the manuscript and final approval of the manuscript. AA, HB, ST and AQ contributed to literature review, final approval of the manuscript. All authors read and approved the final manuscript.

Funding

None to be declared.

Availability of data and materials

Not applicable.

Declarations**Ethics approval and consent to participate**

Not applicable.

Consent for publication

Written informed consent for publication has been acquired from the patient.

Competing interests

The authors declare that they have no competing interests.

Received: 18 October 2022 Accepted: 30 March 2023

Published online: 18 April 2023

References

- Aldera AP, Ramburan A, John J (2022) TFE3-rearranged renal cell carcinoma with osseous metaplasia and indolent behaviour. *Urology Case Reports* 42(1):1–3
- Cakici MC, Kir G, Akalin MK, Yildirim A (2020) Clear cell renal cell carcinoma with osseous metaplasia: two extremely rare cases and review of the literature. *Arch Esp Urol* 73(7):651–654
- Moch H, Cubilla AL, Humphrey PA, Reuter VE, Ulbright TM (2016) The 2016 WHO classification of tumours of the urinary system and male genital organs—part A: renal, penile, and testicular tumours. *Eur Urol* 70(1):93–105
- Prakash A, Mishra S, Tyagi R, Attri P, Bhatnagar A, Kansal S (2017) Thoracic psammomatous spinal meningioma with osseous metaplasia: a very rare case report. *Asian Journal of Neurosurgery* 12(02):270–272
- Odum BR, Bechtold ML, Diaz-Arias A (2012) Osseous metaplasia in an inflammatory polyp of the rectum: a case report and review of the literature. *Gastroenterology Res* 5(2):74
- Mat Q, Mehta R, Tainmont S, Duterme JP (2020) Nasal polyps with osseous metaplasia: a misunderstood situation. *Clinical Case Reports* 8(8):1527–1529
- Agarwal S, Bohara S, Jha R, Khurana N, Agarwal PN (2015) Clear cell renal cell carcinoma with osseous metaplasia: rare case report. *J Cancer Res Ther* 11(4):1039–1041
- Fukuoka T, Honda M, Namiki M, Tada Y, Matsuda M, Sonoda T (1987) Renal cell carcinoma with heterotopic bone formation. *Urol Int* 42(6):458–460
- Mitra AP, Chopra S, Ghodoussipour S, Schuckman AK (2020) Heterotopic bone formation in clear cell renal cell carcinoma. *Urology* 144(1):13–14
- Yamasaki M, Nomura T, Mimata H, Nomura Y (2004) Involvement of bone morphogenetic protein 2 in ossification of renal cell carcinoma. *J Urol* 172(2):475–476
- Ramirez DM, Ramirez MR, Reginato AM, Medici D (2014) Molecular and cellular mechanisms of heterotopic ossification. *Histol Histopathol* 29(10):1281
- Pan H, Wu D, Wang H, Pan Y, Zhang T, Zhou J (2017) Clear cell renal cell carcinoma with extensive osseous metaplasia: report of a rare case. *Urology* 105(1):e3–5
- Greenspan A (1995) Bone island (enostosis): current concept—a review. *Skeletal Radiol* 24(2):111–115
- Capitanio U, Montorsi F (2016) Renal cancer. *The Lancet* 387(10021):894–906
- Ulisse S, Baldini E, Lauro A, Pironi D, Tripodi D, Lori E et al (2021) Papillary thyroid cancer prognosis: An evolving field. *Cancers* 13(21):5567
- Iglesias P, Diez JJ (2009) Thyroid dysfunction and kidney disease. *Eur J Endocrinol* 160(4):503–515
- Bellini MI, Lori E, Forte F, Lauro A, Tripodi D, Amabile MI et al (2022) Thyroid and renal cancers: A bidirectional association. *Front Oncol* 12(1):481
- Van Fossen VL, Wilhelm SM, Eaton JL, McHenry CR (2013) Association of thyroid, breast and renal cell cancer: a population-based study of the prevalence of second malignancies. *Ann Surg Oncol* 20(11):1341–1347
- Bloom TL, Sears CL, Williams TR, Linfesty RL, Amling CL (2003) Multilocular cystic renal cell carcinoma with osseous metaplasia in a 25-year-old woman. *Urology* 61(2):462–464
- O'Connor M, Phillis C, Pardo J, Madelaire C, Terry W Jr (2021) A unique presentation of a rare renal cancer: Appearance of bone metaplasia in tubulocystic renal cell carcinoma. *Urology Case Reports* 39(1):1–3
- Singh V, Sinha RJ, Sankhwar SN, Dalela D (2008) Heterotopic bone formation in renal cell carcinoma: A diagnostic challenge. *Indian J Cancer* 45(3):126–127
- Kefeli M, Yildiz L, Aydin O, Kandemir B, Yilmaz AF (2007) Chromophobe renal cell carcinoma with osseous metaplasia containing fatty bone marrow element: a case report. *Pathology-Research and Practice* 203(10):749–752
- Bielsa O, Lloreta J, Arango O, Serrano S, Gelabert-Mas A (2001) Bone metaplasia in a case of bilateral renal cell carcinoma. *Urol Int* 66(1):55–56

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Submit your manuscript to a SpringerOpen[®] journal and benefit from:

- Convenient online submission
- Rigorous peer review
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

Submit your next manuscript at ► [springeropen.com](https://www.springeropen.com)