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Rare occurrence of renal metastasis from thyroid carcinoma: lessons not to forget in evaluation

Dear Sirs,

I am writing regarding a recent article entitled 'Clinicoradiological characteristics of patients with differentiated thyroid carcinoma and renal metastasis: case series with follow up' by Kand and Basu.[1] In this paper, the authors attempted to demonstrate clinicoradiological characteristics in a series of patients with rare occurrence of renal metastasis from primary thyroid carcinoma. It was surprising that a journal of your repute accepted this paper in which pathological proof of renal metastasis was lacking in half of the patients (two of four patients).

Firstly, the authors' claim that the diagnosis of renal metastasis was primarily confirmed by radioiodine whole-body scintigraphy may not be true. It is well known that radioiodine undergoes physiological excretion through the renal system. Moreover, certain renal abnormalities such as cysts are known to have false positive radioiodine uptake.[2–5] Even if an ultrasound or computed tomography correlation has been obtained, fine needle aspiration of the renal lesion is imperative to establish the diagnosis of renal metastasis.

Secondly, variable expression of sodium iodide symporter in different metastatic sites, or selective loss of sodium iodide symporter expression, could explain the rarity of detection of renal metastatic lesion from a primary site in the thyroid.[6] This is different from a true 'flip-flop' where a lesion that was initially concentrating radioiodine subsequently loses this ability as it undergoes dedifferentiation. No such lesion (i.e. initially radioiodine avid and later (in follow-up scans) fluorine-18 fluorodeoxyglucose avid) was reported by the authors in this paper.

Thirdly, the thyroglobulin secreting nature of these lesions is of immense clinical relevance, as a lower level of thyroglobulin on follow up would demonstrate treatment response. Hence, to state the value of thyroglobulin as more than 250 ng/ml, and not the actual value, may not be clinically relevant in the follow up of these patients.

G MALHOTRA
Radiation Medicine Centre, Bhabha Atomic Research Centre, Parel, Mumbai, India

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Authors' reply

Dear Sirs,

This is in response to the letter related to our paper published in this journal on the clinicoradiological characteristics of renal metastases in differentiated thyroid carcinoma.[1] We believe the author has based his letter on certain unusual imaging findings and case reports reported in the literature without adequately fathoming the rigorous clinical and imaging investigation procedure adopted in this case series, including the follow-up data, which, beyond doubt, rule out the concerns raised.

We have addressed the issues in a point-wise manner below.

The ultrasonography findings of the lesions in our patient series were clearly indicative of neoplastic pathology and not consistent with cystic lesion. Also, no doubt was raised by the ultrasonologist about the possibility of other pathologies except for the lesions in contention. This was sufficient to rule out the possibility of a false positive radioiodine uptake due to pathology such as cystic renal disease which has a characteristic radiological pattern. The value of appropriate investigations and their rational interpretation is pivotal for the correct practice of any branch of clinical medicine; which would prevent over-investigation using invasive procedures.

In addition, the findings of the furosemide-enhanced technetium-99 m diethylene triamine pentaacetic acid renogram, technetium-99 m dimercaptosuccinic acid (III) renal scan and biochemical tests of renal function were adequate to clear any suspicion of tracer stasis or accumulation in the collecting system, or any other benign pathology including cystic renal disease. These results were clearly mentioned in our clinical record.

The lesions were confirmed on the low dose radioiodine (iodine-131) diagnostic scan and the post-treatment radioiodine scan, the latter of which was conducted at least 2 days after the administration of high dose radioiodine (iodine-131) for therapy.

Thus, the meticulous investigation with supportive findings from ultrasonography, the demonstration of renal function using biochemical and scintigraphic techniques, and the highly specific post-therapy scan, are more than adequate to conclude that the renal lesions were metastases from differentiated thyroid carcinoma and not false positive findings, even in the absence of histological confirmation. Indeed, we have highlighted the role of ultrasonography-guided fine needle aspiration cytology (FNAC) for the diagnosis of renal metastasis. However, we have further provided reliable alternatives for clinically challenging situations in order to facilitate the evaluation and management of patients where either the sites for FNAC may not be easily accessible or the sample obtained may not be adequate for definite conclusion. These clinically challenging situations highlight the value of pattern recognition and proper correlation with other supportive investigations, which are integral components of clinical nuclear medicine practice.

The direct implication of the extent of sodium iodide symporter expression in metastatic lesions of differentiated thyroid carcinoma is that the lesions are amenable to radioiodine therapy and the outcome of radioiodine therapy. This is based on the ability of individual lesions to concentrate radioiodine, which has been clearly stated in our record. It is a recognised fact that renal metastatic lesions from differentiated thyroid carcinoma are rare by incidence and occurrence.[2] Non-detection as a result of selective loss of sodium iodide symporter expression is rare if not impossible. Here again, the value of considering common causes first and of reasoning cannot be overemphasised.

Fluorine-18 fluorodeoxyglucose uptake in metastatic lesions from differentiated thyroid carcinoma has been described in the context of both radioiodine concentrating lesions as well as those without radioiodine concentration. The uptake has been shown to be influenced by serum thyroid-stimulating hormone and serum thyroglobulin levels.[3] Differentiated thyroid carcinoma is known to demonstrate polymorphism in its course of expression.[4] Hence, we reported the fluorine-18 fluorodeoxyglucose positron emission tomography (PET)-CT findings for the renal metastatic lesions of our series. Our observation should not be misinterpreted with the clear clinical role of fluorine-18 fluorodeoxyglucose PET in non-iodine concentrating lesions of differentiated thyroid carcinoma with an elevated or rising thyroglobulin level (the so-called thyroglobulin-elevated negative iodine scintigraphy ('TENIS')).[5]

The specific thyroglobulin values alone, although important, cannot serve as reliable markers for evaluating the treatment response, especially in multi-organ and multi-lesion metastases, as the value will be the cumulative result of secretion from all metastatic sites and not just one lesion. Thus, in this setting, it is more appropriate for the thyroglobulin values to be used for assessment of response to therapy in conjunction with scintigraphic or radiological imaging response assessment and not in an isolated manner. Furthermore, in cases of excellent favourable therapeutic response, the thyroglobulin titre is expected to reduce substantially and never be more than 250 ng/ml. The majority of patients in our series had extensive multi-organ involvement (including associated lymph node metastases) or multiple lesions involving various organs including both kidneys. Thus, the clinical interpretation of serum thyroglobulin in this scenario must always be individualised.[6]

Thus, most of the points raised by the author of the letter are either not relevant or are less convincing given the clinical situation; nonetheless, these doubts can be encountered by treating physicians who are relatively less experienced in dealing with this rare occurrence. While all the aforementioned points were already very well addressed in the meticulous, thorough and detailed original clinical record,[1] we believe the detailed explanation in this response will help the readers and the author evolve a clear understanding of the concepts related to the subject, and further consolidate their knowledge on this important subject.

P KAND
S BASU
Radiation Medicine Centre, Bhabha Atomic Research Centre, Parel, Mumbai, India

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