An incidental clear cell lesion of the kidney found at the time of cadaveric renal transplantation

Philip Macklin

Maria Soares

Ian SD Roberts

Lisa Browning

Abstract

We report a case of ectopic adrenal tissue (adrenal rest), found incidentally within a donor kidney being prepared for cadaveric renal transplantation. This is a known important mimic of clear cell renal cell carcinoma and, indeed, the clinical suspicion in this case was of a tumour of the kidney, the confirmation of which would have had implications as to the suitability of the kidney for transplantation. Pre-transplantation frozen section examination suggested the correct diagnosis, which was confirmed by subsequent review of paraffin-embedded sections and supportive findings on immunohistochemistry. We review the topic of developmental anomalies of the adrenal gland and outline an approach to differentiate ectopic adrenal tissue from clear cell renal cell carcinoma.

Keywords adrenal rest; ectopic adrenal tissue; immunohistochemistry; renal cell carcinoma

Clinical history

An intraparenchymal nodule was found in a donor kidney during graft harvesting. Frozen section assessment was requested to exclude malignancy.

Macroscopic description

Yellow nodule, 5 × 5 × 3 mm.

Microscopic description

The frozen section (Figure 1a and 1b) was reported as 'suggestive of ectopic adrenal tissue − clear cell renal cell carcinoma (CCRCC) cannot be ruled out; defer diagnosis to paraffin sections'. Based upon this, together with the small size of the nodule with sufficient margins, the surgical team proceeded with transplantation.

Paraffin sections demonstrated 'apparent adrenal cortical tissue, surrounded by a thin rim of fat' (Figure 2a). The diagnosis of ectopic adrenal tissue/adrenal rest was supported by immunohistochemistry (lesional cells expressed calretinin and inhibin but not PAX8) (Figure 2b−2d).

Diagnosis

Ectopic adrenal tissue/adrenal rest.

Discussion

The adrenal glands are paired endocrine organs consisting of an outer cortex that synthesises steroid hormones and an inner medulla that secretes catecholamines. The cortex is divided into three layers: the outer zona glomerulosa produces mineralocorticoids, the middle zona fasciculata produces glucocorticoids and the inner zona reticularis produces sex hormones, predominantly androgens. The adrenal glands develop from two different primordia: the cortex arises from coelomic mesothelium and the medulla from neural crest ectoderm. Three embryological anomalies have been described[1]:

- Ectopic adrenal tissue ('adrenal rest') − tissue (most commonly cortex) separated from the developing adrenal gland during its embryological migration;
- True adrenal heterotopia − a very rare condition involving incorporation of adrenal tissue into adjacent organs due to incomplete separation from the coelomic mesothelium;
- Adrenal-renal fusion − either developmental (due to failure of formation of the renal and/or adrenal capsule) or acquired (due to post-inflammatory fibrosis).

Autopsy studies demonstrate that ectopic adrenal tissue is present in approximately half of neonates[2] but only 1% of adults,[3] suggesting that it frequently undergoes atrophy with age. Ectopic adrenal tissue may comprise both cortex and medulla or cortical tissue only and may be found anywhere along the line of gonadal descent from the upper abdomen to the gonadal adnexa including the coeliac axis, kidney, liver, broad ligament and spermatic cord. Ectopic adrenal tissue has also been reported at sites that do not have an obvious embryological explanation, such as the lung and central nervous system. Most cases are asymptomatic incidental findings, although they can be functional and very occasionally neoplasms arise within them. In a review of ten cases diagnosed incidentally at surgery, the mean diameter was 0.9 cm, the mean age was 54 years and there was a slight female predominance.[4] In another series of seven cases, most lesions were located within the upper pole of the kidney.[5] The histological appearance of these lesions varied; three were plaque-like, two wedge-shaped, one spherical and one comprised irregular nests located deep within the renal parenchyma.

The lesion we report was yellow in colour and located within the renal parenchyma, hence the suspicion of CCRCC. Histologically, the main differential diagnosis for intrarenal ectopic adrenal tissue is CCRCC as both lesions contain clear cells with a

Philip Macklin *MBChB BSc Specialty Trainee in Histopathology, Department of Cellular Pathology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK. Conflicts of interest: none declared.*

Maria Soares *MD PhD Specialty Doctor in Renal Pathology, Department of Cellular Pathology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK. Conflicts of interest: none declared.*

Ian SD Roberts *MBChB FRCPath Professor of Cellular Pathology and Consultant Histopathologist, Department of Cellular Pathology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK. Conflicts of interest: none declared.*

Lisa Browning *MBBS BSc FRCPath Consultant Histopathologist, Department of Cellular Pathology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK. Conflicts of interest: none declared.*

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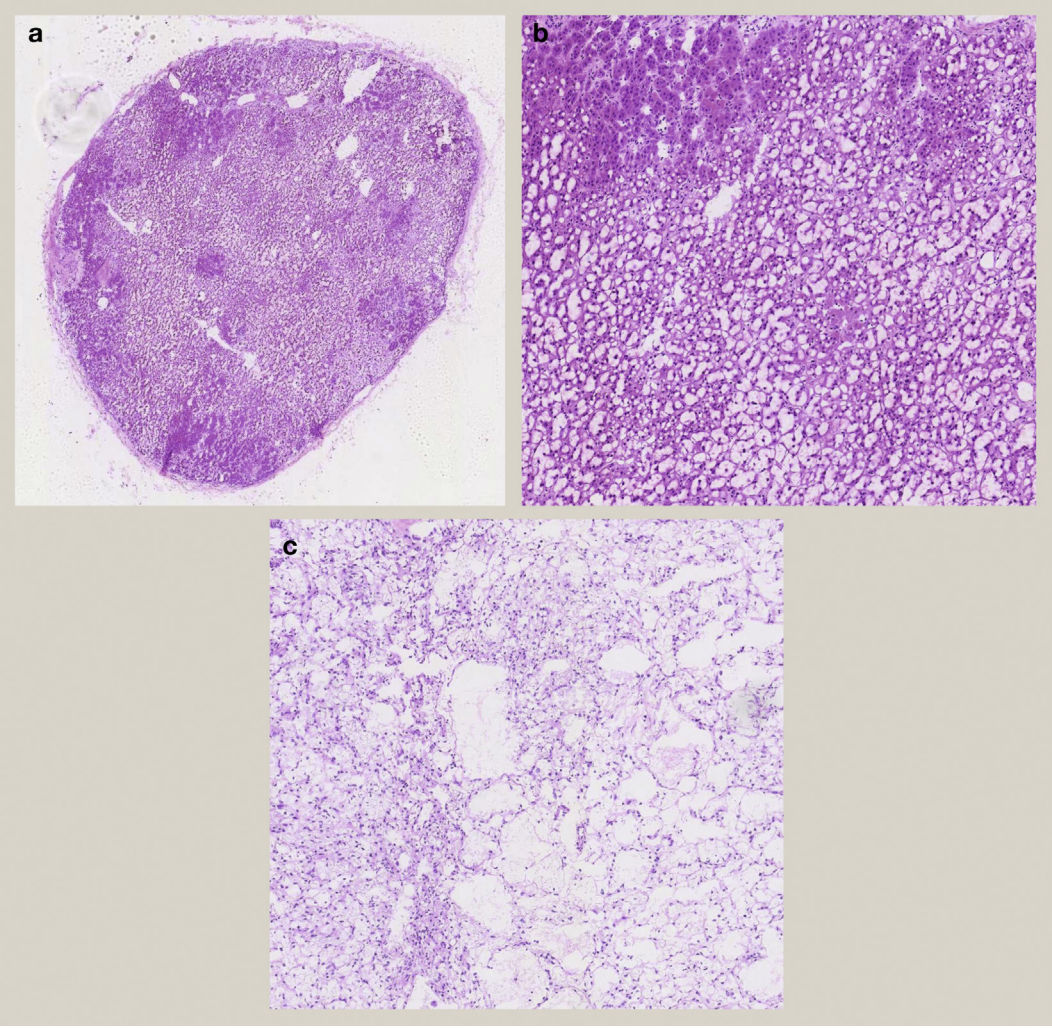

Figure 1 Initial frozen section specimen. (**a**) – Low power view of the initial frozen section specimen, demonstrating a well-circumscribed, nodular lesion (×2.5). (**b**) – At higher magnification, the lesion has a zonal architecture and is composed of both eosinophilic and clear cells, reminiscent of the zona glomerulosa and zona fasciculata, respectively; there is no evidence of cytological atypia, mitotic activity or necrosis (×10). (**c**) – For the purpose of comparison, a photomicrograph from a frozen section of a clear cell renal cell carcinoma, which can also show an admixture of cells with clear and eosinophilic cytoplasm. However, the tissue architecture is not as well-organised, with variability of cells present (×10).

nested arrangement and a prominent, delicate vasculature. Helpful features to differentiate the two include:

- Size – CCRCCs are often larger;
- Architecture – ectopic adrenal tissue often recapitulates a zonal architecture whereas CCRCCs tend to be well-circumscribed with a surrounding pseudocapsule;
- Admixed cells – admixed normal renal tubules and/or adipocytes strongly favour a diagnosis of ectopic adrenal tissue;
- Cytology – cytoplasmic microvesicles favour a diagnosis of ectopic adrenal tissue, although similar features can be seen in CCRCC;
- Other – necrosis is strongly suggestive of CCRCC whilst lymphovascular invasion is not seen in ectopic adrenal tissue.

Differentiation may be complicated when tissue is limited, such as renal mass biopsy, or at frozen section when diagnostic features are less easy to appreciate. For comparison, a photomicrograph of a CCRCC frozen section is presented in Figure 1c.

Immunohistochemistry can facilitate differentiation – markers of adrenal tissue include calretinin, inhibin, melan-A and SF-1 whereas membranous reactivity for carbonic anhydrase IX and RCC and nuclear reactivity for PAX8 are indicative of CCRCC. ◆

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