Renal sclerosing peritubular nodule—how rare is it?

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Introduction

Neurofibromatosis type 2 (NF2) is a rare autosomal-dominant disorder. It affects about 1 in 25 000 people. Approximately 50% of affected people inherit the disorder; in others the disorder is caused by a spontaneous genetic mutation of unknown cause. The hallmark finding in NF2 is the presence of bilateral vestibular schwannomas. Schwannomas may occur along any nerve in the body, including the spinal nerves, cranial nerves and peripheral nerves. As these tumours grow, they may press against and damage nearby structures such as other cranial nerves and the brain stem; compression of the latter may cause serious disability. The gene for NF2 is a tumor suppressor gene located on chromosome 22q12. In contrast to NF1, cutaneous stigmata are generally lacking [1]. Kidney involvement in NF2 has not been studied extensively. A typical histological lesion caused smooth muscle proliferation in the wall of blood vessels, resulting in narrowing of the lumen and ultimately producing hypertension [2]. Rarely, schwannomas have been described in the renal pelvis and perirenal soft tissue [3, 4]. A relatively rare lesion, the renal sclerosing peritubular nodule (RSPN), was first described in a mother and two sons with NF2 who died and underwent autopsy in 1981 [5].

Case report

A 53-year-old man with NF2 was referred for investigation and management of his deteriorating renal function. He was diagnosed with NF2 after developing bilateral vestibular schwannomas in the third decade of life. The surgical history included multiple resections for meningioma and excision of left vestibular schwannoma which left him with residual facial palsy. He also had residual radial nerve palsy from a schwannoma excision. His current deafness, ataxic gait and right wrist drop. At the age of 48, he survived a subarachnoid haemorrhage secondary to a ruptured distal left internal carotid artery aneurysm, which was subsequently successfully coiled. This resulted in a good functional recovery and he continued to work in his construction business. He was noted to have mild hypertension at the time of the haemorrhage; however, this was subsequently well controlled on irbesartan and metoprolol. His only other medications were aspirin and phenytoin. He had no other vascular risk factors. His parents were never tested for NF2; however, his two children have NF2 on genetic studies. He was a non-smoker and non-drinker.

Physical examination revealed multiple subcutaneous schwannomas mainly over the torso, left facial palsy and right wrist drop. His blood pressure was well controlled at 110/60. Serial blood tests had showed declining renal function with a serum creatinine of 113 µmol/L in May 2009, 133 µmol/L in December 2009, 181 µmol/L in August 2012 and 177 µmol/L in April 2013. Urine analysis showed microscopic haematuria (RBC-10/HPF) with no proteinuria. An ultrasound of his renal tract was normal—no hydronephrosis, no renal cysts, and no calyceal abnormalities. Kidney scintigraphy was normal; however, his left kidney was small, measuring 10.5 cm and the right kidney measuring 9.2 cm.

A renal biopsy was performed under ultrasound guidance.

Results

Two cores of renal parenchyma were obtained, one each for light microscopy and immunofluorescence. A small sample of the cortex was reserved prior to processing for electron microscopy if required; however, ultrastructural analysis was not performed as the diagnosis was readily established on light microscopy. Immunofluorescence showed no significant reaction for IgG, IgA, IgM, C3, C1q, kappa or lambda. The core submitted for light microscopy included cortex and medulla, with up to nine glomeruli in a single level. Three of these were globally sclerosed. The intact glomeruli exhibited mild glomerulomegaly, but were otherwise within normal histological limits. Within the interstitium were paucicellular nodules, adjacent to tubules (arrows, Figure 1). These measured up to ∼150 µm in maximum diameter. The nodules were lightly eosinophilic on H&E, PAS negative and argyrophilic on PASM (arrows, Figures 2a–c). The nodules stained blue with Masson trichrome, resembling collagen (arrow, Figure 3). In the context of the clinical history, the morphology of the collagenous nodules was consistent with NF2 (see the Discussion below). Additionally, there was focal mild interstitial inflammation which included eosinophils and lymphocytes, as well as mild hyperplastic arteriolar sclerosis.
and moderate intimal fibroelastosis, suggesting interstitial nephritis and hypertensive nephropathy, respectively (Figure 4).

**Discussion**

To the best of our knowledge, our case represents the first case in a living patient with NF2 with this rare renal lesion on biopsy. There are only two previous case reports which were mentioned from autopsy samples [5,6]. In the first report, which was published in 1981 [5], the lesions were described in detail by light microscopy and EM. In this previous report, nodules were found to be tubulocentric with entrapment of tubule in the middle with a concentric proliferation of spindle cells, and the different developmental
stages of the nodules were characterized in four categories. The origin of the spindle cells was believed to be interstitial cells, and they were unrelated to vessels. Electron microscopy confirmed that the proliferating spindle cells had characteristics of fibroblasts as well as smooth muscle cells. These lesions might be best classified as hamartomas, similar to the renal angiomyolipomas seen in patients with tuberous sclerosis [5]. The second case report of a 24-year-old with a normal renal function showed similarly sized peritubular nodules with four different developmental stages, distributed throughout the cortex in the autopsy sample. The RSPN was unassociated with vessels, unlike the nodular smooth muscle proliferation seen in the vessels of NF2 patients, and the endothelial cell marker CD31 was negative in all nodules [6]. Our microscopy findings were similar to those originally described. We observed similarly sized peritubular nodules almost exactly identical to those previously described for the late-stage lesion of RSPN, although the early-stage lesion with entrapped tubules was not identified in this case.

It has been thought that these nodules do not alter normal kidney function, even when they are extensive [7]; however; none of the previous patients survived in their fifth decade. With increasing frequency of NF2 patients surviving with advanced medical care, RSPN like lesions are more likely to be seen on their renal biopsy. Renal dysfunction in this case could be secondary to interstitial nephritis and hypertension; however, no cause could be found for the interstitial nephritis. Even after adequate control of his blood pressure, his renal function progressively worsened. The role of these RSPN lesions in contributing to renal dysfunction is unclear at this stage as well as its prognostic significance. Since these histological lesions appear to be morphologically progressive (at least in previous cases), early recognition and careful monitoring of the renal function of these NF2 patients may be indicated. As always, the avoidance of potentially nephrotoxic agents is prudent. Bevacizumab (Avastin) is an angiogenesis inhibitor, which is now being increasingly used to reduce the growth of the schwannomas. It has been shown to cause proteinuria, hypertension and renal dysfunction [8]; however; no studies have looked at the effects on these renal lesions in NF2. Hence, due consideration has to be given when they are used in this group of patients.

In summary, we present the third case report of RSPNs in a patient with NF2, with detailed histopathological descriptions. Further studies are needed to understand the pathogenesis and significance of these lesions.

Conflict of interest statement. None declared

References
1. Folkert RD. Chapter 4. Congenital malformations, perinatal diseases, and phakomatoses. In: Prayson RA, Goldblum JR (eds). Human Pathology. Philadelphia, Elsevier: Pennsylvania, 2009, pp. 162–5
2. Immelman EJ, Bunston MR, Goldin AR. Renovascular hypertension in neurofibromatosis. S Afr J Surg 1978; 16: 167
3. Fein RL, Hamm FC. Malignant schwannoma of renal pelvis: a review of the literature and a case report. J Urol 1965; 94: 356
4. Bair ED, Woodside JR, Williams WL et al. Perirenal malignant schwannoma presenting as renal cell carcinoma. Urology 1978; 11: 510
5. Mandybur TI, Weiss MA. Sclerosing peritubular nodules: a hereditary renal abnormality in von Recklinghausen’s disease. Hum Pathol 1981; 12: 704–12
6. Gökdén N, Jamal S, Gökdén M et al. Renal sclerosing peritubular nodules in a patient with neurofibromatosis type 2: a case report with immunohistochemical and electron microscopic studies. Hum Pathol 2009; 40: 1650–1654
7. Liapis H, Winyard P. Cystic diseases and developmental kidney defects. In: Jennette JC et al. (ed). Heptinstall’s Pathology of the Kidney. 6th ed. Philadelphia, USA: Lippincott Williams and Wilkins, 2007, pp. 1294
8. Shenhong Wu, Christi Kim, Lea Baer et al. Bevacizumab increases risk for severe proteinuria in cancer patients. J Am Soc Nephrol 2010; 21: 1381–1389

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