Case Report

Familial interstitial nephritis and retinitis pigmentosa

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Key words: interstitial nephritis; retinitis pigmentosa; Bardet–Biedl syndrome.

Introduction

Numerous hereditary forms of renal disease have been identified over the past 50 years. However, the combination of end-stage renal disease and retinitis pigmentosa remains unusual [1,2] and has been predominantly described in two separate conditions: medullary cystic disease and the Bardet–Biedl syndrome. Herein, we describe two siblings with obesity and retinitis pigmentosa, who developed ESRD secondary to biopsy-proven chronic tubulointerstitial nephritis in the second decade of life. Neither patient fulfills the required diagnostic criteria of any previously described renal–retinal syndrome. The implications of this observation are discussed.

Case 1

A 16-year-old girl, first presented in 1988 with worsening night blindness. She had never previously been hospitalized. There was no history of urinary-tract infections. Family history (to that date) was negative for renal disease. Clinically she was an obese girl. Blood pressure-100/60 mmHg. She had syndactyly affecting the second and third digits of both her hands and feet. Cardiovascular, respiratory, abdominal and pelvic examinations were within normal limits. She had normal secondary sexual characteristics. Fundoscopy revealed retinitis pigmentosa. Her IQ was estimated at 130 (using WAISR, normal 85–115). Biochemistry (all serum) on admission included: creatinine 775 µmol/l (n = 60–120), potassium 6.3 mmol/l (n = 3.5–5.2) and urea 32 mmol/l (n = 2.5–8.5). Her haemoglobin was 8.2 g/dl with normochromic, normocytic indices. Ultrasound of the kidneys showed her to have bilateral shrunken kidneys (size 7.5 cm). There was no evidence of fetal lobulation or calyceal cysts.

Case 2

In 1991, a 19-year-old sibling of case one, presented with increasing malaise over the previous 2 months. At presentation, he was a student studying third-level accountancy. He had previously enjoyed normal health and had never been hospitalized. Clinically he was obese. Blood pressure-160/90 mmHg. Examination by a clinical geneticist revealed that his hands and feet were entirely normal with no evidence of any dystrophic changes. Fundoscopy revealed retinitis pigmentosa. Cardiovascular, respiratory, and abdominal examinations were within normal limits. He had normal secondary sexual characteristics, and in particular the testicular size (4.7 × 3.0 cm, volume 22 ml) was within normal limits. Biochemistry (all serum) on admission included: creatinine 1560 µmol/l, potassium 5.6 mmol/l, FSH 1.9 m.i.u/ml (n = 1–7), LH 7.8 m.i.u/ml (n = 2–14), testosterone 22.1 nmol/l (n = 10.3–34.5). Haemoglobin was 7.7 g% with normochromic and normocytic indices. Ultrasound showed bilateral small kidneys (size 8 cm). There was no evidence of fetal lobulation or calyceal cysts. Renal histology (Figure 1) revealed chronic tubulointerstitial nephritis, with large areas of inflammatory cells consisting mainly of lymphocytes and plasma cells. There were 41 glomeruli, of which 29 were sclerosed. Immunofluorescence was negative. Electron-microscopy did not reveal any splitting of the basement membrane. A diagnosis of chronic tubulointerstitial nephritis was made. She was commenced on CCPD and has subsequently undergone successful cadaveric renal transplantation.

Subsequent evaluation of the three other siblings and the parents revealed no evidence of renal impair-
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The association of retinitis pigmentosa with renal disease occurs mainly in two conditions: medullary cystic disease [1] and the Bardet–Biedl syndrome [2]. Given the complete lack of clinical, radiological, or histological evidence consistent with medullary cystic disease, we quickly eliminated this condition from our differential diagnosis.

In 1920 and 1922, Bardet [3] and Biedl [4] respectively, separately described patients with obesity, retinitis pigmentosa, polydactyly, mental retardation, and hypogonadism. These patients were originally assumed to be similar to four siblings described in 1866, by Laurence and Moon [5]. A new syndrome, the Laurence–Biedl syndrome was named [6]. However, over the last two decades it has become increasingly obvious that the Laurence–Biedl syndrome actually contains two closely related but separate syndromes—

the Laurence–Moon syndrome and the Bardet–Biedl syndrome [7,8]. Polydactyly, which occurs in up to 75% of patients with Bardet–Biedl syndrome, is extremely rare in Laurence–Moon syndrome, whilst the clinical picture in Laurence–Moon syndrome is dominated by neurological disease, which does not occur in Bardet–Biedl syndrome [9].

Schachat and Maurenee [8] reviewed the literature on Bardet–Biedl syndrome in 1982, in an attempt to define the cardinal features of this syndrome. They concluded that an individual patient required four of the following five features in order to make the diagnosis of Bardet–Biedl syndrome: mental retardation, obesity, hypogonadism, retinal dystrophy, and polydactyly.

However, there is more recent evidence to suggest that renal disease also commonly occurs in Bardet–Biedl syndrome, and may be present up to 90% of patients with this syndrome [2,10]. The type of renal involvement is extremely variable, but usually consists of minor structural and functional defects [2]. This may explain why Bardet, Biedl, and researchers for the next 50 years failed to make any reference to the occurrence of renal disease in patients with this syndrome. In a review of renal disease in Bardet–Biedl syndrome, Harnett et al. [2] described the major types of renal involvement in this condition. Almost all of their 32 patients had minor defects, which consisted mainly of urinary concentration and acidification defects. Radiological evidence of calyceal clubbing and blunting were present in 18 of 19 patients examined. Interestingly, of particular note is the fact that only three of 32 patients had chronic renal impairment [2].

This conflicted with Linne et al. [10], who noted ESRD in two of their six patients, all of whom, however, had mental retardation. A possible explanation for this discrepancy is that Harnett’s group were obtained from review of patients attending ophthalmologists with retinitis pigmentosa. In an effort to include renal disease as part of the criteria for a diagnosis of Bardet–Biedl syndrome, Harnett et al. have attempted to redefine Bardet–Biedl syndrome as obesity, mild structural and functional renal disease, retinal dystrophy, dystrophic extremities and, in males only, hypogonadism [2].

When renal tissue has been obtained in patients with Bardet–Biedl syndrome, many different histological lesions have been described including mesangial proliferation, glomerulosclerosis and interstitial fibrosis [11,12]. Chronic tubulointerstitial nephritis with fibrosis dominated the histological picture in both our cases.

We believe that these patients are unique in that they are the first siblings reported with retinitis pigmentosa and end-stage renal disease secondary to interstitial nephritis. Although this histological lesion has been rarely described in association with Bardet–Biedl syndrome [12], this is the first description in patients of normal intelligence. We also believe it noteworthy that there are only two previously reported cases of renal transplantation in patients with

Discussion

Fig. 1. Light-microscopy of the renal biopsy of case no. 2, revealing severe interstitial fibrosis and tubular atrophy with relative glomerular sparing.

ment biochemically, by urinalysis, or on imaging. Interestingly, HLA typing showed only both patients of the family to be A1A2, B8B14, Dr3,Dr7
Bardet–Biedl syndrome [10,13]. Of interest is the observation that both our patients had the same HLA type. Unfortunately it is difficult to interpret the significance of this as HLA testing has not previously been performed in these patients, but it obviously warrants further investigation. The exact classification of our patients remains difficult. They fail to fulfil the accepted criteria, described by Schachat and Maurenee for the diagnosis of Bardet–Biedl syndrome [8]. They are of normal intelligence, and neither had hypogonadism. They also differ from the patients described by Harnett [2] in that they both developed end-stage renal failure. Whether this means that the criteria for the diagnosis of Bardet–Biedl syndrome need to be further revised, or that our patients represent a new renal–retinal syndrome must await further genetic clarification studies.

References

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