Situs inversus: A Rare Extrarenal Association of Alport's Syndrome

R.	Ravindra	Mittal
S.	Sanjiv	Saxena
R.K.		Hotchandani
S.K.		Agarwal
S.C.		Tiwari
S.C.		Dash

Department of Nephrology, AIIMS, New Delhi, India

Dr. Sanjiv Saxena, Asstt. Prof., Department of Nephrology, AIIMS, 110029 New Delhi (India)

Dear Sir,

Alport's syndrome is a form of hereditary nephritis characterised by progressive hematuric nephritis and sensorineural hearing loss occurring in successive generations in a family [1]. A spectrum of ocular, hematological and other extra-renal abnormalities have been reported in patients with Alport's syndrome [2-4]. Only 2 cases of Alport's syndrome with situs inversus have been reported in the literature so far [4,5]. We now report the third case of Alport's syndrome with situs inversus.

A 26-year-old male presented to the Nephrology services of All India Institute of Medical Sciences, New Delhi in April 1992 with a history of pedal edema and facial puffiness off and on for 3 years prior to admission. About 4 months prior to admission, he was found by his local doctors to have moderate hypertension and moderately severe azotemia and was put on conservative management for uremia. The patient gave a history of decreased hearing since the age of 10 years and of decreased visual acuity in both eyes for the last 8 years. He denied any history of gross hematuria in the past. The patient was the eldest of 6 sibs and his 2 younger brothers aged 14 and 16 years also complained of decreased hearing and visual acuity for the last 7-8 years but had not been investigated till date for the same. However, they denied any history of hematuria or anasarca. No other family members had any history of renal disease.

On examination, the patient was found to be very pale and had features of chronic renal failure. There was evidence of situs inversus on clinical examination in the form of dextrocardia and abdominal viscerae on the opposite side. Ocular examination revealed the presence of bilateral anterior and posterior lenticonus with the oil-droplet sign being positive on distant direct ophthalmological examination. The audiometry revealed evidence of bilateral moderate sensorineural deafness.

Laboratory investigations confirmed the presence of severe anemia Hb being 0.65 mmol/l (4.5 mg/dl) with a normal total and differential leucocyte count. The platelets were normal in number and structure. There was evidence of severe azotemia on admission with a serum creatinine of 1056

mmol/l (12 mg/dl). Urine examination revealed 3+ proteinuria and 15-20 RBCs per high power field. Proteinuria was 3.6 g/24 h and the creatinine clearance was 3 ml/min. Skeletal survey

revealed the presence of mixed uremic osteodystrophy. A plain skiagram of the chest and abdomen confirmed the presence of dextrocardia and the gastric fundal shadow on the right side. Electrocardiogram confirmed the presence of dextrocardia. Ultrasonography of the abdomen confirmed the presence of situs inversus and showed both the kidneys to be small and contracted with increased echogenicity -the right and left kidney being 7.8 and 8.2 cm in size, respectively. There was no dilatation of the pelvi-calyceal system and no post-void residue.

The patients' two younger brothers were also investigated. Both had bilateral anterior and posterior lenticonus and bilateral sensorineural deafness. Urine examination in both these sibs revealed proteinuria and microscopic hematuria. However, both these patients had normal renal parameters and a creatinine clearance of 80-90 ml/min. Neither of them had evidence of dextrocardia or situs inversus.

In view of severe azotemia, the index case was put on biweekly maintenance hemodialysis through a right subclavian catheter. An AV fistula was made on his left forearm for future use. Since the kidneys were small and contracted, biopsy was not done. The patient's younger brothers refused kidney biopsy. On the basis of a positive family history, clinical examination and laboratory investigations, a diagnosis of Alport's syndrome with chronic renal failure, end-stage renal disease with situs inversus was made in the patient.

Since its first recognition as a distinct entity by Alport in 1927 [1], a large number of extra-renal abnormalities have been described in association with Alport's syndrome or its variants. Those well recognised include various ocular defects, abnormalities of platelet number and structure, granulo-cyte inclusions, hyperprolinemia, amino-aciduria and oesophageal and genital leiomyomatosis [2, 3].

Besides these, many strange associations have also been described with Alport's syndrome. Interesting amongst them: aortic medianecrosis, cryptorchidism, Marfan-like features, selective IgA deficiency, situs inversus, anti-thyroid antibodies, thyroiditis, hypothyroidism and idiopathic hypoparathyroidism. Most of these are isolated case reports and their authenticity as a true extra renal association of Alport's syndrome has been doubted for want of confirmation in larger studies [4]. Only two cases have been reported in the literature so far describing the coexistence of situs inversus with Alport's syndrome in the same patient [4, 5]. Given the relative individual rarities of situs inversus and Alport's syndrome in the general population per se, the fact that the two have now been described together in the same patient for the third time, situs inversus should now be recognised as a true extra-renal association of Alport's syndrome rather than a simple chance association.

References

- Alport AC: Hereditary familial congenital hemorrhagic nephritis, *Br Med J* 1927; 1:504-506.
Grunfeld JP: The clinical spectrum of hereditary nephritis, *Kidney Int* 1985; 27:83-92.
Gubler MC, Antignac C, Deschenes G, Knebelmann B, Hors Coyle MC, Grunfeld JP, Broyer M, Habib R: Genetic, clinical and morphologic heterogeneity in Alport's syndrome; in Grunfeld JP, Bach JF, Kreis H, Maxwell MH (eds): *Advances in Nephrology*. St Louis, Mosby Year Book, 1993, vol 22, pp 15-36.
Gregory MC, Atkins CL: Alport's syndrome; in Schrier RW, Gottschalk CW (eds): *Diseases of the Kidney*. Boston, Little Brown, 1993, vol 1, pp 571-592.
Hamasaki T, Shimizu K, Seki K: Two cases of Alport's syndrome with incomplete Fanconi's syndrome or with situs inversus viscerum totalis. *Nippon Naika Gakai Zasshi* 1989; 78:410-412.

0028-2766/94/
0683-0390\$8.00/0