Acute tubulointerstitial nephritis and uveitis syndrome in the elderly

P Salu, N Stempels, K Vanden Houte, D Verbeelen

Abstract

A case of acute tubulointerstitial nephritis and uveitis syndrome (TINU syndrome) in an elderly woman is reported. The present case demonstrates that this entity originally observed in children, and more recently in adults, may also occur in the elderly. The aetiology and treatment are briefly discussed.

In December 1985 a 66-year-old Caucasian woman complained of symptoms of anorexia and fatigue. A clinical examination gave normal results. Her blood urea was 8 mmol/l and serum creatinine 133 μ mol/l. A proteinuria of 0.9 g/l and some leucocytes in the urine were found. An x-ray of the chest, barium meal x-ray bone scintigraphy, and abdominal echography were normal.

Renal symptoms. One month later admission was necessary because of acute renal failure. Her blood pressure was 190/100 mmHg and temperature 37.4°C. A clinical examination did not reveal other abnormalities. The evolution of the positive blood tests is shown in Table 1. Serological markers for cytomegalovirus, hantavirus, hepatitis B virus antigen, syphilis, streptococci, rubella, salmonella, toxoplasmosis, Epstein-Barr virus, and herpes simplex virus, as well as repeated blood cultures, tests for rheumatoid arthritis factor, immune complexes, and Coombs's reaction were negative. The patient had not been exposed to toxic agents and denied the use of analgesics, antibiotics, or other drugs.

A renal biopsy was carried out. The proximal and distal tubules showed focal areas of destruction, and the interstitial tissue was swollen by oedema and a dense infiltrate of lymphocytes, plasmocytes, neutrophils, and some eosinophils; small blood vessels had a swollen endothelium. Immunofluorescence showed the presence of complement in the endothelial layer of the small vessels and protein casts in the tubules (Figs 1 and 2).

Idiopathic acute tubulointerstitial nephritis (AIN) was diagnosed and oral treatment of methylpredisone (32 mg/day) was started. Corticosteroid treatment was gradually decreased and stopped in April 1986. The results of follow-up blood and urine examinations progressively returned to normal (Table I and Fig 3).

Ocular symptoms. In June, 5 months after the beginning of the acute renal failure, the patient complained of itching, redness, and pain in the left eye. She was treated with local antibiotic eye drops of Chloransulfa (chloramphenicol 5 mg, sodium sulphacetamide 100 mg/ml, collyrium 10 ml). Two weeks later she complained of loss of vision in the left eye. The visual acuity was 6/6 in

the right eye and 6/12 in the left eye. The anterior segment showed keratic precipitates, Tyndall positivity, and posterior synechiae in the left eye. The inferior fornix was hyperaemic, with secretions and follicles. The intraocular pressure was normal. The diagnosis of anterior uveitis was made. Topical treatment of combined neomycin sulphate, polymyxin B, and dexamethasone drops (Maxitrol) together with atropine 1% was started. Two days later persistent posterior synechiae were successfully treated with a paralimbal injection of 0.1 ml of adrenaline (0.1%). Ten days later the visual acuity of the left eye had increased to 6/9. The treatment with Maxitrol eye drops was discontinued because of increasing intraocular pressure. Twenty months later the patient developed a moderate anterior uveitis in the right eye, with a slight Tyndall positive reaction. This inflammatory reaction resolved completely after a few days of treatment with steroid eye drops (Maxitrol). Classical tests for uveitis remained negative.

Discussion

Since 1975 several cases of an association of acute interstitial nephritis (AIN) with uveitis without any obvious aetiology have been described in children.¹⁻¹² Later a few cases of this oculo-renal syndrome have been reported in adult females.¹⁰⁻¹⁴ (Table II). Eighteen out of 28 patients were younger than 20 and the oldest was 56. Our case illustrates that this syndrome can appear at any age. It is interesting to note that the uveitis may appear before, simultaneously with, or after the renal failure. The uveitis appeared as a first symptom in only three cases and simultaneously with the nephritis in five cases. The uveitis was preceded by AIN in 18 cases, with an interval of two to seven months. In 17 cases (70%) the two eyes were involved within two months. In the present case the contralateral eye was involved after 20 months.

In general the anterior uveitis responds well to topical corticosteroid treatment, as the present case confirms. Good results in the treatment of

TABLE 1 Evolution of blood and urine analysis data during and after AIN

	Jan 1986	Feb 1986	May 1986
ESR (mm/1 h)	70	36	13
Haemoglobin (g/dl)	12.6	9.4	12.7
Leucocytosis ($\times 10^9/l$)	9.3	9.6	4.0
Neutrophils (%)	57	65	48
Eosinophils (%)	3	6	6
Lymphocytes (%)	39	20	29
Blood urea (mmol/l)	18	12	10
Blood creatinine (μ mol/l)	592	194	141
Creatinine clearance (ml/min/1.73 m ²)	8.2		
Proteinuria (g/l)	0.5	0.5	1.0
Glucosuria (g/l)	3.2	2.5	1.2

University of Brussels
(VUB), Brussels, Belgium

Department of
Ophthalmology
P Salu
N Stempels

Department of Pathology
K Vanden Houte

Department of
Nephrology
D Verbeelen

Correspondence to: Dr P Salu,
Academisch Ziekenhuis, Vrije
Universiteit Brussel,
Laarbeeklaan 101, 1090
Brussels, Belgium.

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Figure 1: Photomicrograph of renal biopsy showing normal glomerulus, normal blood vessel, and interstitial infiltrate consisting of inflammatory cells. (PAS, $\times 200$.)

Figure 2: Photomicrograph of the renal biopsy showing the inflammatory infiltrate composed of lymphocytes, plasmocytes, neutrophils, and some eosinophils (indicated by arrows). (PAS, $\times 320$.)

Figure 3: Clinical course of AIN and uveitis.

TABLE II Uveitis in TINU syndrome

Author	Year	Sex	Age	Uveitis		Unit/bi*	Months†
				Ant.	Post.		
Dobrin <i>et al</i> ¹	1975	F	14	+	—	bi	+3
Guesry and Loirat ²	1976	F	17	—	—	bi	0
		M	11	—	—		<1
		F	10	—	—		+2
Kikkawa <i>et al</i> ³	1977	F	14	—	—		<1
		F	13	+	—	bi	+1
		F	14	+	—	bi	<1
Van Acker <i>et al</i> ⁴	1980	F	14	+	—	bi	+2
		id	—	—	+		+3
Levy ⁵	1983	F	10	—	—		
Roth and Laberke ⁶	1983	M	13	—	—		0
		M	15	+	+‡	uni	0
Burghard <i>et al</i> ⁷	1984	F	14	+	—	bi	0
		F	11	+	—	bi	+3
Steinman and Silva	1984 ¹³	F	27	+	—	uni	0
Vanhaesebrouck <i>et al</i> ⁸	1985	F	15	+	—	bi	+2
Leumann <i>et al</i> ⁹	1985	M	14	+	—	bi	+3 (RE)/+5 (LE)
Noël <i>et al</i> ¹⁰	1986	F	15	+	—	uni	+4
		F	26	+	—	uni	—3
		F	30	+	—	uni	+3
Burnier <i>et al</i> ¹⁴	1986	F	56	+	—	bi	—1 (LE)/0 (RE)
Mouillon <i>et al</i> ¹¹	1986	F	48	+	—	bi	—1 (RE+LE)
		id	—	—	—		+6
		F	12	+	+	bi	0
Rossenbaum ¹²	1988	F	43	+	+‡	bi	+7
		M	13	+	—	bi	+3
		F	42	+	+§	bi	+3
		M	54	+	—	bi	+5
Present case	1988	F	52	+	—	bi	<1
		F	66	+	—	uni	+5 LE/+20 (RE)

*Bi=bilateral uveitis diagnosed at the same moment or with an interval of no more than two months between both eyes.

†Months before (—), less than (<), concurrent with (0), or after (+) AIN.

‡Cystoid maculopathy.

§Pars planitis.

interstitial nephritis by oral corticosteroids have been reported.^{1,6,7,9-13} Two patients¹⁵ needed cytotoxic agents in addition to steroids for the control of the nephrotic syndrome. In some patients renal abnormalities improved spontaneously.^{4,12,14,15} The correlation between the improvement of renal function and corticosteroid administration suggests a beneficial effect of corticosteroids. However, there is no proof of their necessity. In no case has a relapse of the renal disease been observed, whereas the uveitis relapses frequently and after varying periods of time.

The aetiology of the TINU syndrome remains unknown. Classical causes of interstitial nephritis and/or uveitis (as may be shown by serological markers or by bacterial or viral cultures, toxic agents, etc) have not been shown

to be responsible for this syndrome. Systemic disease and a drug induced nephritis have been excluded.

An immunological disorder accompanying or causing this syndrome is most likely since: (1) the interstitial infiltrate consists of lymphocytes; (2) a hypergammaglobulinaemia (IgG) is found in most cases; (3) the response to steroid treatment is favourable.

CONCLUSION

The oculorenal syndrome or TINU syndrome is probably of immunological origin; is accompanied by uni- or bilateral anterior uveitis, which may follow, concur with, or even precede the renal failure; and is most frequently seen in children and adult females, but can occur at any age as the present case illustrates.

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