

[CASE REPORT]

IgA Vasculitis in an Oldest-old Patient Successfully Treated with Glucocorticoid

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Abstract:

A 94-year-old man was diagnosed with immunoglobulin A vasculitis (IgAV), and losartan was initiated. His renal function rapidly deteriorated over a month; therefore, methylprednisolone was administered intravenously for three days followed by oral prednisolone. Renal function improvement and both proteinuria and hematuria remission were observed within six months. Prednisolone tapering was completed at eight months. In this case, we monitored the patient carefully and started glucocorticoids as soon as the patient's renal function deteriorated. We were thus able to treat the patient with a relatively small dose of glucocorticoids in a short treatment period without any adverse events due to glucocorticoids.

Key words: IgA vasculitis, oldest-old, glucocorticoid

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Introduction

Immunoglobulin A-associated vasculitis (IgAV), formerly referred to as Henoch-Schönlein purpura, is an immune-mediated small-vessel vasculitis. It is the most common vasculitis in children and has a good prognosis (1-3). IgAV in adults is rare, and it is associated with poorer clinical prognosis than childhood IgAV (4). A few studies have reported the prognosis of IgAN in the elderly to be particularly poor; however, there are almost no reports of the outcomes in the oldest-old (>90 years old).

We herein report a case of IgAV in an oldest-old patient who was successfully treated with glucocorticoid therapy.

Case Report

A 94-year-old man presented with a history of bilateral lower limb purpuric rash and edema that progressed over a few weeks. There was no preceding illness or change in medications. His medical history included hypertension and diet-controlled type 2 diabetes mellitus. His family history

was unremarkable.

On an examination, he was alert, afebrile (temperature 36.5°C), and had a slightly elevated blood pressure (149/86 mmHg) and normal pulse rate (88 beats/min). His body weight was 68.4 kg. A clinical examination revealed small palpable purpuras and pitting edema of the lower limbs bilaterally. A clinical examination was otherwise unremarkable.

The laboratory data are provided in Table. A urinalysis and urine sediment examination showed dysmorphic hematuria, oval fat bodies, hyaline casts and granular casts. The urine protein-creatinine (Cr) ratio (P/C) was 2.55 g/gCr. His serum albumin level was slightly low (3.4 g/dL), and C-reactive protein (3.2 mg/dL), immunoglobulin A (IgA) (652 mg/dL), glucose (233 mg/dL) and glycosylated hemoglobin (HbA1c) (7.0%) levels were elevated. Abdominal non-contrast computed tomography showed no kidney abnormalities.

The patient was reviewed by the dermatology and nephrology teams, and a skin biopsy was performed. Light microscopy showed nuclear enlargement of endothelial cells, extravasated red blood cells, fibrin, neutrophils, and nuclear

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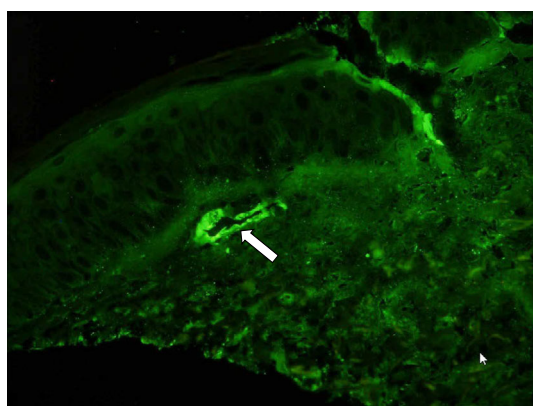
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Table. Laboratory Data.

Urinalysis		BUN (mg/dL)	14.8
Protein (g/gCr)	2.55	Cr (mg/dL)	0.77
Glucose	-	Na (mEq/L)	137.5
RBC	>100/HPF	K (mEq/L)	4.5
WBC	5-9/HPF	Cl (mEq/L)	101.7
Oval fat body	+	Ca (mg/dL)	8.7
Hyaline cast	+	P (mg/dL)	2.7
Granular cast	+	HbA1c (%)	7
Blood count		Serological test	
WBC (μ L)	7,820	CRP (mg/dL)	3.2
RBC ($\times 10^4/\mu$ L)	468	RF	-
Hb (g/dL)	14	ANA	-
Platelets ($\times 10^4/\mu$ L)	26.2	C3 (mg/dL)	103
Biochemical test		C4 (mg/dL)	22
Total protein (g/dL)	7.2	IgG (mg/dL)	1,735
Albumin (g/dL)	3.4	IgA (mg/dL)	652
AST (IU/L)	24	IgM (mg/dL)	56
ALT (IU/L)	15	PR3-ANCA (IU/mL)	0.6
LDH (IU/L)	157	MPO-ANCA (IU/mL)	<0.5

WBC: white blood cell, RBC: red blood cell, HPF: high power field, Hb: hemoglobin, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, BUN: blood urea nitrogen, Cr: creatinine, CRP: C-reactive protein, RF: rheumatoid factor, ANA: antinuclear antibody, Ig: immunoglobulin, PR3-ANCA: proteinase 3 anti-neutrophil cytoplasmic antibody, MPO-ANCA: myeloperoxidase anti-neutrophil cytoplasmic antibody

**Figure 2. C3 deposition within the dermal vessels (arrow, immunofluorescent staining $\times 400$).**

dust around small vessels in the dermal layer (Fig. 1). These findings are consistent with leukocytoclastic vasculitis. Immunofluorescent staining showed only C3 deposition (Fig. 2). Although IgA deposition was not shown in immunofluorescent staining due to the extended duration from the emergence of purpuras to the biopsy, the patient was definitively diagnosed with IgA vasculitis based on the American College of Rheumatology (ACR) (5) and European League Against Rheumatism/Paediatric Rheumatology International Trials Organisation/Paediatric Rheumatology European Society (EULAR/PRINTO/PRES) (6) criteria and did not undergo a renal biopsy.

The patient's clinical course is shown in Fig. 3. Given his

**Figure 1. A skin biopsy showing leukocytoclastic vasculitis; nuclear enlargement of endothelial cells (arrow), fibrin (arrowhead), extravasated red blood cells (asterisks), neutrophil infiltration with nuclear dusts (yellow arrow) within and surrounding the dermal vessel (Hematoxylin and Eosin staining $\times 400$).**

advanced age and co-morbidities and the minimal purpura and relatively well-preserved renal function at the time of the diagnosis, we opted for treatment with losartan 25 mg/day, withholding glucocorticoids. Four weeks later, he developed worsening edema and a rapidly deteriorating renal function (serum Cr increased from 0.77 mg/dL to 1.67 mg/dL) along with an increase in proteinuria (P/C 2.55 g/gCr to 5.04 g/gCr). Preceding infection, new medication use other than losartan and urinary retention were denied by his recent medical history and physical examinations. In addition, dehydration and hypotension, which are risk factors of a reduction in the renal function with ARBs, were also denied by his recent medical history, physical examination findings and daily blood pressure records. Hyperkalemia was absent at the time of the renal function decline, and the dose of losartan was relatively small. For these reasons, we considered IgAV progression as a cause of his rapid renal function decline rather than losartan and decided to initiate glucocorticoid therapy.

We admitted the patient and administered methylprednisolone 500 mg/day intravenously for 3 days followed by oral prednisolone (30 mg/day). The dose of glucocorticoids was relatively small considering the patient's age, comorbidities and risk of adverse effects. We strictly monitored his blood glucose levels, vital signs and general condition during the treatment. We initiated sitagliptin phosphate hydrate, and subcutaneous injection of insulin was administered when the blood glucose level increased (>200 mg/dL). We started sulfamethoxazole-trimethoprim to prevent pneumocystis pneumonia. We completed glucocorticoid therapy safely, and the patient was discharged on day 18 without any complications.

The small purpuras disappeared after one month. The renal function gradually improved and stabilized to Cr 1 mg/dL, and proteinuria and hematuria resolved at 3 and 6 months, respectively. His diabetes mellitus was stable, with HbA1c $<7\%$ with oral sitagliptin phosphate hydrate only.

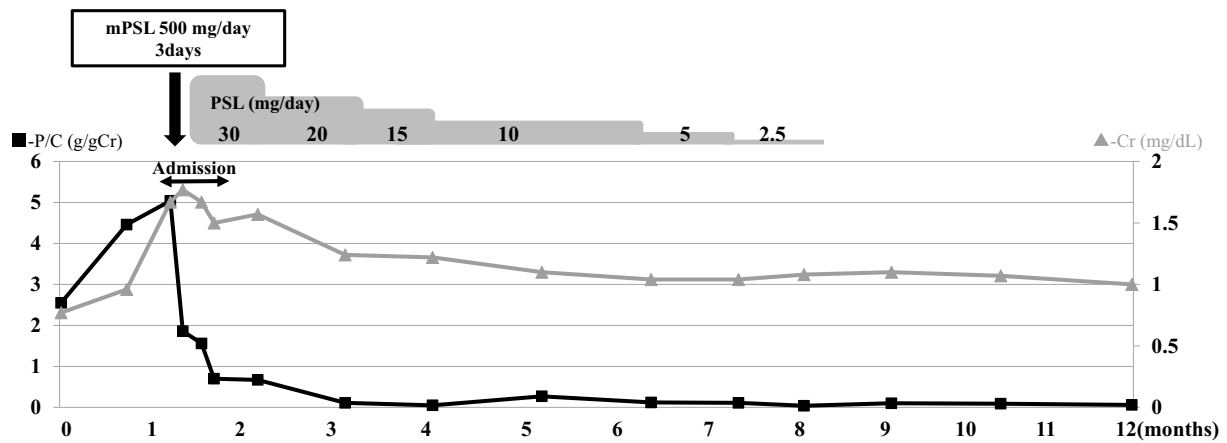


Figure 3. Clinical course of the patient. The renal function was stabilized to Cr 1 mg/dL, and the proteinuria had resolved after 3 months. mPSL: methylprednisolone, PSL: prednisolone, Cr: creatinine, P/C: protein-creatinine ratio

The patient completed prednisolone tapering at eight months. No adverse events related to glucocorticoid treatment were observed during treatment. At 12-month follow-up, his renal function was stable, and there was no proteinuria.

Discussion

We herein report a rare case of IgAV in an oldest-old patient successfully treated with a short course of relatively low-dose glucocorticoids.

IgAV is an immune-mediated small-vessel vasculitis. Palpable purpura, arthritis, abdominal pain and renal involvement are major clinical manifestations. Histologically, leukocytoclastic vasculitis and IgA deposition in the vascular wall are characteristic features of IgAV (7).

IgAV is diagnosed based on the ACR criteria (5) or EULAR/PRINTO/PRES criteria (6). Both criteria include clinical manifestations and histological findings. IgAV is the most common vasculitis in childhood and has been extensively studied in children (1). The annual incidence of IgAV in children is approximately 20 cases per 100,000 and is highest between the ages of 4 and 6 years old (70 cases per 100,000) (8). Childhood IgAV is often self-limited, with 94% of children experiencing complete recovery (2, 3). Renal involvement occurs in 30-50% of cases and is more common in older children (11-15 years old) than in younger ones (9). Histologically, microscopic dermal edema and perivascular deposition of C3 on direct immunofluorescence are reported to be predictive of renal involvement in childhood IgAV (10). The prognosis of childhood IgAV with renal involvement is good in most cases (11).

IgAV in adults is less common, and renal involvement is more frequent and associated with a worse prognosis than in children (4). The annual incidence of IgAV in adults is reported to be only 1.3 per 100,000 (12), with a 50-90% rate of renal involvement (13, 14). In a retrospective study of 250 adult patients with IgAV confirmed on a renal biopsy,

the patient survival rate was only 74%, and 14% had moderate renal insufficiency (creatinine clearance <50 mL/min), 13% had severe renal failure (creatinine clearance <30 mL/min), and 11% reached end-stage renal failure during a median follow-up of 14.8 years (15).

Due to its rarity, there are few studies of IgAV in elderly patients, and the treatment strategy of IgAV in this group has not been established. Miura et al. reviewed the clinical course of 28 IgAV patients >60 years old and reported a mortality rate of 25.9%, indicating that an age over 60 years old at the onset of IgAV was associated with a poor prognosis (16). In contrast, a Japanese study of 13 elderly IgAV patients (60-85 years old) and 10 younger patients (10-59 years old) treated with glucocorticoids reported comparable renal prognoses. However, that study reported a higher risk of adverse events associated with glucocorticoid administration in elderly patients (9/13: 69%) than in younger patients (1/10: 10%). Of note, three elderly patients died of severe infection (17). A cohort study of 152 adult IgAV (19-84 years old) patients who underwent a renal biopsy reported that an older age (>65 years old) and hypoalbuminemia were independent prognostic factors of a worsening renal function, and aggressive treatment with corticosteroids and renin-angiotensin system blockade was associated with a good renal prognosis (18).

To our knowledge, only one previous case of IgAV in an oldest-old patient has been reported, being noted in a 99-year-old Japanese woman with hypertension and diabetes mellitus who presented with bilateral lower limb purpura, abdominal pain and acute kidney injury (Cr 2.65 mg/dL) (19). The patient was diagnosed with IgAV based on clinical manifestations, and a skin biopsy confirmed leukocytoclastic vasculitis. Although oral prednisolone 30 mg/day was immediately initiated, the patient died of renal failure on day 24.

Although these previous studies have reported that elderly patients with IgAV have a worse prognosis and are at an increased risk of adverse events associated with glucocorti-

coids compared with their younger counterparts, we monitored the present patient carefully and started glucocorticoids as soon as the patient's renal function deteriorated. We considered the disease progression to be severe, and oral prednisolone alone was not sufficient to treat the patient with reference to above previous case of a 99-year-old patient (19); therefore, we started methylprednisolone half pulse to obtain faster and stronger efficacy and to avoid the need for the long-term use of oral prednisolone. As a result, we were able to treat the patient in a short period without any adverse events using relatively low doses of glucocorticoids. Our case suggests that methylprednisolone half-pulse followed by oral prednisolone has potential efficacy, even in oldest-old IgAV patients with comorbidities. If the disease progresses rapidly, as shown in our case, it may be important to consider the use of glucocorticoids with careful monitoring.

Although further studies are warranted to establish a treatment strategy for extremely old IgAV patients, this case shows that therapy is a promising treatment option. We hope that our findings will inform the management of similar cases.

Conclusion

IgAV occurs even in oldest-old patients. Although the treatment of IgAV in such patients has not been established, glucocorticoids might be a valuable potent therapeutic option with careful monitoring.

Consent for the publication of this case report was obtained from the patient and his daughter.

The authors state that they have no Conflict of Interest (COI).

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