2014/5/16 (第 4 回)　C プリント

Rapidly progressive glomerulonephritis: defined as a decrease in the glomerular filtration rate by more than 50% in a 3-month period

Table 2. Causes of Rapidly Progressive Glomerulonephritis.*

Anti–glomerular basement membrane disease
Antineutrophil cytoplasmic antibody–associated vasculitis
Immune-complex–mediated glomerulonephritis
In patients with normal complement levels:
- IgA nephropathy
- Henoch–Schönlein purpura
- Fibrillary glomerulonephritis, immunotactoid glomerulonephritis

In patients with low complement levels:
- SLE
- Poststreptococcal glomerulonephritis
- Membranoproliferative glomerulonephritis
  - Infections (HCV, HBV, HIV)
  - Genetic
  - Collagen vascular disease (SLE, Sjögren's syndrome)
  - Monoclonal gammopathies
- Endocarditis
- Cryoglobulinemia
  - Type I (may be associated with myeloma, lymphoma, or Waldenström's macroglobulinemia)
  - Type II (may be associated with myeloma, lymphoma, Waldenström's macroglobulinemia, HCV, or Sjögren's syndrome)
  - Type III (may be associated with HCV or endocarditis)

Clinical diagnosis: acute glomerulonephritis, possibly due to Henoch-Schonlein purpura or cryoglobulinemia

Occasionally, the rash of Henoch-Schnlein puroura appears after the gastrointestinal and renal manifestations.

The diagnostic tests should be testing for the presence of a cryoglobulin and a paraprotein (M protein) on a specimen of warm blood and a renal biopsy.

The absence of an M component could be explained by the specimen's being at room temperature, which would lead to precipitation of the M component as part of the cryoprecipitate.

Anatomical diagnosis: Type II　cryoglobulinemia with acute glomerulonephritis and renal vasculitis, monoclonal B-cell population of unknown significance

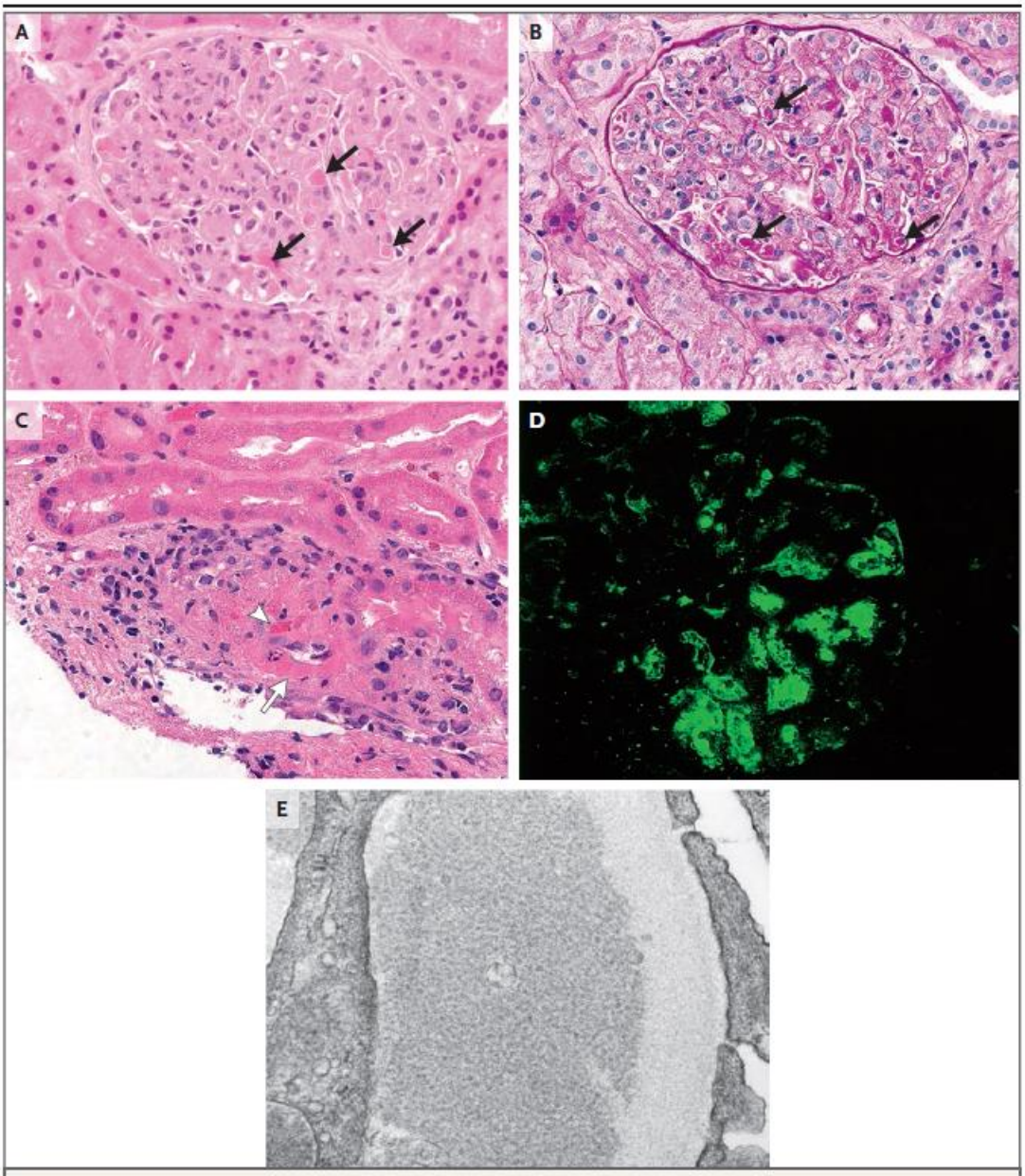

Figure 2. Renal-Biopsy Specimen.

Glomeruli have pseudothrombi (arrows), swollen endothelial cells, and endocapillary inflammatory cells (Panel A, hematoxylin and eosin; and Panel B, periodic acid–Schiff). Vessels with reactive endothelial cells, mural cryoglobulin deposits (Panel C, arrow; hematoxylin and eosin), extravasated red cells (arrowhead), and karyorrhectic debris are present. IgM immunofluorescence (Panel D) revealed granular staining of capillary loops and positive pseudothrombi. An electron micrograph (Panel E) shows a subendothelial deposit with a tubular substructure. (In all images, the Smart Sharpen filter [Photoshop CS] was used for white balance and sharpening, with identical settings for each image.)

Glomerular pseudothrombi are pathgnomonic for cryoglobulinemic glomerulonephritis. Key features supporting a diagnosis of cryoglobulinemic glomerulonephritis are the predominance of a macrophages in the glomerular infiltrate and a tubular substructure on electron microscopy. (Fibrin: PAS－　pseudothrombi: PAS+)

Cryoglobulinemia

Cryoprecipitates: blood proteins which precipitate at temperatures lower than 37°C

Cryoglobulin: the precipitate from an individual's serum and plasma
consists of immunoglobulins and complement components

Cryofibrinogen: the precipitate from plasma only

Cryoglobulinemia has three types.

Type I: monoclonal immunoglobulin (Ig)

Type II: mixed monoclonal Ig and polyclonal Ig with rheumatoid factor activity

Type III: mixed polyclonal Ig

	Type I	Type II	Type III
Associated diseases	LPD >>>	HCV >>	HCV >>
	MGUS >	> CTD	CTD >>
	Idiopathic	> Idiopathic	Idiopathic
		> LPD > other infections	> Other infections
Symptoms and signs			
Purpura	+	+++	+++
Gangrene/acrocyanosis	+++	+ to ++	±
Athralgias >> arthritis	+	++	+++
Renal	+	++	+
Neurologic	+	++	++
Liver	±	++	+++

Treatment: high-dose glucocorticoids and cyclophosphamide if the patients have nephropathy or renal complications

Treatment:

methylprednisolonesodium succinate followed by prednisone taper

→plasmapheresis because of a rising creatinine level

→cyclophosphamide and rituximab because apheresis can lead to rebound, in which cryoglobulin production increases after the cessation of apheresis

→the symptoms improved, but…

Two months later, cutaneous purpura appeared over the patient's legs, and night sweats developed!!

→The rash resolved after a single dose of rituximab, but she continued to have mild influenza-like symptoms.

→Three months later, oral cyclophosphamide and prednisone were begun because of increasing creatinine levels and worsening constitutional symptoms of malaise, fatigue and night sweats.

→The constitutional symptoms improved, but two months later the patient had increasing shortness of breath!

→cyclophosphamide was stopped and bortezomib was started!

→The patient now has a good quality of life with maintenance prednisone/

Teaching points

① Even though the patient's presentation is missing some key findings such as the rash, these features may evolve over time.

② In rapidly progressive glomerulonephritis, the empirical therapy (high doses of methylprednicolone) outweighs the risk of harm.