CASE REPORT

IgA Vasculitis Triggered by Infective Endocarditis of Pulmonary Artery with Congenitally Corrected Transposition of the Great Arteries
A Case Report and Literature Review

Midori Akagi, MD, Nozomi Iwanaga, MD, Yuichi Torisu, MD, Hisayuki Fujita, MT, Chieko Kawahara, MD, Yoshiro Horai, MD, Yasumori Izumi, MD and Atsushi Kawakami, MD

Summary
A man in his 40s with a history of congenitally corrected transposition of the great arteries (CCTGA) and closure of ventricular septal defect was referred to our hospital with purpura and hematuria. Presence of purpura, renal damage, and pathological findings on skin biopsy led to the diagnosis of IgA vasculitis (IgAV). Oral prednisolone (PSL) was initiated. However, Streptococcus pseudoporcinus was isolated from blood cultures, and transthoracic echocardiogram revealed vegetation on the pulmonary valve. From these findings, the diagnosis of infective endocarditis (IE) was made. Although the patient’s condition improved after PSL interruption and antibiotic administration, his purpura relapsed. PSL readministration improved symptoms, with no further relapse even after gradual PSL dose reduction. The present case raises awareness of the importance of recognizing the occurrence of IE in IgAV patients, especially in those with congenital heart disease. CCTGA should be acknowledged as a risk factor for IE in the right-sided heart.

Key words: Leukocytoclastic vasculitis, Caries, Streptococcus pseudoporcinus, Congenital heart disease

IgA vasculitis (IgAV) is a form of leukocytoclastic vasculitis characterized by IgA-immune deposits and immune complexes. It is presumed that bacterial and viral infections take part in IgAV pathogenesis. However, cases of IgAV complicated by infective endocarditis (IE) are rarely reported. Although IE mainly affects mitral and aortic valve, IE of pulmonary artery (PA) is rare. Congenitally corrected transposition of the great arteries (CCTGA), a form of congenital heart disease (CHD) that often complicates pulmonary valve (PV) stenosis (PS), may be a risk factor for IE of PA. There are currently no reports of IgAV linked to IE in a patient with CCTGA.

The case of a male diagnosed with IgAV triggered by IE of PA with CCTGA is herein described.

Case Report
A man in his 40s with CCTGA and a history of closure of ventricular septal defect (VSD) was admitted to our hospital with purpura and hematuria; the date of operation was unknown. He had been hospitalized in a psychiatric hospital for 12 years because of schizophrenia and developed generalized edema one month before admission to our hospital. Upon admission, his body temperature was compatible with intermittent fever ranging from 37.1°C to 38.5°C. Pulse rate was regular (89 beats per minute), and blood pressure was 106/63 mmHg. Oxygen saturation on room air was 95%. No signs of anemia and jaundice were found in his eyes, but a great number of caries were present in the oral cavity. Neck lymph nodes were not palpable. Systolic murmur was present at the second left sternal border. Crackles were audible on both lower lung fields. No abdominal distension, rigidity, or tenderness was noted. Arthralgia was not apparent. Pitting edema was found in both legs. Palpable purpura was prominent on the lower half of the extension side of both legs. Results of subsequent laboratory investigations showed leukocytosis with a shift to the left, anemia, and thrombocytopenia. Fibrinogen degenerative product and D-dimer levels were elevated. Serum albumin and haptoglobin...
| Variable | Value |
|----------|-------|
| **Blood tests** |       |
| WBC      | 8,300 /μL |
| Neutrophils | 84.8 % |
| Lymphocytes | 11.1 % |
| Monocytes | 3.5 % |
| Eosinophils | 0.5 % |
| Basophils | 0.1 % |
| RBC      | 2.4 x 10⁶ /μL |
| Hemoglobin | 7.3 g/dL |
| Reticulocytes | 32.5 % |
| Platelets | 7.9 x 10⁹ /μL |
| ESR      | 75 mm/h |
| TP       | 7.1 g/dL |
| Alb      | 2.5 g/dL |
| AST      | 40 IU/L |
| ALT      | 7 IU/L |
| LDH      | 350 IU/L |
| ALP      | 202 IU/L |
| BUN      | 20.7 mg/dL |
| Cr       | 1.94 mg/dL |
| CRP      | 6.22 mg/dL |
| Na       | 139 mEq/L |
| K        | 3.0 mEq/L |
| Cl       | 102 mEq/L |
| Ferritin | 304 ng/dL |
| IgG      | 2.768 mg/dL |
| IgA      | 407 mg/dL |
| IgM      | 84 mg/dL |
| C3       | 79 mg/dL |
| C4       | 12 mg/dL |
| PAIgG    | 670 ng/10⁶ cells |
| anti-dsDNA Ab | (−) |
| anti-Sm Ab | (−) |
| anti-SS-A Ab | (−) |
| anti-SS-B Ab | (−) |
| anti-U1RNP Ab | (−) |
| MPO-ANCA | (−) |
| PR3-ANCA | (−) |
| LAC (dRVVT) | 1.1 |
| anti-CLβ2GPI Ab | < 0.7 U/mL |
| Factor XIII | 82 % |
| Haptoglobin | < 10 mg/dL |
| ADAMTS-13 activity | 85 % |
| PT (%) | 67.2 % |
| APTT | 33.3 s |
| Fibrinogen | 234.0 mg/dL |
| D-dimer | 6.9 μg/dL |
| **Urinalysis** |       |
| Protein | (−) |
| Occult Blood | (3+) |
| Sugar | (−) |
| Nitrite | (−) |
| RBC | > 100 /HPF |
| WBC | 1-4 /HPF |
| UPCR | 0.69 g/gCre |
| β2-microglobulin | 2.350 μg/L |

**Ab** indicates antibody; **ADAMTS-13**, a disintegrin-like and metalloproteinase with thrombospondin type 1 motifs 13; **Alb**, albumin; **ALT**, alanine transaminase; **ANCA**, antineutrophil cytoplasmic antibody; **APTT**, activated partial thromboplastin time; **AST**, aspartate transaminase; **BUN**, blood urea nitrogen; **Cl**, chloride; **Cr**, creatinine; **CRP**, C-reactive protein; **ESR**, erythrocyte sedimentation rate; **Ig**, immunoglobulin; **K**, potassium; **LAC** (dRVVT), lupus anticoagulant dilute Russell's viper venom test; **LDH**, lactate dehydrogenase; **MPO**, myeloperoxidase; **Na**, sodium; **PT**, prothrombin time; **PP3**, proteinase3; **RBC**, red blood cells; **RN**, ribonucleoprotein; **TP**, total protein; **UPCR**, urinary protein-to-creatinine ratio; and **WBC**, white blood cells.

globin levels were decreased, whereas blood urea nitrogen, serum creatinine, C-reactive protein (CRP), ferritin, immunoglobulin G (IgG), IgA, and platelet-associated IgG levels were elevated. Antinuclear antibody titer was ×40, with speckled pattern. Urine was dark red, the result of urinary dipstick test for hematuria was 3+, urinary protein-to-creatinine ratio was 0.69 g/Cr, and urinary β2-microglobulin was 2.350 μg/L (Table 1).

Skin biopsy specimen taken from the purpuric lesion revealed leukocytoclastic vasculitis (Figure 1). Computed tomography revealed a nodular shadow with cavity in the left upper lobe and another nodular shadow adjacent to the pleura in the right lung (Figure 2A). Transbronchial lung biopsy specimen revealed pulmonary capillaritis (Figure 2B).

Upon admission, a form of vasculitis such as IgAV was suspected based on physical manifestations and laboratory findings, and administration of 55 mg/day (≈ 1 mg/kg/day) of prednisolone (PSL) was allocated. However, *Streptococcus pseudoporeninus* was subsequently isolated from two independent blood culture sets taken from the peripheral veins after admission. Transesophageal echocardiogram revealed the anatomical right ventricle with hypertrophied trabeculae carneae (Figure 3A). The aorta originated from the anatomical right ventricle, whereas the PA originated from the anatomical left ventricle, which was compatible with CCTGA. Mosaic blood flow with 4 m/s of peak velocity and 68 mmHg of peak gradient, which suggested a presence of moderate to severe PS, was observed at PV. Vegetation on the PV (1.7 × 1.2 cm in size) was identified (Figure 3B). Left-to-right atrial shunt flow, suggesting the presence of atrial septal defect, was found (Figure 3C). Left-to-right ventricular shunt flow was not apparent.

The presence of fever, history of CHD, and vegetation on PV found thereafter led to the diagnosis of IE. Computed tomography on admission suggested septic pulmonary embolism. PSL treatment was concluded on the fourth day of admission, and antibiotic administration was performed.

Caries were associated with bacterial entry, and five teeth were extracted by the dentist. Purpura gradually disappeared, and the levels of serum creatinine and CRP declined. Antibiotic discontinuation was scheduled for 6 weeks from then. However, macrohematuria persisted, and reappearance of purpura under continuous antibiotic administration was observed. Considering purpura, renal damage, and pathological findings on skin biopsy, the condition was diagnosed as IgAV, and administration of 55 mg/day of PSL was restarted. Purpura and macrohematuria improved after PSL resumption, and CRP levels normalized. No relapses were observed even after the gradual PSL decrease, and blood culture reassessment results were negative. Although systolic murmur present upon admission persisted, enlargement of the vegetation was not shown by repeated echocardiography. PSL dose was decreased to 20 mg/day during admission, and the patient was subsequently transferred to the initial psychiatric hospital (Figure 4).
Discussion

IgAV, formerly designated Henoch-Schölein purpura,7) is a form of vasculitis with IgA-immune complexes affecting small vessels of the skin, joints, digestive tracts, and kidneys. Upper respiratory tract infections precede most cases of IgAV,8) and A β-hemolytic Streptococcus, Staphylococcus, and parainfluenza viruses are commonly associated pathogens.9) Streptococcus strains and Staphylococcus strains are also common IE causative agents, with their common places of entry in the organism often associated with untreated caries and dental treatments. Although Streptococcus bovis group is known as a common cause of IE, a case of IE linked to Streptococcus dysgalactiae infection, a rare cause of IE, has also been reported.10) Other than caries lesions, atopic dermatitis is reported as a portal of bacterial entry into the bloodstream.11) Streptococcus pseudoporcinus, found in blood cultures in the present case, is a Streptococcus strain isolated from human rectum, upper respiratory, and genital tracts.12) The full physical examination on admission suggested that the oral cavity was the only potential site of bacterial entry. In the presented case, S. pseudoporcinus was presumed to invade the bloodstream through the oral cavity, where several caries were present. Previously re-
reported cases of IgA V and IE are shown in Table II.\textsuperscript{13-19} Streptococcus strains were identified as IE causative agents in four out of the seven cases, whereas there are currently no reports of IgA V and IE linked to \textit{S. pseudo-}
porcinus infection. Although preceding respiratory symptoms were not apparent in the presented case, physicians should be aware that \textit{S. pseudoporcinus} may be a pathogen that causes IgA V and IE concomitantly.

It is well known that cyanotic CHD, such as tetralogy of Fallot, are risk factors for IE. In Japanese Circulation Society 2017 Guideline on Prevention and Treatment of IE, the highest-risk group for IE includes cyanotic CHD, and moderate-risk group includes right-sided valvular diseases.\textsuperscript{20} Although in the presented case VSD had been closed, IE is reported to develop even after VSD closure.\textsuperscript{21} PV IE is extremely rare, occurring in only 1.5%-2% of total IE cases. A presumed reason for this entity’s rarity is the lower pressure within the right compared with the left heart.\textsuperscript{22} Connelly et al. reported 74% of patients > 18 years old who had a diagnosis of CCTGA complicated PS.\textsuperscript{3} In the present case, it is presumed that the patient had PS with CCTGA and that the PS caused the infective endocarditis.

As mentioned, bacterial infections are thought to take part in IgA V development. However, IgA V triggered by IE is rare. As shown in Table II, three out of the seven cases were complicated with CHD. Therefore, complications of IE should be considered in cases of IgA V with CHD. Al-

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**Table II.** Cases of IgA Vasculitis with Infective Endocarditis

| Case | Age | Sex | Causative bacteria | CHA | Affected sites | Therapy | Outcome | References |
|------|-----|-----|--------------------|-----|---------------|---------|---------|------------|
| 1    | 36  | M   | MSSA               | n.p.| Skin, joint, digestive tract, kidney | Antibiotics, steroid | Recovered | 13         |
| 2    | 37  | M   | \textit{Staphylococcus sp.} | n.p.| Skin, digestive tract, kidney | Antibiotics, small bowel resection, steroid, PE | Recovered | 14         |
| 3    | 49  | M   | Unknown            | VSD | Skin, joint, kidney | Antibiotics, VSD closure | Recovered | 15         |
| 4    | 47  | M   | \textit{Streptococcus galollyticus} | n.p.| Skin, kidney | Antibiotics, heart valve replacement | Recovered | 16         |
| 5    | 44  | F   | \textit{Streptococcus mitis} | VSD | Skin, kidney | Antibiotics | Recovered | 17         |
| 6    | 41  | F   | \textit{Streptococcus sp.} | n.p.| Skin, joint, digestive tract, kidney | Antibiotics, heart valve replacement | Recovered | 18         |
| 7    | 70  | F   | \textit{Streptococcus viridans} | n.p.| Skin | Antibiotics | Recovered | 19         |
| 8    | 48  | M   | \textit{Streptococcus pseudoporcinus} | CCTGA, VSD (closure), ASD | Skin, kidney, lung | Antibiotics, steroid | Recovered | Presented case |

ASD indicates atrial septal defect; CCTGA, congenitally corrected transposition of the great arteries; CHA, congenital heart anomalies; F, female; M, male; MSSA, methicillin-susceptible \textit{Staphylococcus aureus}; PE, plasmapheresis; and VSD, ventricular septal defect.
though spontaneous remission may be achieved in IgAV, immunosuppressants including steroids should be considered for IgAV depending on disease severity, particularly in cases of renal dysfunction. As depicted in Table II, several patients improved with antibiotic use, whereas steroid treatment was necessary in four cases. Further analyses are required to clarify the pathophysiology and optimal treatment of IE-related IgAV. To the best of our knowledge, there are currently no reports of IE-associated IgAV with underlying CCTGA. As previously mentioned, PS due to CCTGA may contribute to vegetation on PA. Therefore, this case suggests that CCTGA may be a risk factor for rare PV IE, and careful attention, together with proper dental care for patients with CCTGA, is important.

The present report describes the first case of IgAV triggered by PV IE with CCTGA. *Streptococcus* strains, including *S. pseudoporcinus*, may cause IgAV and IE concomitantly. It raises awareness of the importance of recognizing the occurrence of IE in IgAV patients, especially in those with CHD. CCTGA should be acknowledged as a risk factor for IE in the right-sided heart.

**Disclosure**

**Conflicts of interest:** None.

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