Fatal gastrointestinal bleeding due to IgA vasculitis complicated with tuberculous lymphadenitis: A case report and literature review

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Abstract
We report a case of IgA vasculitis that developed during the treatment of tuberculosis. Patients with tuberculosis who are on antituberculosis treatment can be administered steroids for severe disease or complications.

KEYWORDS
gastrointestinal bleeding, Henoch-Schönlein purpura, IgA vasculitis, leukocytoclastic vasculitis, tuberculosis

1 | INTRODUCTION

Immunoglobulin A vasculitis (IgAV), formerly called Henoch-Schönlein purpura, is a small vessel vasculitis that commonly occurs in children but can also affect people of all ages. Patients with this condition typically exhibit lower extremity purpura, arthritis, and hematuria. The gastrointestinal tract is affected in approximately one-half of patients with IgAV. Gastrointestinal symptoms include abdominal pain, nausea, vomiting, and occult or overt intestinal bleeding. The condition is generally self-limiting, and patients are usually managed with symptomatic treatment, but there are also severe cases with gastrointestinal bleeding, intussusception, infarction, and perforation.1-3 Although various infectious and chemical triggers are recognized, the underlying cause of IgAV remains unknown to date.4

We report the case of a patient with IgAV that developed during treatment of tuberculous lymphadenitis and later proved fatal because of deterioration of gastrointestinal lesions.

2 | CASE REPORT

A 71-year-old man with diabetes mellitus presented to our institution complaining of left axillary lymphadenopathy, which lasted for 1 month. Whole-body CT revealed lymphadenopathy with central necrosis in the left clavicle, axilla, and abdomen. Scars and nonspecific fibrosis were observed in the apex of both lungs, but no active lesions or tumors were found in the lungs or other organs. Mycobacterium tuberculosis was detected from the exudate of the left axillary lymph nodes but not from the sputum, and tuberculous lymphadenitis diagnosis was made. Thereafter, the patient was treated with isoniazid (300 mg), rifampicin (450 mg), pyrazinamide (1.5 g), and ethambutol (1 g) daily. On the 19th day of treatment, he complained of abdominal pain and diarrhea, and on day 20, palpable purpura appeared on both of his legs (Figure 1A).

Laboratory findings were as follows: white blood cell count, 11.3 × 10^3/μL; eosinophils, 0.2%; hemoglobin level, 13.2 g/dL; platelet count, 498 × 10^3/μL; international normalized ratio, 1.05; D-dimer, 61.9 μg/mL; percentage factor XIII...
activity, 77%; serum urea level, 20.9 mg/dL; creatinine level, 0.55 mg/dL; C-reactive protein level, 12.5 mg/dL; serum, IgA 472 mg/dL; IgE, 122 IU/mL. Meanwhile, the results of serologic tests for antinuclear antibodies, rheumatoid factor, antineutrophil cytoplasmic antibodies, and hepatitis B and C viruses were all negative. Urinalysis showed a protein level of 50 mg/dL, and the patient tested negative for occult blood. Abdominal computed tomography showed wall thickening of the duodenum and small intestine, and mild to moderate ascites (Figure 2). An endoscopic examination demonstrated highly reddish erosions in the antrum of the stomach (Figure 3A) and circular ulcers in the descending part of the duodenum (Figure 3B). Biopsy of skin lesions showed leukocytoclastic vasculitis (Figure 1B). The deposition of IgA on the vascular wall was not proven, and we reached a diagnosis of IgAV in combination with palpable purpura and digestive symptoms.

The clinical course is shown in Figure 4. We considered corticosteroid administration to improve his abdominal symptoms, but we believed that this also carried a risk of worsening of tuberculosis and diabetes, so we opted to manage the patient with fasting and rest instead. A small amount of bloody stool was noted on day 27, but upper and lower gastrointestinal endoscopy did not reveal a definite source of bleeding. On day 30, the patient suffered hypovolemic shock as a result of massive blood loss, and we started systemic management, blood transfusion, and venous corticosteroid administration. Simultaneously, acute respiratory distress syndrome caused by aspiration pneumonia, and acute kidney injury occurred, which indicated that the patient required artificial respiration and hemodialysis. Hemorrhage was relieved temporarily, but a large amount of bloody stool reappeared on day 50, making it impossible to manage his condition by conservative treatment. Although we considered performing abdominal surgery, his general condition was deemed too severe for this approach. Therefore, abdominal angiography was performed with sufficient informed consent. Because the extravasation of contrast agent was observed in the jejunum, we performed transcatheter arterial embolization. Consequently, blood loss decreased, but gastrointestinal perforation merged. The patient died on day 56. His relatives did not accept the autopsy.

3 | DISCUSSION

We report a patient who developed leukocytoclastic vasculitis during mycobacterial infection treatment. Leukocytoclastic vasculitis is a term for pathological finding, and several vasculitides show this finding. Among these vasculitides, IgAV was defined as vasculitis with IgA1-dominant immune deposits that invades small blood vessels in the skin and gastrointestinal tract and often cause arthritis. However, IgA deposition cannot be proven in all cases, and some cases are difficult to diagnose. In the present case, there was no opportunity to prove IgA deposition.
Biopsies from the gastric and duodenal mucosa did not contain appropriately sized blood vessels, and the involvement of vasculitis could not be pointed out. Therefore, we made the diagnosis of IgAV from clinical symptoms (ie, palpable purpura and abdominal pain) on the basis of the conventional criteria for Henoch-Schönlein purpura proposed by the American College of Rheumatology (ACR) and the European League Against Rheumatism.
| Reference         | Age (year) | Sex | Type of tuberculosis                      | Renal symptoms | Arthralgia/arthritis | Gastrointestinal symptoms | LCV | IgA deposit<sup>a</sup> | Treatment                                      | Outcome |
|-------------------|------------|-----|-------------------------------------------|----------------|----------------------|---------------------------|-----|-----------------------|-----------------------------------------------|---------|
| Dalgleish and Ansell | 44         | M   | Pulmonary tuberculosis                    | +              | −                    | +                         | NR  | NR                    | Supportive therapy                            | Survive |
|                   | 31         | F   | Pulmonary tuberculosis                    | +              | −                    | +                         | NR  | NR                    | Supportive therapy                            | Death   |
|                   | 47         | M   | Pulmonary tuberculosis                    | −              | +                    | −                         | NR  | NR                    | Supportive therapy                            | Survive |
| Washio et al      | 21         | M   | Tuberculous pleurisy                      | +              | −                    | −                         | NR  | +                     | Tuberculosis treatment                         | Survive |
| Sais et al        | 61         | F   | Tuberculous lymphadenitis                 | −              | −                    | −                         | +   | +                     | Tuberculosis treatment, Colchicine             | Survive |
| Lee et al         | 15         | F   | Pulmonary tuberculosis                    | −              | +                    | −                         | +   | NR                    | Tuberculosis treatment                         | Survive |
|                   | 13         | F   | Positive for blood mononuclear cell PCR   | −              | −                    | +                         | +   | NR                    | Tuberculosis treatment                         | Survive |
| Minguez et al     | 36         | M   | Pulmonary tuberculosis, Tuberculous pleurisy | −              | +                    | −                         | +   | NR                    | Tuberculosis treatment, NSAIDs                 | Survive |
| Islek et al       | 8          | F   | Pulmonary tuberculosis                    | −              | −                    | +                         | NR  | NR                    | Tuberculosis treatment                         | Survive |
| Kim et al         | 49         | M   | Tuberculous lymphadenitis                 | −              | +                    | −                         | +   | NR                    | Tuberculosis treatment                         | Survive |
| Isebe et al       | 54         | M   | Pulmonary tuberculosis                    | +              | −                    | −                         | +   | +                     | Tuberculosis treatment, Systemic corticosteroid| Survive |
| Carvalho et al    | 50         | M   | Pulmonary tuberculosis                    | −              | +                    | −                         | +   | NR                    | NSAIDs, antihistamines                         | Survive |
| Bueno Filho et al| 45         | F   | Tuberculous lymphadenitis                 | +              | −                    | −                         | +   | +                     | Tuberculosis treatment                         | Survive |
| Meziane et al     | 19         | M   | Pulmonary tuberculosis, Tuberculous pleurisy, Anal tuberculosis | −              | +                    | +                         | +   | −                     | Tuberculosis treatment                         | Survive |

Abbreviations: F, female; LCV, leukocytoclastic vasculitis; M, male; NR, not reported.
<sup>a</sup>IgA deposition in the vessels of skin or kidney.
| Reference | Age (year) | Sex | Type of tuberculosis          | Antituberculosis drugs | Interval\(^a\) (days) | Renal symptoms | Arthralgia/arthritis | Gastrointestinal symptoms | LCV | IgA deposit\(^b\) | Treatment | Outcome       |
|-----------|-----------|-----|-------------------------------|------------------------|------------------------|----------------|---------------------|--------------------------|-----|-----------------|-----------|---------------|
| McLachlan | 34        | M   | Tuberculous pericarditis,     | SM, INH               | 20                     | +              | +                   | +                        | NR | NR              | Systemic corticosteroid, ACTH | Survive         |
|           | 21        | M   | Pulmonary tuberculosis        | SM, INH               | >400                   | +              | +                   | +                        | NR | NR              | Withdrawal of antituberculosis drugs, Systemic corticosteroid | Survive         |
| Chan et al| 64        | M   | Pulmonary tuberculosis,       | INH, RFP, PZA, EB    | 150                    | +              | −                   | −                        | +  | +               | Withdrawal of antituberculosis drugs | Survive         |
|           | 41        | M   | Pulmonary tuberculosis        | INH, RFP, PZA, EB    | 120                    | +              | −                   | −                        | +  | +               | Withdrawal of antituberculosis drugs | Death           |
| Mishima et al | 34   | M   | Pulmonary tuberculosis,       | INH, RFP, SM         | 150                    | −              | +                   | −                        | NR | NR              | Systemic corticosteroid | Survive         |
| Han et al | 41        | M   | Disseminated tuberculosis     | Unknown              | 15                     | +              | −                   | −                        | +  | +               | Tuberculosis treatment | Survive         |
| Kitamura et al | 38  | M   | Pulmonary tuberculosis        | INH, RFP, PZA, EB    | 90                     | +              | +                   | +                        | +  | +               | Systemic corticosteroid | Survive         |
| Chanprapaph et al | 62 | M   | Pulmonary tuberculosis        | INH, RFP, EB         | 14                     | −              | −                   | −                        | +  | +               | Withdrawal of antituberculosis drugs, Topical corticosteroid, Antihistamines | Survive         |
| Bhatia et al | 14     | M   | Disseminated tuberculosis     | INH, RFP, PZA, EB    | 42                     | −              | −                   | −                        | +  | −               | Withdrawal of antituberculosis drugs, Systemic corticosteroid | Survive         |
| AVCU      | 12        | F   | Pulmonary tuberculosis        | INH, RFP, PZA, EB    | 29                     | −              | −                   | −                        | +  | NR              | Withdrawal of antituberculosis drugs, Systemic corticosteroid, Antihistamines | Survive         |
| Gargouri et al | 29  | M   | Pulmonary tuberculosis        | INH, RFP, PZA, EB    | 3                      | −              | +                   | −                        | +  | +               | Withdrawal of antituberculosis drugs | Survive         |
| Shim and Jung | 72     | M   | Pulmonary tuberculosis        | INH, RFP, EB         | 14                     | −              | −                   | +                        | +  | −               | Withdrawal of antituberculosis drugs, Systemic corticosteroid | Survive         |
| This case | 71        | M   | Tuberculous lymphadenitis     | INH, RFP, PZA, EB    | 19                     | +              | −                   | +                        | +  | NR              | Systemic corticosteroid | Death           |

Abbreviations: EB, ethambutol; F, female; INH, isoniazid; LCV, leukocytoclastic vasculitis; M, male; NR, not reported; PZA, pyrazinamide; RFP, rifampicin; SM, streptomycin.

\(^a\)Interval between the start of tuberculosis treatment and onset of symptoms of IgA vasculitis.

\(^b\)IgA deposition in the vessels of skin or kidney.
Gastrointestinal symptoms of IgAV include abdominal pain, nausea, vomiting, and occult or overt intestinal bleeding.\textsuperscript{1-3} The small intestine is the most frequently involved site in the gastrointestinal tract. The descending part of the duodenum is characteristically involved more often than the bulb. Endoscopic findings exhibit various forms such as diffuse mucosal redness, petechiae, hemorrhagic erosions, and ulcers.\textsuperscript{30} Although symptomatic treatment alone often improves symptoms of IgAV, corticosteroids are useful in cases with severe abdominal symptoms. Corticosteroids should be considered early in cases with severe abdominal symptoms, because early corticosteroid therapy has been reported to reduce the need for abdominal surgery.\textsuperscript{31} We delayed the use of corticosteroids for fear of worsening the course of tuberculosis, but this was not necessary because corticosteroids have also been reported to improve the prognosis of tuberculosis.\textsuperscript{32} In addition, we could have used higher doses of corticosteroids because rifampicin has been reported to reduce the effectiveness of corticosteroids.\textsuperscript{33} On the other hand, deaths caused by infections associated with the use of glucocorticoids have been reported in older adults with IgAV, and it is thought that their use requires careful attention.\textsuperscript{34}

In summary, there are only a few reports of IgAV complicated with tuberculosis, and the case we have presented marks the first fatal case attributed to gastrointestinal tract lesions. If IgAV caused by antituberculosis drugs is suspected, discontinuation of tuberculosis treatment is usually considered, but in cases marked by severe abdominal pain or gastrointestinal bleeding, use of corticosteroids should be considered. There is no need to withhold the use of corticosteroids because of the coexistence of tuberculosis. On the contrary, patients taking rifampicin may usually need more steroids. Careful attention should be paid when administering steroids to elderly patients with IgAV, as deaths from infections have been reported.

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CONFLICT OF INTEREST
The authors declare that there is no conflict of interest regarding the publication of this article.

AUTHOR CONTRIBUTIONS
NY: wrote the manuscript. ST, SK, AO, MK, TA, TM, JY and AM: revised the manuscript. SF: supervised the final draft.

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