Autoimmune polyglandular syndrome type III associated with antineutrophil cytoplasmic autoantibody-mediated crescentic glomerulonephritis

A case report and literature review

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Abstract

Rationale: Polyglandular autoimmune syndromes (PAS) are a heterogeneous group of rare diseases characterized by the association of at least 2 organ-specific autoimmune disorders, concerning both the endocrine and nonendocrine organs. Type III is defined as the combination of autoimmune thyroid disease and other autoimmune conditions (other than Addison disease), and is divided into 4 subtypes. We describe a patient with Hashimoto thyroiditis, adult-onset Still disease, alopecia, vasculitis, antineutrophil cytoplasmic antibody (ANCA)-mediated crescentic glomerulonephritis, and hyperparathyroidism. Co-occurrence of these 5 diseases allowed us to diagnose PAS type IIIc. The rare combination of these different diseases has not been reported before.

Patient concerns: A 51-year-old woman was admitted in April, 2019 after the complaint of an enlarged thyroid. She was diagnosed with Hashimoto thyroiditis at the age of 36. At age 40, she was diagnosed with an adult-onset Still disease. Three months before admission, she experienced renal insufficiency. After admission, she was diagnosed with hyperparathyroidism.

Diagnosis: Renal biopsy revealed renal vasculitis and crescentic nephritis. Antineutrophil cytoplasmic autoantibody showed that human perinuclear ANCA and myeloperoxidase ANCA were positive. Therefore, the patient was diagnosed with vasculitis and ANCA-mediated crescentic glomerulonephritis. After admission, parathyroid single-photon emission computed tomography/computed tomography fusion image demonstrated the presence of hyperparathyroidism.

Interventions: The patient was treated with high-dose methylprednisolone pulse therapy (0.1 g/d) for vasculitis and ANCA-mediated crescentic glomerulonephritis, calcium and vitamin D3 (600 mg/d elemental calcium [calcium carbonate] and 2.5 μg/d active vitamin D₃) for hyperparathyroidism, and levotiroxine sodium (50 μg/d) for Hashimoto thyroiditis.

Outcomes: Up to now, serum thyroid-stimulating hormone, total triiodothyronine, total thyroxine, free triiodothyronine, and free thyroxine were within the normal ranges. Patient’s renal function did not deteriorate.

Lessons: We report a patient with Hashimoto thyroiditis, adult-onset Still disease, alopecia, vasculitis, ANCA-mediated crescentic glomerulonephritis, and hyperparathyroidism, which is a very rare combination. We present this case as evidence for the coexistence of several different immune-mediated diseases in the clinical context of a PAS IIIc.

Abbreviations: anti-Tg = antithyroglobulin, anti-TPO = antithyroid peroxidase, ANCA = antineutrophil cytoplasmic antibody, FT₃ = free triiodothyronine, FT₄ = free thyroxine, PAS = polyglandular autoimmune syndromes, TSH = thyroid-stimulating hormone, TT₃ = total triiodothyronine, TT₄ = total thyroxine.

Keywords: adult-onset Still disease, antineutrophil cytoplasmic autoantibody, autoimmune polyglandular syndromes, crescentic glomerulonephritis, Hashimoto disease
1. Introduction

As the incidence of autoimmune disease has gradually increased over the past 10 years, polyglandular autoimmune syndromes (PAS) should be paid significant attention by physicians. PAS are a group of autoimmune disorders characterized by endocrine tissue destruction causing multiple gland malfunction. The classification of PAS proposed in 1980 by Neufeld and Blizzard[1] based on clinical features included 4 main types of PAS: type I, type II, type III, and type IV. In PAS III, autoimmune thyroiditis occurs together with another organ-specific autoimmune disease. PAS III can be further divided into 3 subtypes: PAS IIIa, autoimmune thyroiditis with immune-mediated diabetes mellitus; PAS IIIb, autoimmune thyroiditis with pernicious anaemia; and PAS IIIc, autoimmune thyroiditis with vitiligo, alopecia, and/or other organ-specific autoimmune disease.[2] In this article, we present a rare case of patient affected by PAS IIIc (Hashimoto thyroiditis accompanied with vasculitis, antineutrophil cytoplasmic antibody [ANCA]-mediated crescentic glomerulonephritis, adult-onset Still disease, and hyperparathyroidism).

2. Case report

A 51-year-old woman was admitted in April, 2019 after the complaint of an enlarged thyroid. Fifteen years before admission, during her annual physical examination, her titers of antithyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) increased in the serum. Thyroid ultrasound revealed an enlarged thyroid gland with diffuse hypoechoic lesion. Her free thyroxine (FT4) slightly decreased, and her thyroid-stimulating hormone (TSH) increased. She was diagnosed with Hashimoto thyroiditis and treated with levothyroxine sodium (Na) (50 μg/d). After 3 years, she stopped taking levothyroxine Na. At age 40, she was diagnosed with adult-onset Still disease due to fever, rash, and arthralgia. She was treated with methylprednisolone for 18 days, and her condition sufficiently improved. Hence, she was discharged from the hospital.

Three months before admission, she experienced alopecia and renal insufficiency (creatinine 265 μmol/L; glomerular filtration rate 22.03 mL/min). Considering her renal insufficiency, renal biopsy was performed. Light microscopy revealed renal vasculitis and crescentic nephritis (Fig. 1A). Serum antinuclear antibodies were positive (1:100). Antineutrophil cytoplasmic autoantibody

Figure 1. (A) Renal biopsy (hematoxylin and eosin staining ×200) showing the interstitial and perivascular infiltrate comprising lymphocytes and eosinophils, fibrinoid necrosis, and glomerular, parietal epithelial cell hyperplasia. (B) ⁹⁹Tc technetium scan revealing a high tracer uptake in the left upper thyroid. (C) Parathyroid single-photon emission computed tomography/computed tomography fusion image showing a slightly lower density below the left thyroid with a slightly higher concentration of radioactivity (as indicated by the red arrows).
showed that perinuclear ANCA and myeloperoxidase ANCA were positive. Therefore, vasculitis and ANCA-mediated crescentic glomerulonephritis were considered. The patient was treated with high-dose methylprednisolone pulse therapy (0.1 g/d).

**Table 1**

**Laboratory data on admission.**

| Test                          | Value               |
|-------------------------------|---------------------|
| Fasting glucose              | 5.74 (normal, 3.9–6.1 mmol/L) |
| Urea nitrogen                | 9.13 (normal, 2.8–7.6 mmol/L) |
| Creatinine                   | 162.65 (normal, 48–100 μmol/L) |
| Na                            | 137.6 (normal, 136–145 mmol/L) |
| K                             | 4.42 (normal, 3.5–5.2 mmol/L) |
| Ca                            | 2.16 (normal, 2.1–2.65 mmol/L) |
| P                             | 1.44 (normal, 0.81–1.45 mmol/L) |
| Aspartate transaminase        | 1.735 (normal, 0.08–2.2 U/L)  |
| Alanine aminotransferase      | 1.735 (normal, 0.08–2.2 U/L)  |
| Albumin                       | 39.99 (normal, 35–52 g/L)     |
| Lactate dehydrogenase         | 164.02 (normal, 80–248 μmol/L) |
| γ-glutamyl transferase        | 42.41 (normal, 6–87 μmol/L)    |
| Alkaline phosphatase          | 52.24 (normal, 30–120 μmol/L)  |
| Total bilirubin               | 8.7 (normal, 5–21 μmol/L)      |
| Ferritin                      | 173.5 (normal, 5–130 mg/mL)    |
| Folate                        | 7.4 (normal, ≥3.2 mg/mL)       |
| Vitamin B12                   | 207.4 (normal, 180–916 μg/mL)  |
| Hemoglobin                    | 88 (normal, 110–150 g/L)       |
| Red blood cells               | 3.24 (normal, 3.5–5.0 × 10^{12}/L) |
| White blood cells             | 7.46 (normal, 4.0–10.0 × 10^{12}/L) |
| Lymphocyte                    | 2.81 (normal, 0.8–4.0 × 10^{11}/L) |
| Platelets                     | 477 (normal, 100–300 × 10^{9}/L) |
| Mean corpuscular volume       | 81.8 (normal, 80–100 μL)        |
| Mean corpuscular hemoglobin   | 26.5 (normal, 27–34 pg)         |
| Mean corpuscular hemoglobin concentration | 325 (normal, 320–360 μL) |
| Parathyroid hormone           | 152.4 (normal, 15–65 pg/ml)     |

| Test                          | Value               |
|-------------------------------|---------------------|
| Urinalysis                     |                     |
| Protein                       | 2±                  |
| Glucose                       | Negative            |
| Blood                         | Negative            |
| Ketone                        | Negative            |
| Autoantibodies                |                     |
| Anti-TPO                      |                     |
| Anti-Tg                       |                     |
| Anti-TRAb                     |                     |
| Isolet cell antibody          |                     |
| Anti-SSA                      |                     |
| Anti-SSB                      |                     |
| Anti-SM/RNP                   |                     |
| Antinuclear antibodies        |                     |
| Anti-ASMA                     |                     |
| Anti-SID-70                   |                     |
| Anti-ds DNA                   |                     |
| Anti-mitochondrial antibodies |                     |
| Anti-Jo-1                     |                     |
| cANCA                         |                     |
| pANCA                         |                     |
| MPO-ANCA                      |                     |
| Rheumatic factor              |                     |
| Antinuclear antibody          |                     |
| Immunoglobulin G              | 20 (normal, <0.2 μg/L) |
| Immunoglobulin M              | 23.2 (normal, 8–16 μg/L) |
|      | 3.1 (normal, 0.5–2.2 μg/L) |

Abnormal values are indicated in bold.

**Table 2**

The results of thyroid hormone follow-up.

| Hormone analyses                  | First test (2019–2–28) | Second test (2019–3–15) | Third test (2019–4–15) | Last test (2019–5–16) |
|-----------------------------------|------------------------|-------------------------|------------------------|-----------------------|
| TSH (normal, 0.372–4.94 mU/L)     | 0.005                  | 0.284                   | 5.08                   | 4.82                  |
| TT3 (normal, 1.35–5.15 nmol/L)    | None                   | 1.29                    | 1.19                   | 2.88                  |
| FT4 (normal, 70–106 pmol/L)       | None                   | 46.5                    | 38                     | 78                    |
| FT3 (normal, 3.1–6.8 pmol/L)      | 10.76                  | 2.49                    | 2.28                   | 3.56                  |
| FT4 (normal, 12–22 pmol/L)        | 30.3                   | 6.4                     | 5.6                    | 13                   |

FT3 = free triiodothyronine, FT4 = free thyroxine, TSH = thyroid-stimulating hormone, TT3 = total triiodothyronine, TT4 = total thyroxine.
This study was conducted in accordance with the recommendations of the Ethics Committee of the China-Japan Union Hospital of Jilin University, and all the participants provided written informed consent for the publication of this case report.

3. Discussion

Considering the subtle manifestations of Hashimoto thyroiditis and its insufficient clinical features, the early detection of this disease is significantly hard. Hashimoto thyroiditis has a variety of clinical manifestations, which can be characterized by hyperthyroidism, hypothyroidism, and a normal gland. In our case, hormone analyses on admission (2019-2-28) showed increased circulating FT3 (10.76 pmol/L) and FT4 (30.3 pmol/L) with a decreased TSH level (0.005 mIU/mL) in the serum. Hormone analysis after hospital discharge showed that TSH level gradually increased, and FT3, FT4, total triiodothyronine (TT3), and total thyroxine (TT4) gradually decreased. The third hormone analysis (2019-4-15) showed the low level of circulating TT3 and TT4 (TT3, 1.19 nmol/L; TT4, 2.28 pmol/L) and TT4 (TT4, 38 nmol/L; FT4, 5.6 pmol/L) with an increased TSH level (5.08 mIU/mL) in the serum. This was due to the release of thyroxine after thyroid follicle damage, rather than increased thyroxine synthesis; thyroxine levels will decrease over time. Subsequently, hyperthyroidism disappeared and even transitioned into hypothyroidism. In our case, the patient was finally diagnosed with hypothyroidism and received levothyroxine Na (0.5 mg/d). The last hormone analysis (2019-5-16) showed that the sera TSH, TT3, TT4, FT3, and FT4 were within the normal ranges. In the case of the presented patient, chronic kidney disease was due to hyperparathyroidism. Patients with chronic kidney disease are at risk of calcium and phosphorus metabolism disorders and osteoporosis. The parathyroid gland was stimulated by hypocalcemia and hyperphosphatemia for a long time, and it was easy to secrete a large amount of parathyroid hormone; subsequently, parathyroid hyperplasia was observed.

Polyglandular autoimmune syndrome is defined as multiple endocrine endorgan failure presenting over a variable period of time. Patients with PAS have an increased incidence of autoimmune diseases affecting both the endocrine and nonendocrine organs. The latter disorders include alopecia, vitiligo, pernicious anemia, Addison disease, insulin-dependent type 1 diabetes, rheumatoid arthritis, myasthenia gravis, chronic active hepatitis, and primary biliary cirrhosis. PAS III includes autoimmune thyroid disease plus another autoimmune disorder in the absence of Addison disease. If the other autoimmune disorder is insulin-dependent diabetes mellitus, it is designated as type IIIa. Type IIIb involves pernicious anemia, whereas type IIIc includes vitiligo, alopecia, and/or other organ-specific autoimmune disease. Our patient had Hashimoto thyroiditis, alopecia, adult-onset Still disease, vasculitis, ANCA-mediated crescentic glomerulonephritis, and hyperparathyroidism. Accordingly, she was classified as type IIIc. By reviewing the literature (Table 3), we confirm that this is a rare combination that has never been reported. Moss et al. described a patient with type IIIc PAS who presented with antifibroblast membrane antibody disease. They incorporated the antibasement membrane antibody disease into the spectrum of PAS. Shimomura et al. reported a case with PAS III associated with Sjögren syndrome and autoimmune neutropenia. They considered autoimmune disorders as the cause of this condition. In our case, multiple autoimmune disorders including autoimmune thyroiditis, adult-onset Still disease, and positive autoantibodies might be associated with the onset of vasculitis and ANCA-mediated crescentic glomerulonephritis. At present, the mechanism of PAS is unclear, but its occurrence is associated with the genetic susceptibility associated with the human leukocyte antigen. Tadmor et al. have hypothesized that organs derived from the same embryonal germ layer share

Table 3

| Year   | Authors                       | Sex/age | Clinical manifestation | Type          |
|--------|-------------------------------|---------|------------------------|---------------|
| 1989   | Takamatsu et al.
1989   | F/40                           | Type 1 diabetes mellitus | PAS IIIa      |
| 1993   | Papadopoulou and Haldengen    | F/52    | Hashimoto thyroiditis  | PAS IIIa      |
| 1994   | Kim et al.                    | F/24    | Pernicious anemia      | PAS IIIb      |
| 1994   | Moss et al.                   | N/A     | Antibasement membrane antibody disease | PAS IIIc      |
| 1995   | Rodriguez Quinones et al.     | F/16    | Type 1 diabetes mellitus | PAS IIIa      |
| 2000   | Berberoglu et al.             | F/14    | Chronic atrophic gastritis | PAS IIIc      |
| 2003   | Papi et al.                   | F/41    | Thyroid hemiagenesis   | PAS IIIc      |
| 2003   | Shimomura et al.              | F/57    | Premature ovarian failure | PAS IIIa      |
| 2004   | Bahceci et al.                | F/24    | Common variable immunodeficiency | PAS IIIc      |
| 2004   | Ugur-Altm et al.              | N/A     | Thyroid autoimmunity   | PAS IIIc      |
| 2006   | Melnikuk and Vompan          | N/A     | Thyroiditis            | None          |
| 2006   | Oki et al.                    | F/58    | Graves disease         | PAS IIIa      |
| 2006   | Furuuchi et al.               | F/51    | Type 1 diabetes mellitus | PAS IIIa      |
| 2007   | Molina-Garrido et al.         | M/54    | Hyperparathyroidism    | PAS IIIc      |
| 2007   | Rodriguez Martin et al.       | F/28    | Thyroid autoimmunity   | PAS IIIb      |
| 2008   | Efthimiou et al.              | N/A     | Autoimmune thyroid disease | PAS IIIa      |
| 2008   | Lubraska et al.               | F/20    | Hashimoto thyroiditis  | PAS IIIa      |

(continued)
Table 3 (continued).

| Year       | Authors                  | Sex/age | Clinical manifestation                      | Type               |
|------------|--------------------------|---------|---------------------------------------------|--------------------|
| 2009       | Briscoe et al[23]        | M/37    | Myasthenia gravis                           | None               |
|            |                          |         | Vascular hemophilia                         |                    |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
| 2009       | Fujikawa et al[24]       | F/55    | Pernicious anemia                           | PAS IIIa           |
|            |                          |         | Ulcerative colitis                          |                    |
|            |                          |         | Alopecia areata                             |                    |
| 2010       | Mazzolaki et al[25]      | F/38    | Type 1 diabetes mellitus                    | PAS IIIa           |
|            |                          |         | Hashimoto thyroiditis                        |                    |
|            |                          |         | Autoimmune gastritis                         |                    |
|            |                          |         | Vitiligo                                     |                    |
| 2011       | Quinlivan et al[26]      | M/33    | Autoimmune hypothyroidism                   | PAS IIIc           |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
|            |                          |         | Graves disease                               |                    |
| 2011       | Katsanis et al[27]       | M/19    | Type 1 diabetes mellitus                    | PAS IIIa           |
|            |                          |         | Graves disease                               |                    |
| 2012       | Farkas et al[28]         | M/37    | Insulin-dependent diabetes mellitus         | PAS IIIc           |
|            |                          |         | Ulcerative colitis                           |                    |
|            |                          |         | Hashimoto thyroiditis                        |                    |
|            |                          |         | Vitiligo                                     |                    |
| 2013       | Krysiak et al[29]        | N/A     | Cushing syndrome                             | None               |
|            |                          |         | Autoimmune endocrine disorders              |                    |
|            |                          |         | Graves disease                               |                    |
| 2014       | Trivedi et al[30]        | F/17    | Insulin-dependent diabetes mellitus         | PAS IIIa           |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
|            |                          |         | Graves disease                               |                    |
| 2014       | Choudhury et al[31]      | F/35    | Type 1 diabetes mellitus                    | PAS IIIc           |
|            |                          |         | Hypothyroidism                               |                    |
|            |                          |         | Hydropsytyroidal thymectomy                 |                    |
| 2012       | Yokote et al[32]         | F/73    | Type 1 diabetes mellitus                    | PAS IIIa           |
|            |                          |         | Chronic thyroiditis                          |                    |
|            |                          |         | Late-onset multiple sclerosis               |                    |
| 2013       | Mizokami et al[33]       | F/41    | Type 1 diabetes mellitus                    | PAS IIIa           |
|            |                          |         | Graves disease                               |                    |
| 2013       | Iwashashi et al[34]      | F/42    | Type 1 diabetes mellitus                    | PAS IIIa           |
|            |                          |         | Graves disease                               |                    |
| 2013       | Kanazawa et al[35]       | M/40    | Type 1 diabetes mellitus                    | PAS IIIa           |
|            |                          |         | Chronic thyroiditis                          |                    |
|            |                          |         | Idiopathic portal hypertension              |                    |
| 2013       | Wei et al[36]            | F/62    | Insulin-dependent diabetes mellitus         | PAS IIIb           |
|            |                          |         | Acute pontal thyroiditis                     |                    |
|            |                          |         | Pernicious anemia                           |                    |
| 2013       | Melcscu et al[37]        | F/34    | Graves disease                               | PAS IIIc           |
|            |                          |         | Hypothyroidism                               |                    |
|            |                          |         | Alopecia                                     |                    |
| 2014       | Kaszycki and Drzewowski[38]| F/37 | Systemic lupus erythematosus                | PAS IIIa           |
|            |                          |         | Hashimoto thyroiditis                        |                    |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
|            |                          |         | Vitiligo                                     |                    |
|            |                          |         | Autoimmune urticaria                         |                    |
| 2014       | Ocampo Chaparro et al[39]| M/92    | Insulin-dependent diabetes mellitus         | PAS IIIa           |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
|            |                          |         | Autoimmune hypothyroidism                   |                    |
| 2014       | Inoke et al[40]          | F/51    | Hypothyroidism                               | PAS IIIa           |
|            |                          |         | Autoimmune hypothyroidism                   |                    |
|            |                          |         | Celiac disease                               |                    |
|            |                          |         | Sicca syndrome                               |                    |

Table 3 (continued).

| Year       | Authors                  | Sex/age | Clinical manifestation                      | Type               |
|------------|--------------------------|---------|---------------------------------------------|--------------------|
| 2014       | Hadwen et al[41]         | F/30    | Insulin-dependent diabetes mellitus         | PAS IIIa           |
|            |                          |         | Graves disease                               |                    |
|            |                          |         | Vitiligo                                     |                    |
| 2014       | Batra et al[42]          | F/6     | Autoimmune thyroiditis                       | PAS IIIa           |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
| 2014       | Duman et al[43]          | M/1     | Anti-TPO-positive hypothyroidism             | PAS IIIc           |
|            |                          |         | Hashimoto thyroiditis                        |                    |
|            |                          |         | Alopecia                                     |                    |
| 2014       | Bujak et al[44]          | F/10    | Chronic urticaria                            | PAS IIIa           |
|            |                          |         | Anti-smooth muscle antibody                  |                    |
|            |                          |         | Pernicious anemia                            |                    |
| 2014       | Noraisykin et al[45]     | F/62    | Pernicious anemia                            | PAS IIIb           |
|            |                          |         | Autoimmune thyroiditis                       |                    |
| 2014       | Kim et al[46]            | F/32    | Type 1 diabetes mellitus                    | PAS IIIa           |
|            |                          |         | Autoimmune thyroiditis                       |                    |
|            |                          |         | Primary hypothyroidism                       |                    |
| 2015       | Krysiak and Okole[47]    | F       | Insulin-dependent diabetes mellitus         | PAS IIIa           |
| 2015       | De Marco et al[48]       | F/51    | Autoimmune thyroiditis                       | APS III             |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
|            |                          |         | Pernicious anemia                            |                    |
| 2015       | de Sousa et al[49]       | F/34    | Autoimmune thyroiditis                       | PAS IIIb           |
| 2015       | Kurzumi et al[50]        | M/40    | Pernicious anemia                            | PAS IIIa           |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
| 2015       | Cucci et al[51]          | N/A     | Vogt-Koyanagi-Harada syndrome               | PAS IIIc           |
|            |                          |         | Common variable immunodeficiency             |                    |
| 2016       | Pescione et al[52]       | F/34    | Type 1 diabetes mellitus                    | PAS IIIa           |
|            |                          |         | Autoimmune Hashimoto thyroiditis            |                    |
| 2016       | Ciapol and Amero[53]     | F/52    | Celiac disease                               | PAS IIIc           |
|            |                          |         | Autoimmune thyroiditis                       |                    |
|            |                          |         | Vitiligo                                     |                    |
| 2016       | Honey et al[54]          | F/71    | Autoimmune thyroid disease                   | PAS IIIb           |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
|            |                          |         | Pernicious anemia                            |                    |
| 2016       | Takahashi et al[55]      | F/66    | Deep vein thrombosis                         | PAS IIIb           |
|            |                          |         | Graves disease                               |                    |
| 2017       | Kohki et al[56]          | F/54    | Autoimmune thyroiditis                       | PAS IIIc           |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
|            |                          |         | Vitiligo                                     |                    |
| 2017       | Sato et al[57]           | F/49    | Chronic spontaneous urticaria                | PAS IIIc           |
|            |                          |         | Graves disease                               |                    |
| 2018       | Alam and Elzawawy[58]    | F/22    | Hashimoto thyroiditis                        | PAS III             |
|            |                          |         | Autoimmune hypothyroidism                   |                    |
|            |                          |         | Celiac disease                               |                    |
| 2018       | Morita et al[59]         | M/6     | Hashimoto thyroiditis                        | PAS II              |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
|            |                          |         | Pernicious anemia                            |                    |
| 2018       | Orwa et al[60]           | F/51    | Autoimmune Hashimoto thyroiditis            | PAS IIIc           |
|            |                          |         | Type 1 diabetes mellitus                    |                    |
|            |                          |         | Pernicious anemia                            |                    |
| 2018       | Jamrólska and Bossowski[61]| F/15 | Graves disease                               | PAS IIIc           |
|            |                          |         | Myasthenia gravis                            |                    |
|            |                          |         | Autoimmune thyroiditis                       |                    |
|            |                          |         | Ectodermal dysplasia                         |                    |
|            |                          |         | Immune deficiency                            |                    |
|            |                          |         | Hypothyroidal urticaria                      |                    |
|            |                          |         | Growth hormone deficiency                    |                    |
|            |                          |         | Myasthenia gravis                            |                    |
| 2019       | Our case                 | F/51    | Pernicious anemia                            | PAS IIIc           |
|            |                          |         | Graves disease                               |                    |
|            |                          |         | Myasthenia gravis                            |                    |
|            |                          |         | Autoimmune thyroiditis                       |                    |
|            |                          |         | Hyperparathyroidism                          |                    |
|            |                          |         | Adult Still disease                          |                    |
|            |                          |         | Sarcoid disease                              |                    |

(continued)
common specific antigens. Recent studies have shown that polymorphisms of the T-cell regulatory gene (cytotoxic T-lymphocyte-associated antigen 4) are associated with PAS.\textsuperscript{[61]}

Evidently, the immunological mechanisms are crucial in the development of the autoimmune disease, and the intervention of activated self-reacting T cell is considered to be necessary in the majority of the cases to achieve complete destruction of the target organ.\textsuperscript{[62]}

Therapies regarding the different components of PAS III are similar whether they occur as single or in multiple associations with other autoimmune diseases. However, it is worth noting that Hashimoto disease can present as transient thyrotoxicosis; hence, antithyroid drugs and radiotherapy with iodine-131 must be carefully considered when treating Hashimoto disease. Additionally, the thyroid hormone replacement therapy in patients with autoimmune hypothyroidism may result in adrenal failure because thyroxine may enhance hepatic corticosteroid metabolism. Thus, before initiating the therapy with thyroxine, it is crucial to investigate the possible coexistence of an underlying adrenal insufficiency.\textsuperscript{[67]}

4. Conclusions
We report a patient with Hashimoto thyroiditis, adult-onset Still disease, alopecia, vasculitis, ANCA-mediated crescentic glomerulonephritis, and hyperparathyroidism, which is a very rare disease, alopecia, vasculitis, ANCA-mediated crescentic glomerulonephritis, and hyperparathyroidism are associated with PAS.\textsuperscript{[65]}

We present this case as evidence for the coexistence of several different immune-mediated diseases in the clinical context of a PAS III.

Author contributions
Data curation: Shiyuan Tian.
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