

Generalised Blisters and Respiratory distress: A Case of Bullous Systemic Lupus Erythematosus

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Abstract: Tjasma's syndrome is a benign combination of ascites, pleural effusion, and elevated CA-125 occurring in patients with systemic lupus erythematosus. Reports of Tjasma's syndrome are scarce. An elevated CA-125 level often suggests the possibility of the presence of a malignant tumor. We report a case of generalised erythema and blisters with pruritus, massive unilateral pleural effusion and elevated CA-125. This patient was finally diagnosed with bullous systemic lupus erythematosus after exclusion of tumour and other maculopapular disorders. We hope that this particular case may provide a more comprehensive and novel diagnostic idea of systemic lupus erythematosus and pleural effusion, avoiding unnecessary anxiety, laboratory tests and surgical interventions.

Keywords: systemic lupus erythematosus, bullous systemic lupus erythematosus, pleural effusion, Tjasma's syndrome, CA-125

Clinical Information

A 27-year-old female patient recently presented to our dermatology department. The patient had erythema and blisters distributed across her back with significant itching that had been noticed five months prior to the consultation. Following treatment with topical glucocorticosteroids, the patient experienced slight relief from the rash and itching. In the three months leading up to the consultation, the patient began to experience chest tightness and shortness of breath after physical activity. The erythema and blisters on her skin gradually spread throughout her body, including the face, trunk, and extremities, accompanied by intense itching. Upon inquiry, we discovered that the patient had no history of other diseases or suspicious medication use, and there was no family history of autoimmune diseases. Subsequently, a detailed physical examination and laboratory tests were conducted. The patient exhibited numerous erythema and blisters with varying morphology scattered widely on her face, trunk, and limbs, as shown in [Figure 1](#). The examination findings suggested a decreased white blood cell count, antinuclear antibody titre of 1:1000, and the presence of a large pleural effusion in the right lung. Chest CT is shown in [Figure 2](#). Pleural fluid analysis shows: (1)Positive Rivalta test; (2)Cell count of 800×10^6 /L, WBC count of 600×10^6 /L; (3)CRP of 8.88 mg/L; Albumin of 28.8 g/L; (4)ADA of 13.00 U/L;LDH of 119 U/L; (5) No fungi or acid-fast bacilli detected; (6)No malignant cells in pathology. The subepidermal blistering and a neutrophil-predominant dermal infiltrate can be seen on dermatopathological examination of the tissue taken from the skin of the left leg. Inflammatory cell infiltration with predominantly neutrophils was seen in the superficial dermis, as shown in [Figure 3](#). Direct immunofluorescence examination suggested that IgG and C3 could be seen as linear deposits in the basement membrane zone, as shown in [Figure 4](#). The diagnosis of bullous systemic lupus erythematosus (BSLE) is based on the diagnostic criteria developed by Yell:¹ (1) Systemic lupus erythematosus (SLE) fulfilling the criteria of the American Rheumatism Association (ARA); (2) a chronic, widespread, non-scar- ring blistering eruption, a subepidermal blister with acute neutrophil-predominant inflammation in the upper dermis without evidence of LE; (3) immunoglobulin (Ig) and complement deposition at the BMZ on direct immunofluorescence (DIF), and immune deposits ultra- structurally localized on or beneath the lamina densa. The patient met the 2019 diagnostic criteria for SLE:² white blood cell count $2750/\text{mm}^3$ (3 points); serosal: pleural exudate (5



Figure 1 The erythematous macules and vesicles are scatteredly distributed on the patient's face, trunk, and extremities. (A). Front face; (B).Side of the face; (C). Hands; (D). Legs).

points); and complement C3 0.36 g/L (normal value 0.78–2.10 g/L) (3 points), totalling 11 points. This criterion suggests that a diagnosis of SLE can be made by meeting the criteria of an elevated ANA and a score greater than 10 points. This patient also presented with an elevated CA-125 (95.8 U/mL), which is often indicative of tumour risk. After a tuberculosis gamma interferon release test, Desmoglein 1 and 3, anti-BP180 and 230 antibodies and imaging studies, we excluded the patient from having tuberculosis infection, autoimmune subepidermal blistering disease (including bullous pemphigoid, linear IgA bullous dermatosis) and tumour. The patient's pleural fluid ADA was below 45 U/L, and the tuberculosis gamma interferon release assay (IGRA) and tuberculosis-specific cellular immune response (TB-IGRA) were both negative, which do not match the characteristics of tuberculous pleurisy. The patient underwent a lymph node puncture biopsy, which indicated lymphoid hyperplastic changes, suggesting an inflammatory process. Thoracentesis and pleural fluid tests, including fungal smear, acid-fast smear, and pathological examination, were performed, and all results were negative. Ultimately, we considered that the patient might have BSLE combined with benign pleural effusion based on the relevant diagnostic criteria.¹ The patient's rash and symptoms such as itching and dyspnoea gradually improved after receiving methylprednisolone, hydroxychloroquine and symptomatic treatment. The patient has been followed up for a year and a half and has not experienced any recurrence.

Discussion

SLE is an immunological disease involving multiple systems. BSLE is a rare type of systemic lupus erythematosus, with an incidence of less than 1%. Its clinical features are mainly manifested as the appearance of tense



Figure 2 A large amount of pleural effusion is noted in the right lung on chest CT.

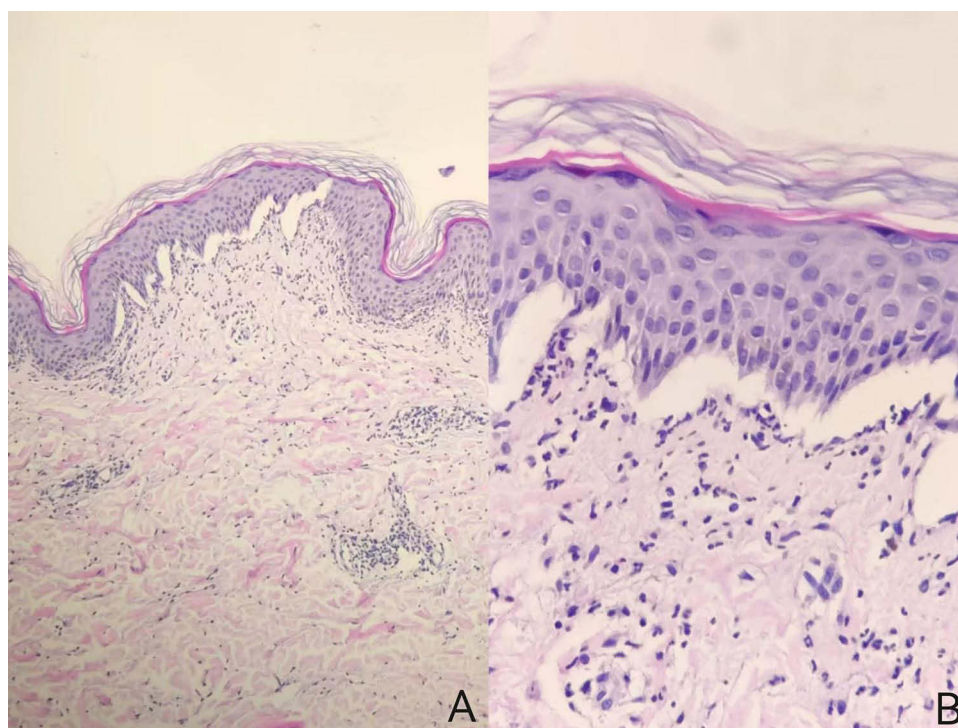


Figure 3 The dermis is infiltrated by inflammatory cells predominantly consisting of neutrophils. (A). H&E, $\times 40$; (B). H&E, $\times 100$.

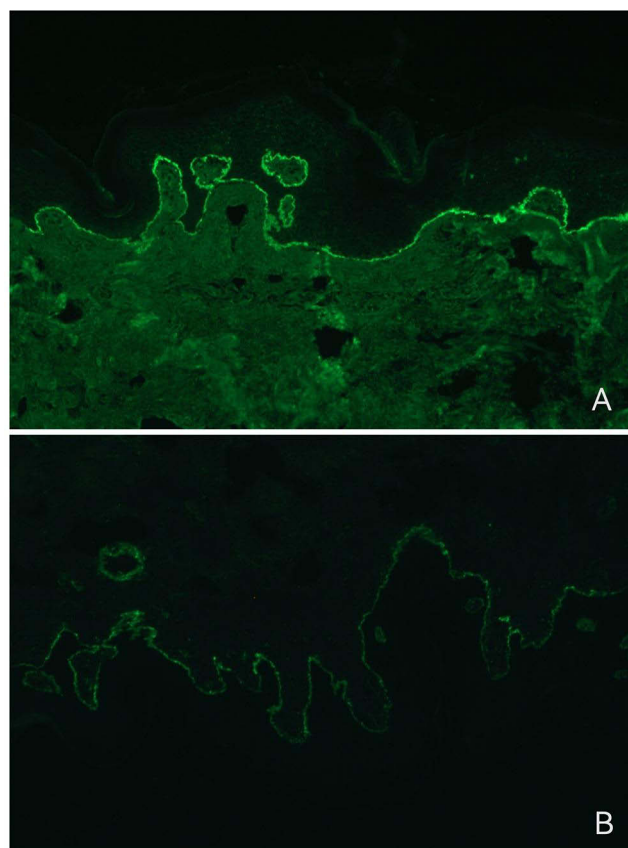


Figure 4 Linear deposition of IgG and C3 at the basement membrane zone on direct immunofluorescence examination. (A).IgG; (B).C3).

blisters and macules of varying sizes on the basis of erythema or normal skin, and the blister fluid is clear or bloody. The lesions are often widely distributed, occurring on sun-exposed or non-sun-exposed areas.³ Tjasma's syndrome is a benign combination of ascites, pleural effusion, and elevated CA-125 occurring in patients with systemic lupus erythematosus.⁴ In recent years, there have been several case reports of SLE combined with pleural effusion, ascites, and elevated CA 125 in Tjasma's syndrome.^{5–8}

When SLE presents with pleuritis, it typically shows bilateral small or moderate pleural effusions. Large unilateral pleural effusion as the initial manifestation of SLE is uncommon and is often misdiagnosed as tuberculous pleurisy. The patient's tumor marker results showed CA-125 levels above the normal range, and superficial lymph nodes (cervical, axillary, and inguinal) were enlarged.

Under normal conditions, CA-125 is synthesized in various tissues throughout the body and is maintained at a relatively low level, such as in the cornea and conjunctiva of the ocular surface, the respiratory tract, the endometrium of the fallopian tubes, the endometrium of the cervix, the endometrium of the uterus, the pleura, the pericardium, the peritoneum, and secretory breast tissue. However, when these tissues are stimulated or become pathological, the synthesis of CA-125 increases, leading to an elevated serum CA-125 level. CA-125 is elevated to varying degrees in benign conditions such as chronic kidney failure, adenomyosis, endometriosis, hepatitis, and cirrhosis. In this particular case, we suspect that damage to the aforementioned tissues during the progression of SLE has led to an increase in CA-125 levels.

Considering the patient's autoantibody results and clinical presentation, we concluded that the pleural effusion was caused by bullous systemic lupus erythematosus. This phenomenon is relatively rare and has not attracted much attention, and the etiology of the disease is still unclear. There are few reports of patients with BSLE.

Conclusion

We hope that this case will provide a more comprehensive and novel diagnostic idea of BSLE and pleural effusion, avoiding unnecessary anxiety, laboratory tests and surgical interventions. When encountering patients in clinical practice with unilateral pleural effusion, elevated CA-125, and multiple blisters, do not overlook the possibility of BSLE. For patients presenting with dyspnea as the chief complaint, clinicians often pay more attention to respiratory or circulatory system diseases. We also hope that this will raise public awareness and emphasis on skin lesions. Revealing the pathogenesis of this combination of disease and symptoms will be a direction we can delve into in the future.

Ethics and Consent Statements

Our institution does not require ethical approval for reporting individual cases or case series. We have obtained written informed consent from the patient to include his anonymized information, including images, in this publication.

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Disclosure

Mingyuan Ren and Yijia He are co-first authors for this study. The authors have no conflicts of interest to declare in this work.

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