Pancytopenia as a first presentation of Late-onset SLE; A Case Report

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Abstract

Introduction:
Systemic lupus erythematosus (SLE) is a systemic immune condition, classically seen in young to middle-aged females and can present with cutaneous, renal, hematological, neurological, and/or other manifestations at the time of diagnosis or may develop over the course of the disease. Late-onset SLE or SLE in the elderly is a subtype that differs from the classic SLE in age group, clinical presentation, involvement of organs, and severity.

Case presentation: A 63 years old Syrian female noted to have pancytopenia. The patient was diagnosed with lupus upon obtaining clinical presentations and serological marker, along with high titers of the antinuclear antibody (ANA) and/or anti-double-stranded DNA (anti-dsDNA) antibody. The patient was managed with glucocorticoids and mycophenolate mofetil therapy, which led to a rapid response.

Conclusion: This case underscores the importance of acknowledging any abnormal presentation of SLE when clinical suspicion remains high and conducting further investigation. It is also vital to formulate a personalized management plan for each patient based on their comorbidities and tolerance to immunosuppressive medications, leading to improvement in overall patient prognosis.

Keywords: Pancytopenia, SLE, Elderly SLE, prednisone, mycophenolate mofetil, Thrombocytopenia

Introduction
Systemic lupus erythematosus (SLE) is a systemic, immune condition with unknown etiology, classically seen in young to middle-aged females, with a wide variable course and prognosis (1).

Its generalized symptoms include fever, arthralgia, weight loss, and fatigue. In addition, other manifestations such as cutaneous, renal, hematological, neurological, and/or others at the time of diagnosis may develop throughout the disease (2).

According to several epidemiological reports, late-onset SLE has been noted to be present in patients over the age of 50-60 in the past 25 years(1).

Although it is rare and uncommon, the term SLE in the elderly is used to differentiate it from the classic SLE (1). Fewer than 10% of patients may first present with a single, severe manifestation from one organ system, such as the kidneys or central nervous system(3), which related to high morbidity and increased mortality rate
The spectrum of hematologic manifestations in SLE is very broad, including lymphopenia, anemia, thrombocytopenia, or pancytopenia. In some cases, lymphadenopathy and/or splenomegaly are also found. The vast majority of these manifestations correlate with high disease activity. However, many of these alterations have a multifactorial cause that must be taken into account to decide the suitable therapeutic approach (4). We report the case of a geriatric female in whom late-onset SLE with pancytopenia was discovered. We hope that this report serves as an aid to future health professionals during the diagnosis and management of this disease.

Case history/Examination:

A 63-year-old Syrian female with a past medical history of hypertension, presented to the outpatient clinic at Modern Medical Hospital in January 2023, with an oral ulcer, fever of 38.2°C, and fatigue for the past three months. Medications before admission were amlodipine 10 mg, and aspirin 81 mg.

The physical examination was unremarkable except for pallor seen on the conjunctiva, and ulcers on the lips (Figure-1). Her blood pressure was 135/82 mmHg with a pulse of 76 beats per minute.

Figure-1: Ulcers on the lower lip

Laboratory examination revealed leukopenia: 2300/mm³ (n=4000-11000), anemia: hemoglobin 8.3 g/l(n:12-14), and thrombocytopenia: 132,000 (n=150,000-400,000), elevated inflammatory marker: C-reactive protein 23.8 mg/dl (n<6), and erythrocyte sedimentation rate 128 mm/h (n=0-20). The rest of the chemical tests were normal. Protein electrophoresis showed a polyclonal peak on gamma. Bone marrow aspiration was compatible with pancytopenia, with no evidence of malignancies (normocytic normochromic anemia, leukopenia, and thrombocytopenia) (Figure-2,3).

Figure-1; pancytopenia
Figure-2: pancytopenia
The patient’s chest X-ray showed no acute cardiopulmonary abnormality. A CT scan of the chest abdomen and pelvis was also ordered, which showed no abnormalities.

Further, the workup revealed a strongly positive antinuclear antibody (ANA) screen (1:320 titers) with normal anti-Sm, anti-SS-A (Ro), anti-SS-B (La), anti-Scl-70, anti-Jo-1, anti-dsDNA, and C3 and C4 levels.

**Differential diagnosis, investigation and treatment:**

Additionally, cryoglobulins, antineutrophil cytoplasmic antibodies (ANCA), and anti-GBM antibodies. Virology including EBV, parvovirus, herpes simplex 1/2, HIV, and hepatitis panels was all negative. Blood and urine cultures were negative.

In line with the recommendations, the patient has started prednisone 60 mg once daily, and 200mg/day hydroxychloroquine, with improvement of fatigue, absence of fever, and increased level of white blood cells(3600mm³), hemoglobin(8.5g/l), platelet(152000), in addition to decreases in ESR(98mm/h) and
CRP (13.3 mg/dl) levels after 15 days. 4 weeks later, the patient had no clinical complaints, and she gained 2 kilograms of weight. The laboratory tests were white blood cells (5200 mm³), hemoglobin (8.9 g/l), platelet (252000 mm³), ESR (45 mm/h) and CRP (3.4 mg/dl) levels. We had begun to taper the prednisone dose 5 mg/week, and continued on 200 mg/day hydroxychloroquine, with a follow-up duration every 3 months.

**Outcome and follow up:**

In August during a routine follow-up, after 6 months of disease onset, she had no clinical complaints, and she gained 10 kilograms of weight. Her laboratory tests were white blood cells (9600 mm³), hemoglobin (9.6 g/l), platelet (348000), ESR (32 mm/h) and CRP (1.3 mg/dl) levels. She continued on 200 mg/day hydroxychloroquine.

**Discussion**

SLE is a chronic systemic disorder, commonly affecting young women (1). The patient in our case is a 63-year-old Syrian female known to have late-onset SLE despite lacking the typical constellation of symptoms.

In patients with an initial atypical presentation, the American College of Rheumatology (ACR) /EULAR 2019 criteria can help in diagnosis. The ACR classifications require at least six clinical manifestations and serological markers, with positive ANA at >1/80, for diagnosing SLE (Image-1) (5).

Image-1:
Our patient had a fever, fatigue, oral ulcers, leukopenia, anemia, and thrombocytopenia, in addition to the positivity of ANA1/160.

Late-onset SLE constituted 2-12%, representing a specific group of SLE, older than 50 years as the minimum age of disease onset (1, 3), and often initially missed leading to a significant delay in diagnosis (3). Delay in diagnosis is often due to the decreased prevalence of frequent disease presentations such as oral ulcers, photosensitivity, or malar rash and attributing symptoms to other comorbid conditions seen in elderly patients (1,3). The time from symptom onset to diagnosis was reported as being as high as 60 months for late-onset SLE compared with 19 to 24 months for adult-onset SLE (2,3).

Late-onset SLE is different from early-onset SLE in sex and ethnic prevalence, clinical symptoms and signs, organ involvement manifestation, disease activity and severity, and prognosis (1,3). These differences are due to age-related variations in environmental and/or host factors responsible for disease expression and variations in sex hormones (1, 3,6). For example, mucocutaneous manifestations are less frequent; while serositis, cytopenias, and pulmonary involvement are more frequent (1-4). Our patient had constitutional symptoms and pancytopenia. Aggressive management of pancytopenia is necessary because it is a significant risk factor for morbidity and mortality in SLE (1,3).

Some studies have also shown that late-onset SLE patients have an increased prevalence of positive RF, and anti-Ro/anti-La antibodies, hypocomplementemia, and higher incidence of elevated creatinine and a decreased creatinine clearance. These patients also have a higher incidence of Sjögren’s syndrome, which often coexists with SLE, although the exact rationale for this has not been clarified (1,3). These tests were negative in our case, and the patient had no symptoms of eye or mouth dryness.

Therapy aimed to control the disease activity and prevent its flares. All lupus patients should receive hydroxychloroquine, at a dose not exceeding 5 mg/kg/day. During chronic maintenance treatment, glucocorticoids should be minimized to less than 7.5 mg/day and, when possible, withdrawn. Immunomodulatory medications such as methotrexate, azathioprine, and mycophenolate can expedite the tapering/discontinuation of glucocorticoids. In persistently active or relapsing flaring disease, belimumab should be considered; rituximab or cyclophosphamide may be considered in organ-threatening and refractory disease. First-line treatment for pancytopenia is glucocorticoid, but there is no consensus to guide second-line therapy. Rituximab and immunosuppressive drugs can be used in refractory cases (1). Induction therapy with glucocorticoids can inhibit inflammation, whereas maintenance therapy with immunosuppressive medication can dampen the immune-mediated damage to the organs. However, these patients do not require immunosuppression as frequently due to lower rates of nephritis (1). Our patient had managed in line with the recommendations, as he was treated with 60 mg/day of predlone that was withdrawn, and 200 mg/day of hydroxychloroquine.

Fortunately, the prognosis for newly diagnosed (SLE) patients has improved markedly over the past several decades (6). However, it is important to highlight that late-onset SLE presents with less systemic involvement compared to classic SLE. Late-onset SLE patients were more likely to die due to treatment complications and sepsis. Age >50 years, male gender, and low C3 levels may be linked to an increased risk of death due to SLE (7,8).

According to the study by Boddaert J, et al. (1), there were no late-onset SLE presented with hematological manifestations.

We found 2 cases in the literature of late-onset SLE, but with nephritis (6,10), and one case with pancytopenia and macrophage-activated syndrome (7).

Herein, we found some cases of young SLE presented with pancytopenia (8).

The key take-home points from this case are the following: (1) Consider the diagnosis of late-onset SLE and LN in elderly patients with pancytopenia; and other typical SLE symptoms, (2) Serology tests, imaging, and other procedures such as renal biopsy should be used when available.

**Conclusion**:
Late-onset SLE or SLE in the elderly is a subtype that differs from the classic SLE in age group, clinical presentation, involvement of organs, and severity.

underscores the importance of acknowledging any abnormal presentation of SLE when clinical suspicion remains high and conducting further investigation.

It is also vital to formulate a personalized management plan for each patient based on their comorbidities and tolerance to immunosuppressive medications, leading to improvement in overall patient prognosis.

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Conflict of interest
No competing interests exist.

Human Ethics
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The data used to support the finding of the study are available from the corresponding author upon request.

References


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