Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Pancytopenia as a first presentation of late-onset systemic lupus erythematosus: a case report

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Introduction: Systemic lupus erythematosus (SLE) is a systemic immune disease that classically occurs in young to middle-aged women and may present with cutaneous, renal, haematologic, neurological, and/or other symptoms at the time of diagnosis. Late-onset SLE or SLE in the elderly is a subtype that differs from classic SLE in terms of age group, clinical symptoms, organ involvement and severity.

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

Discussion: Late-onset SLE accounts for 2–12% of SLE patients with a minimum age of onset of 50 years and older, leading to significant delays in diagnosis. Late-onset SLE differs from early-onset SLE in terms of sex and ethnicity prevalence, clinical symptoms and signs, development of organ damage, disease activity and severity, and prognosis .Some studies have also shown that late-stage SLE patients have higher rates of RF and anti-Ro/anti-La antibody positivity, lower complement titre, and higher incidence of elevated creatinine and decreased creatinine clearance. First-line treatment of pancytopenia is glucocorticoid. In refractory cases, rituximab and immunosuppressants can be used.

Conclusion: It is important to assess any unusual presentation of SLEs when clinical suspicion remains high and conducting further laboratory and imaging investigation.

Keywords: elderly SLE, mycophenolate mofetil, pancytopenia, prednisone, SLE, thrombocytopenia

Introduction

Systemic lupus erythematosus (SLE) is a systemic immune disease of unknown aetiology that classically occurs in young to middle-aged women[1]. Frequent symptoms include fever, joint pain, weight loss, and fatigue. In addition, other systemic organs symptoms may find at the disease onset or develop as the disease progresses[2]. Late-onset SLE was found to occur in patients over 50–60 years of age[1]. Although rare and not frequent, the term geriatric SLE is used to distinguish it from classic SLE[1]. Less than 10% of patients may initially experience a single severe symptom such as kidneys or central nervous system involvement[3]. The spectrum of haematologic manifestations in SLE is very wide and includes lymphopenia, anaemia, thrombocytopenia, or pancytopenia, and in some cases, lymphadenopathy and/or splenomegaly may occur. However, many of these changes have multifactorial causes and must be considered when determining the appropriate treatment approach[4]. We report a case of an elderly woman diagnosed with late-onset SLE with pancytopenia. We hope that this report will be useful for future medical professionals in diagnosing and treating this disease.

Our case is compliant with SCARE 2023 criteria[5], and this work is submitted on the research registry dashboard.

HIGHLIGHTS

- Late-onset systemic lupus erythematosus (SLE) accounts for 2–12% of SLE patients with a minimum age of onset of 50 years and older, leading to significant delays in diagnosis.
- Late-onset SLE differs from early-onset SLE in terms of sex and ethnicity prevalence, clinical symptoms and signs, development of organ damage, disease activity and severity, and prognosis.
- It is important to assess any unusual presentation of SLE when clinical suspicion remains high.

Case history/examination

A 63-year-old female with a past medical history of hypertension, presented to the outpatient clinic in January 2023, with recurrent oral ulcer, fever of 38.2°C*, and fatigue for the past three months.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2024) 86:3025–3028

Received 21 October 2023; Accepted 19 February 2024

Published online 6 March 2024

http://dx.doi.org/10.1097/MS9.0000000000001891

Medications before admission were amlodipine 10 mg, and aspirin 81 mg.

The physical examination including the musculoskeletal examination, skin examination was unremarkable except for pallor seen on the conjunctiva, and ulcers on the lips (Fig. 1). Her blood pressure was 135/82 mmHg with a pulse of 76 beats per min. No enlargement in lymph nodes was observed. No hepatospelomegaly was found.

Laboratory examination revealed leukopenia: 2300 mm^3 ($n = 4000–1100$), anaemia: haemoglobin 8.3 g/l (n:12–14), and thrombocytopenia:132 000) ($n = 150\ 000–400\ 000$),iron value 48 mcg/dl ($n = 60–170$), total iron binding capacity 298 mcg/dl ($n = 240–450$), serum ferritin 87 ng/ml ($n = 12–150$), direct coombs was negative, reticulocyte 1% ($n = 0.5–2.5\%$),vitamin B6 4.2 ug/l ($n = 3.4–65.2$), vitamin B12645 pg/ml (1 $n = 60–950$), vitamin B1 3.2 µg/dl ($n = 2.5–7.5$), vitamin D 23 ng/ml ($n = 20$ and 40), elevated inflammatory marker: C-reactive protein (CRP) 23.8 mg/dl ($n < 6$), and erythrocyte sedimentation rate128 mm/h^1) ($n = 0–20$).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 or atypical cells, normocytic normochromic red blood cells, leukopenia, and thrombocytopenia, with normal maturation and proliferation (Fig. 2).

The patient's chest X-ray showed no acute cardiopulmonary abnormality. A computed tomography (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 titres, homogenous pattern) 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.

The patient was diagnosed to have SLE, due to the positive ANA, in addition to fever, fatigue, recurrent oral ulcers, anaemia, thrombocytopenia, and leukopenia , and the role out of other causes.

In line with the recommendations, the patient has started prednisone 60 mg once daily, and 200 mg/d hydroxychloroquine,

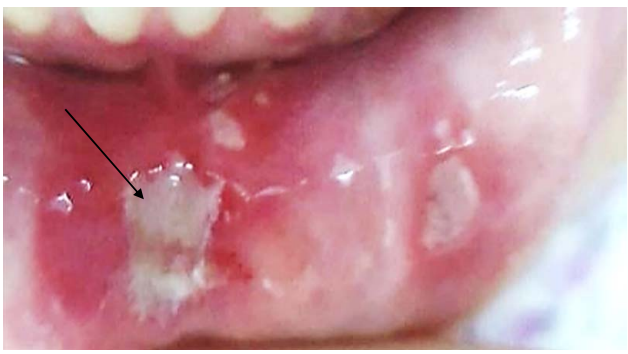

Figure 1. Ulcers on the lower lip.

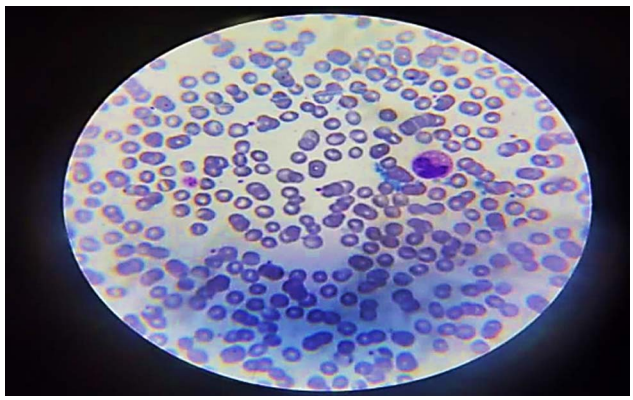

Figure 2. Pancytopenia.

with improvement of fatigue, absence of fever, and increased level of white blood cells (3600 mm^3), haemoglobin (8.5 g/l), platelet (152 000), in addition to decreases in ESR (98 mm/h^1 and CRP (13.3 mg/dl) levels after 15 days.4 weeks later, the patient had no clinical complaints, and she gained 2 kg of weight. The laboratory tests were white blood cells (5200 mm^3), haemoglobin (8.9 g/l), platelet (252 000 mmm), ESR (45 mm/h1 and CRP (3.4 mg/dl) levels. We had begun to taper the predlone dose 5 mg/wk, and continued on 200 mg/d 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 kg of weight Her laboratory tests were white blood cells (9600 mm^3), haemoglobin (9.6 g/l), platelet (348 000), ESR (32 mm/h1 and CRP (1.3 mg/dl) levels. She continued on 200 mg/d hydroxychloroquine.

Discussion

SLE often affects young women[1]. Our patient is a 63-year-old Syrian woman. For patients who initially present with atypical symptoms, the American College of Rheumatology/European League against Rheumatism (ACR)/EULAR) 2019 criteria may be helpful in diagnosis, which requires at least six clinical symptoms and positive serological markers with an ANA greater than 1/80 to diagnose SLE[4], as in our patient. In addition to being ANA1/160 positive, our patient had fever, malaise, oral ulcers, leukopenia, anaemia, and thrombocytopenia.

Late-onset SLE accounts for 2–12% of SLE patients with a minimum age of onset of 50 years and older, leading to significant delays in diagnosis[3]. The period from symptom onset to diagnosis has been reported to be up to 60 months for late-onset SLE, compared to 19–24 months for adult-onset SLE[2,3]. Late-onset SLE differs from early-onset SLE in terms of gender and ethnicity prevalence, clinical symptoms and signs, development of organ damage, disease activity and severity, and prognosis[3]. These differences are due to changes in sex hormones as well as age-related variations in environmental and/or host factors that contribute to disease expression[6]. Pancytopenia is a significant

risk factor for morbidity and mortality in SLE and therefore requires aggressive treatment[4].

Some studies have also shown that late-stage SLE patients have higher rates of RF and anti-Ro/anti-La antibody positivity, lower complement titre, and higher incidence of elevated creatinine and decreased creatinine clearance[7]. All lupus patients should receive hydroxychloroquine at dose not exceeding 5 mg/kg/d[8]. During chronic maintenance therapy, glucocorticoids should be reduced to less than 7.5 mg/d and discontinued if possible[9]. Immunomodulatory drugs such as methotrexate, azathioprine, and mycophenolate may accelerate glucocorticoid taper/discontinuation[1]. Research on belimumab, rituximab, calcineurin inhibitors, and IFN-blocking agents has advanced in the recent period[10]. Belimumab should be considered for persistently active or recurrent disease. Rituximab or cyclophosphamide may be considered for organ-threatening, refractory disease[11]. Higher complete remission rates and a more favourable safety profile suggest that low-dose IL-2, obinutuzumab, rituximab, and belimumab may be superior to the current control as treatments for lupus nephritis[12]. The interferon (IFN) pathway has been extensively studied in the context of autoimmunity pathogenesis, given that multiple genetic polymorphisms are associated with an increased risk of developing SLE. The elevation in IFN levels promotes the survival and differentiation of B cells by inducing BAFF[10]. Calcineurin inhibitors such as voclosporin, cyclosporine, and tacrolimus act directly against T lymphocytes, aiming to decrease their activation and the release of cytokines resulting from it. These drugs are used as a second-line treatment in combination with mycophenolate mofetil[13]. First-line treatment of pancytopenia is glucocorticoid. In refractory cases, rituximab and immunosuppressants can be used[11–13].

Induction therapy with glucocorticoids can suppress inflammation, whereas maintenance therapy with immunosuppressants can reduce immune-mediated organ damage[14]. However, these patients require less frequent immunosuppression due to their lower incidence of nephritis[15]. Our patient was treated with discontinued predrone 60 mg per day and hydroxychloroquine 200 mg per day. Fortunately, the prognosis of newly diagnosed (SLE) patients has improved significantly in recent decades[6]. However, it is important to emphasize that late-onset SLE has less systemic involvement than classic SLE. Patients with late-onset SLE were more likely to die from treatment complications and sepsis[16]. Age older than 50 years, male sex, and low C3 levels may be associated with an increased risk of death[17]. According to a study by Boddaert *et al*.[6], there was no late-onset SLE with haematologic manifestations. We found two cases with late-onset SLE with nephritis in the literature[6,18]. A case of pancytopenia and macrophage activation syndrome[17]. The key finding from our case is to consider the diagnosis of SLE in elderly patients with pancytopenia. Other diagnostic procedures such as serology, imaging, and renal biopsy should be performed when possible.

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 disease severity.

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

Ethical approval

This Case Series was approved by The Ethical approval was given by the Ethical committee of the Faculty of Medicine, Damascus University (CD: 7823,2023).

Consent

Written informed consent was obtained from patient for publication and any accompanying images. Copies of the written consent are available for review by the Editor-in-Chief of this journal on request.

Source of funding

None.

Author contribution

N.K. wrote the discussion, G.H. wrote the abstract and the results, M.H.S. wrote the discussion, T.D. examined the patient, and M.K. re-write and reviewed the study acknowledgements given by any of the authors.

Conflicts of interest disclosure

The author declares no conflicts of interest.

Research registration unique identifying number (UIN)

1. Name of the registry: Ghina Hiader.
2. Unique Identifying number or regiistration ID: research registry9585.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-theregistry#home/registrationdetails/652154daa9e51e0028c57b44/.

Guarantor

Ghina Hiader.

Data availability

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

Provenance and peer review

Not commissioned, externally peer-reviewed.

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