Sultan Qaboos University Med J, November 2014, Vol. 14, Iss. 4, pp. e582–584, Epub. 14TH Oct 14
Submitted 3RD Dec 13
Revisions Req. 6TH Feb & 7TH May 14; Revisions Recd. 14TH Apr & 19TH May 14
Accepted 5TH Jun 14

ONLINE CASE REPORT

# A Possible Case of Systemic Lupus Erythematosus Presenting with Generalised Oedema

*Kawther T. El-Shafie,[1] Ali Al-Shirawi,[2] Buthaina Al-Maskari,[3] Nafisa Samir[1]

# حالة محتملة لمرض الذئبة الحمامية الجهازية ظهر في شكل تورم عام في الجسم

كوثر الشفيع، علي الشيراوي، بثينة المسكري، نفيسة سمير

**ABSTRACT:** Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown aetiology affecting various systems within the body. We report the case of a patient with generalised subcutaneous oedema as the only presenting feature, which led to the possible diagnosis of SLE without a specific cause. The patient presented to the Sultan Qaboos University Hospital in Muscat, Oman, in April 2013. The oedema had been present for two years before admission. Other potential causes of oedema in patients with SLE were excluded, including SLE of renal origin and SLE due to protein-losing enteropathy or drugs. This was confirmed by the patient's normal serum albumin level and negative proteinuria. Laboratory investigations showed high levels of positive antinuclear antibodies (>1:640), positive anti-double-stranded deoxyribonucleic acid results, high levels of anti-$\beta_2$-glycoprotein 1 and immunoglobulin M and low levels of both complement components 3 and 4. The oedema improved immediately in response to steroids and immunosuppressive medications. Physicians should be aware that generalised subcutaneous oedema can be the only manifestation of SLE.

***Keywords:*** Edema; Systemic Lupus Erythematosus; Case Report; Oman.

**الملخص:** الذئبة الحمامية الجهازية هو أحد أمراض المناعة الذاتية وسببه غير معروف، وهو يؤثر على أجهزة مختلفة داخل الجسم. وهنا ننشر حالة مريض كان يشكو فقط من تورم عام تحت الجلد، وهو ما قادنا إلى إمكانية تشخيص الحالة كحالة الذئبة الحمامية الجهازية دون سبب محدد. زار المريض مستشفى جامعة السلطان قابوس في مسقط، عمان خلال شهر أبريل 2013. كان التورم موجوداً لمدة سنتين. وتم استبعاد الأسباب المحتملة الأخرى للتورم في المرضى المصابين بمرض الذئبة الحمراء، بما في ذلك فقد بروتينات بواسطة الكلى أو الأمعاء. وتم التأكد من ذلك لأن تركيزالألبومين في مصل الدم كان طبيعيا ، ولم يوجد بروتين في البول. أظهرت الفحوصات المخبرية مستويات عالية من إيجابية الأجسام المضادة للنواة (1:640>)، ونتائج إيجابية الحمض الخلوي الصبغي المضادة، ووجود مستويات منخفضة من كل من مكونات تكملة 3 و 4. وتحسن التورم فورا عقب إعطاء الاستيرودات والأدوية المثبطة للمناعة. نقترح أن يدرك الأطباء أن التورم تحت الجلد المعمم يمكن أن يكون مظهرا من مظاهر الذئبة الحمامية الجهازية.

**مفتاح الكلمات:** ورم؛ الذئبة الحمامية الجهازية؛ تقرير حالة؛ عمان.

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) is an autoimmune disease of unknown aetiology affecting various systems within the body. It has various clinical and laboratory manifestations and a variable course and prognosis. Polyserositis and subcutaneous oedema are common manifestations of SLE. They are usually associated with nephrotic syndrome, constrictive pericarditis, congestive heart failure, portal hypertension, malignancy and pleural infection.[1] However, generalised subcutaneous oedema as the first manifestation of SLE and without a specific cause is rare.[1] A case of a young female with generalised subcutaneous oedema as the initial and only presenting feature of SLE is reported.

## Case Report

A 21-year-old unmarried female university student with no previous medical problems presented to the Sultan Qaboos University Hospital in Muscat, Oman, in April 2013 with symptoms of generalised swelling of the body which had been present for two years. The swelling was located mainly in the face, abdomen and lower limbs and was gradually increasing over time. The swelling was at its worst in the morning, to the extent that sometimes she was unable to open her eyes fully for 30 minutes after waking. Over the two-year period, the patient noted that her weight had increased by 17 kg; she had begun regular exercise, but had not succeeded in losing any weight. The patient denied experiencing any of the following symptoms: joint pain, chest pain, shortness of breath, palpitations, dizziness, skin rashes, oral ulcers, hair loss, changes in appetite or menstrual problems. There was no history of allergies or any significant family history. The patient was not currently taking any medication.

A physical examination revealed puffiness of the face and pitting pedal oedema extending up to the

*Departments of [1]Family Medicine & Public Health and [2]Medicine, Sultan Qaboos University Hospital; [3]Family Medicine Training Programme, Oman Medical Specialty Board, Muscat, Oman*
**Corresponding Author e-mail: kawther@squ.edu.om*

**Table 1:** Investigation results indicative of a diagnosis of systemic lupus erythematosus in the reported patient

| Investigation | Result | Normal range |
|---|---|---|
| ESR in mm/hour | 2 | 35–52 |
| C-reactive protein in mg/L | <1 | 0–5 |
| Albumin-adjusted calcium in mmol/L | 2.31 | 2.15–2.55 |
| Phosphate in mmol/L | 1.2 | 0.81–1.45 |
| Serum creatinine in µmol/L | 43 | 45–84 |
| Urea in mmol/L | 2.7 | 2.8–8.1 |
| Potassium in mmol/L | 3.6 | 3.5–5.1 |
| Sodium in mmol/L | 139 | 135–145 |
| Urine | Negative for blood and protein | - |
| Urine excretion over 24 hours in g | 0.09 | 0.05–0.14 |
| Urine albumin in mg/L | <3 | 3.0–400 |
| Total creatine kinase in U/L | 48 | 26–192 |
| Serum cortisol in nmol/L | 359 | 185–624 |
| Complement component 3 in g/L | 0.50 | 0.79–1.52 |
| Complement component 4 in g/L | 0.07 | 0.16–0.38 |
| Total protein in g/L | 69 | 66–87 |
| Antinuclear antibody levels | >1:640 | - |
| Anti n-DNA antibody levels in IU/mL | 150* | 0–45 |
| Rheumatoid factor | Negative | - |
| Extractable nuclear antigens | Strong positive anti-Sjögren's syndrome antigen A | - |
| Anti-ribonuclear proteins | Positive | - |
| Anti-Ro52 antibodies | Positive | - |
| Anti-histones antibodies | Moderately positive | - |
| Anti-Smith antigen | Weakly positive | - |
| Other nuclear antigens | Negative | - |
| Anti-β-$_2$ glycoprotein 1 (immunoglobulin G) in U/mL | 1 | 0–20 |
| Anti-β-$_2$ glycoprotein 1 (immunoglobulin M) in U/mL | 105† | 0–20 |
| Anti-cardiolipin antibody (immunoglobulin G) in U/mL | 9 | 0–12 |
| Anti-cardiolipin antibody (immunoglobulin M) in U/mL | 51 | 0–12 |
| Complete blood count | Normal | - |
| Liver function tests | Normal | - |
| Thyroid function tests | Normal | - |
| Thyroid antibodies | Negative | - |
| Uric acid | Normal | - |
| Lipids | Normal | - |
| Electrocardiogram | Normal | - |
| Chest X-ray | Normal | - |

*ESR = erythrocyte sedimentation rate; n-DNA = native double-stranded nuclear deoxyribonucleic acid. *Highly suggestive of systemic lupus erythematosus. †Strongly positive.*

knees. There were no indicators of pallor, jaundice or lymphadenopathy and all of her vital signs were within the normal range. Her weight was 60 kg and a systematic examination was normal, apart from oedema of the abdominal wall without ascites.

The investigation results favoured a diagnosis of SLE [Table 1]. The patient's antinuclear antibody (ANA) level was positive (>1:640) and her anti native double-stranded nuclear deoxyribonucleic acid (n-DNA) count was 150 IU/mL (normal range: 0–45 IU/mL). These results were highly suggestive of SLE. Accordingly, she was started on a regimen of hydroxychloroquine, mycophenolate and prednisolone. Over the following six months, the patient began to show marked improvement and her oedema subsided.

## Discussion

The most likely diagnosis for the findings observed in the current patient was SLE, due to the high levels of positive ANA and anti n-DNA antibodies recorded. However, her clinical condition fulfilled neither the diagnostic criteria of SLE (according to the revised guidelines of the American College of Rheumatology)[2] nor those of mixed connective tissue disease or undifferentiated connective tissue disease.[3,4] The diagnosis was predominantly based on immunological findings. Since her autoimmune profile was strongly indicative of SLE, it was thought likely that this was a possible case of SLE, potentially progressing to definite SLE in the future. The response of the oedema to immunosuppressive therapy also supported this diagnosis.

More common causes of subcutaneous oedema (such as heart failure, liver disease, malnutrition, renal disease or drugs) were excluded in this patient by a careful history-taking as well as clinical and other relevant investigations. Oedema, especially the localised form, has been reported in the literature as a rare presenting symptom of SLE.[5–9] There are reports of periorbital oedema,[5] lower limb pitting oedema,[6] facial oedema,[7] remitting asymmetrical pitting oedema[8] and angioedema,[9] all as initial presentations of SLE. There are several cases of SLE presenting with generalised oedema due to either protein-losing enteropathy (PLE),[10–12] an association with idiopathic nephrotic syndrome,[13] or polyserositis in the form of massive bilateral pleural and pericardial effusions.[1] Nephrotic syndrome as a cause of oedema in this patient was excluded by the absence of urinary protein. Moreover, PLE was unlikely to be the cause of the generalised subcutaneous oedema in this patient, as patients with

PLE usually have low serum protein and albumin measurements.[10–12] As a result, tests to detect PLE, such as technetium-$^{99m}$ albumin scintigraphy or a 24-hour stool alpha-1-antitrypsin clearance test, were not justified in this case.[7,8]

The underlying cause of generalised oedema in SLE patients without systemic manifestations, such as renal disease, is not yet clear. Günaydin *et al*. postulated that the localised oedema observed in his reported case was most likely due to vasculitis, which had led to an obstruction of the lymphatic vessels.[6] The aetiology of localised periorbital oedema in patients with SLE flares is also not apparent. A case series reported by Gómez-Puerta *et al*. found that while some cases were related to nephrosis, there was no evidence in others.[14] Pittau *et al*. believed that oedema may be due to a transient impairment in lymphatic drainage or pre-existing increased capillary permeability, as demonstrated in patients with connective tissue disorders.[8] Marks *et al*. proposed that there was an increase in vascular permeability in patients with connective tissue diseases.[15] In yet another patient with periorbital oedema, increased dermal mucin deposits were observed during a biopsy.[16] Angioedema due to C1-inhibitor deficiency has also been described in the literature.[17]

The findings of this case report are limited by certain factors. Photographs of the patient were not taken before the initiation of treatment and a skin biopsy was not sent to a pathologist to determine the exact pathophysiological mechanisms of the patient's symptoms.

## Conclusion

The first possible case of SLE presenting with generalised subcutaneous oedema without a definite cause is described. The cause of oedema in this patient could not be explained by other reported causes of generalised oedema associated with SLE, such as PLE, nephrotic syndrome or polyserositis. The presence of generalised oedema is a rare cutaneous manifestation of SLE and can be the initial and sole manifestation of this disease.

## References


1. Lu L, Zhao Z, Cai H. Generalized subcutaneous edema and polyserositis as unusual presentation in systemic lupus erythematosus. Int J Rheum Dis 2012; 15:e50–2. doi: 10.1111/j.1756-185X.2011.01695.x.
2. Petri M, Orbai AM, Alarcón GS, Gordon C, Merrill JT, Fortin PR, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum 2012; 64:2677–86. doi: 10.1002/art.34473.
3. Cappelli S, Bellando Randone S, Martinović D, Tamas MM, Pasalić K, Allanore Y, et al. "To be or not To be," ten years after: Evidence for mixed connective tissue disease as a distinct entity. Semin Arthritis Rheum 2012; 41:589–98. doi: 10.1016/j.semarthrit.2011.07.010.
4. Conti V, Esposito A, Cagliuso M, Fantauzzi A, Pastori D, Mezzaroma I, et al. Undifferentiated connective tissue disease - an unsolved problem: Revision of literature and case studies. Int J Immunopathol Pharmacol 2010; 23:271–8.
5. Erras S, Benjilali L, Essaadouni L. Periorbital edema as initial manifestation of chronic cutaneous lupus erythematosus. Pan Afr Med J 2012; 12:57.
6. Günaydin I, Daikeler T, Mohren M, Kanz L, Kötter I. Lower limb pitting edema in systemic lupus erythematosus. Rheumatol Int 1999; 18:159–60. doi: 10.1007/s002960050077.
7. Anzai M, Maezawai R, Ohara T, Kodama K, Fukuda T, Kurasawa K. Systemic lupus erythematosus associated with facial edema, overproduction of interleukin-5, and eosinophilia. J Clin Rheumatol 2008; 14:361–2. doi: 10.1097/RHU.0b013e31818f3b15.
8. Pittau E, Passiu G, Mathieu A. Remitting asymmetrical pitting oedema in systemic lupus erythematosus: Two cases studied with magnetic resonance imaging. Joint Bone Spine 2000; 67:544–9. doi: 10.1016/S1297-319X(00)00217-7.
9. Lahiri M, Lim AY. Angioedema and systemic lupus erythematosus: A complementary association? Ann Acad Med Singapore 2007; 36:142–5.
10. Wu CC, Lin SH, Chu P, Lai JH, Chang DM, Lin YF. An unrecognized cause of oedema in a patient with lupus nephritis: Protein losing enteropathy. Nephrol Dial Transplant 2004; 19:2149–50. doi: 10.1093/ndt/gfh226.
11. Ratnayake EC, Riyaaz AA, Wijesiriwardena BC. Systemic lupus erythematosus presenting with protein losing enteropathy in a resource limited centre: A case report. Int Arch Med 2012; 5:1. doi: 10.1186/1755-7682-5-1.
12. Ranawaka N, Atukorala I, Fernandopulle N, Nawarathna M. An unusual cause of generalized oedema in systemic lupus erythematosus. Rheumatology (Oxford) 2012; 51:2298–300. doi: 10.1093/rheumatology/kes157.
13. Hertig A, Droz D, Lesavre P, Grünfeld JP, Rieu P. SLE and idiopathic nephrotic syndrome: Coincidence or not? Am J Kidney Dis 2002; 40:1179–84. doi: 10.1053/ajkd.2002.36875.
14. Gómez-Puerta JA, Levy S, Khamashta MA, Hughes GR. Periorbital oedema in systemic lupus erythematosus. Lupus 2003; 12:866–9. doi: 10.1191/0961203303lu455xx.
15. Marks J, Birkett DA, Shuster S. "Capillary permeability" in patients with collagen vascular diseases. Br Med J 1972; 1:782–4. doi: 10.1136/bmj.1.5803.782 .
16. Maeguchi M, Nogita T, Ishiguro N, Nihei H, Kawashima M. Periorbital oedema and erythema in systemic lupus erythematosus. Br J Dermatol 1996; 134:601–2. doi: 10.1046/j.1365-2133.1996.t01-5-53778.x.
17. Thong BY, Thumboo J, Howe HS, Feng PH. Life-threatening angioedema in systemic lupus erythematosus. Lupus 2001; 10:304–8. doi: 10.1191/096120301680417011.