

# A fatal case of seronegative, late-onset systemic lupus erythematosus presenting with motor sensory axonal polyneuropathy

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**Abstract** Systemic lupus erythematosus is a multisystemic, autoimmune, inflammatory disorder predominantly affecting young females. Its onset may be abrupt or insidious, presenting with a broad range of clinical and immunological features. We report an unusual case of elderly-onset systemic lupus erythematosus in a woman initially diagnosed with discoid lupus, and subsequently admitted to hospital due to a progressive psycho-motor deficit. Electrophysiological measurements suggested a diagnosis of acute motor sensory axonal neuropathy. Unusual clinical features and negative serology led to diagnostic uncertainty. This case report offers information on the course of the disease through the entire chain of the health care delivery (from primary to tertiary). Despite the efforts of the hospital staff, it was not possible to save the life of the woman.

**Keywords** Discoid lupus · Lupus pneumonitis · Lupus erythematosus systemic · Motor sensory axonal polyneuropathy

## Background

Systemic lupus erythematosus (SLE) is a chronic, autoimmune connective tissue disorder, with multi-organ involvement and a variable clinical course [1]. In 1982, the American College of Rheumatology (ACR) published revised criteria for the classification of SLE [1].

The diagnosis of SLE may be made if four or more of the 11 ACR criteria are present [1]. Women of reproductive age are more often affected. Onset of SLE beyond the age of 50 years is rare [2]. It can present with a wide range of non-specific or atypical clinical manifestations, challenging the physicians involved to achieve a timely diagnosis [3]. We report a case of a woman with late-onset SLE admitted due to a progressive psychomotor deficit caused by acute motor sensory axonal neuropathy (AMSAN).

## Case report

A 77-year-old woman attended a primary care setting due to a 7-day history of a non-pruritic erythematosus macular rash with desquamation, distributed on the nasal bridge and upper extremities. Her medical history was unremarkable except for osteoporosis treated with ibandronic acid and calcium. Clinical examination did not reveal any abnormal findings. Laboratory examination disclosed an abnormal erythrocyte sedimentation rate (ESR) of 30 mm/h (normal range 1–20 mm/h); C-reactive protein 2.70 mg/l (normal range 0–10 mg/l); Urea 46 mg/dl (normal range 13–43 mg/dl);

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Creatinine 0.6 mg/dl (normal range 0.5–1.2 mg/dl). Complete blood count was normal. Due to the progressive extension of the rash and the abnormal ESR, our patient was referred to a private dermatologist.

A skin lesion biopsy was performed. Histological findings (hyperkeratosis, atrophy of the epidermis, vacuolar degeneration of the basal cells, lymphocytic infiltrate of perivascular and subepidermal area) were consistent with a diagnosis of discoid lupus erythematosus. Autoimmune serology tests including anti-nuclear antibodies (ANA), anti-SSA (Ro) Anti-SSB (La), anti-double stranded DNA, p ANCA, c ANCA, were negative. Total haemolytic complement, C3, C4 and rheumatoid factor (RF) were normal. Urine examination was also normal. Topical corticosteroids were initiated along with daily repetitive applications of sunblock creams.

Four weeks afterwards the patient was admitted to a secondary care unit due to a marked progressive generalized muscular weakness of upper and lower extremities, arthralgias and bradypsychism. Limb weakness was symmetrical with proximal to distal distribution manifesting initially as difficulty holding upper extremities over the head, going up stairs and rising from a chair, making the patient seriously disabled with a peak level noted four weeks after the onset. There was no previous history of infectious disease, abdominal pain or diarrhea. Due to the positive history of discoid lupus and the unusual presentation, the patient was referred to a tertiary hospital. On admission the patient, although well oriented in place and time, was inattentive, with delayed speech. Neurological examination revealed decreased muscular strength (2/5 on upper and lower limbs in all the muscular groups bilaterally). Major deep tendon reflexes were absent. Other findings from physical examination included a maculopapular rash located on the face, neck and elbows and a non-deforming arthritis involving metacarpophalangeal and interphalangeal joints bilaterally. Pulmonary auscultation revealed reduced vesicular murmur on both lungs.

Her vital signs were as follows: blood pressure 105/68 mmHg; pulse 150 per min; oxygen saturation 93 % on ambient air; temperature 37.8 °C. Electrocardiogram revealed sinus tachycardia. Complete blood count disclosed marked thrombocytopenia [39 K/ $\mu$ l (normal range 150–450)] and lymphopenia [0.2 K/ $\mu$ l (normal range 1.5–3.6 K/ $\mu$ l)] with normal white blood cell count [4.7 K/ $\mu$ l (normal range 3.8–10.5)]. C-reactive protein levels were 0.48 mg/dl (normal range 0.08–0.8 mg/dl) and ESR 25 mm/h. Renal function tests and urine analysis were normal. Blood cultures and sputum gram smears were negative for infection. Testing for current or past viral infection with cytomegalovirus, human immunodeficiency virus, hepatitis A, B, C, Parvovirus B19 and Epstein Barr was negative. Stool culture for *Campylobacter jejuni*

infection was negative. Serological testing for autoantigenic peripheral nerve gangliosides, including monosialoganglioside (GM1), disialoganglioside (GD1a), asialoganglioside (ASGM1), GD1b and GQ1b was also negative. A bone marrow aspiration and biopsy were also performed with no pathological findings.

Computed tomography (CT) of the brain was unremarkable. Lumbar puncture was consequently performed and cerebrospinal fluid analysis (CSF) revealed an elevated protein level 64 mg/dl (normal range 15–40 mg/dl) with normal glucose levels [85 mg/dl (normal range 60–70 mg/dl)]. White blood cell (WBC) count and red blood cell (RBC) count on CSF were found to be 0.

Serological testing for auto-antibodies (ANA, anti-Sm, anti-ds-DNA, ANCA, p ANCA, c ANCA, anti-DNA cri-thidial and anti-phospholipid antibodies) was negative. Serum complement levels were found to be 79.8 mg/dl (normal range 87–187 mg/dl) for C3 and 18.6 mg/dl (normal range 15–47) for C4. In view of the patient's clinical signs (generalized muscular weakness) and laboratory findings (elevated protein with normal WBC on CSF) a presumed diagnosis of Guillian-Barre-syndrome (GBS) variant secondary to active autoimmune systematic disease was made. A 5-day course of intravenous (iv) administration of immune globulin (IG) at 0.4 g/kg/day (30 g) in parallel with iv administration of prednisolone (25 mg) once a day was initiated. Electromyography with a nerve conduction study performed on the 3rd hospital day revealed findings suggestive of AMSAN (normal distal motor latencies, normal conduction velocities combined with a marked reduction of compound motor action potentials as well as sensory nerve action potentials).

Despite therapy, no improvement was recorded in the patient's motor function. A 3-day course of iv administration of 1 g methylprednisolone was commenced. However, on the 5th hospital day the patient developed hypoxemia [arterial oxygen tension ( $P_a O_2$ ) 53.5 mmHg with 50 % inspired oxygen] with normocapnia [arterial carbon dioxide tension ( $P_a CO_2$ ) 37.4 mmHg]. A rapid and irregular heart rate (128 per min) was also recorded. ECG data were consistent with multifocal atrial tachycardia. High resolution CT of the lungs disclosed small pleural effusions (Fig. 1) with diffuse subsegmental areas of ground-glass attenuation in all lung fields (Fig. 2). Bronchial lavage fluid examination was negative for pneumocystis carinii antibodies. Similarly, urine cultures were sterile and negative for the presence of any pathological microorganism. The patient was placed on non-invasive positive pressure ventilation (NIPPV) using a bilevel positive airway pressure (BPAP) mode at 15 l/min. After exclusion of infection and pulmonary embolism, lupus pneumonitis was the most possible diagnosis. Urine analysis revealed abnormal urinary sediment with proteinuria





**Fig. 1** Thoracic computed tomography showing pleural effusions



**Fig. 2** Thoracic computed tomography showing areas of ground-glass attenuation

(3+), hematuria (3+) and granular casts. Hypoalbuminemia (1.5 g/dl) was also present. A single dose of 500 mg cyclophosphamide was administered i.v. However, the patient's respiratory status continued to deteriorate ( $P_{aO_2} = 49.3$  mmHg;  $P_{aCO_2} = 36.8$  mmHg; Oxygen saturation 86.9 %) requiring transfer to the intensive care unit (ICU) for respiratory failure type 1. During her stay in the ICU she developed Acute Respiratory Distress Syndrome (ARDS) and died 5 days after. A schematic overview of the described episode of care is shown in Fig. 3.

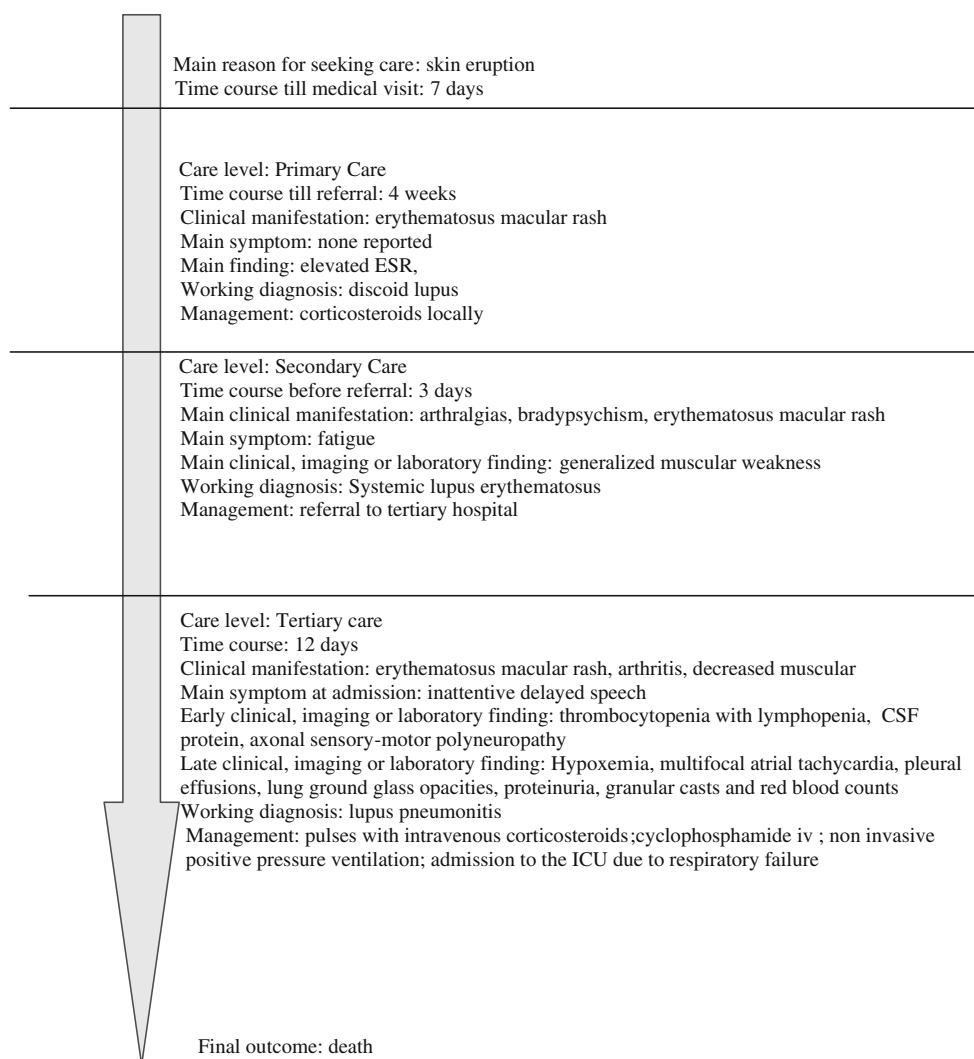
## Discussion

Our patient, during the course of the disease, fulfilled the 1982 revised criteria of the American College of Rheumatology [1]. More specifically, she presented 4 of the 11 criteria with nonerosive arthritis, thrombocytopenia with lymphopenia, proteinuria and discoid rash. This is an unusual case of late-onset SLE presenting with motor sensory axonal polyneuropathy at the beginning of the disease. Occurrence of SLE beyond the 5th decade of life is considered relatively rare [2]. The low frequency of SLE in the elderly combined with the atypical clinical features at onset can lead to significant delays in diagnosis [3]. Font et al. [4] reported an increased interval from the beginning of the disease to diagnosis in elderly compared to younger patients with SLE (5 vs. 3 years). It is also remarkable that aging influences disease evolution with regard to clinical features, course and prognosis [5]. Published data suggest that pulmonary manifestations and serositis tend to occur more often in the late onset SLE [2, 5] while arthritis, renal involvement and skin lesions are less frequent manifestations [2, 5]. Consistently with our case, peripheral nervous system symptomatology was recorded more often in the elderly SLE group [6].

Differences were also recorded with regard to serological abnormalities of SLE in the elderly patients [2, 5]. ANA and RF were more often detected in the elderly while anti-ds-DNA antibodies and anti-Smith were rarely present [2, 5, 6]. Concerning the course and prognosis of the disease, results from the 1,000 faces of lupus study reported that late-onset SLE is not a benign condition [7], but is associated with greater disease activity and organ damage [7]. Consequently in terms of survival, poorer outcomes are recorded in the older onset sub-group of patients with SLE [5].

Reports in the literature refer to the involvement of the peripheral nervous system in patients with SLE, with a predilection to inflammatory demyelinating polyneuropathies [8, 9]. Although peripheral nervous system manifestations in patients with SLE are considered relatively common [10], acute axonal polyneuropathy followed by albumino-cytological dissociation in the CSF (increased CSF protein in the absence of increased WBCs) is extremely rare in the context of SLE [8]. Ubogu et al. [11] reported a case of a young female presenting with AMSAN associated with active SLE and positive anticardiolipin antibodies. This type of peripheral neuropathy represents an axonal variant of GBS with slow recovery and poor prognosis, caused probably by an immune mediated attack on axonal epitopes [11, 12]. This later results in axonal degeneration due to macrophage induced phagocytosis and finally to Wallerian-like degeneration of myelinated motor and sensory nerve roots [11, 12]. Association of the axonal





**Fig. 3** Schematic overview of the reported care episode

form of the Guillain–Barre syndrome with previous *Campylobacter jejuni* infection and positive anti-ganglioside antibodies has been reported [11]. Clinical progression of AMSAN ranges from 7 to 28 days [11]. It is usually presents with severe motor and sensory dysfunction [11]. Cranial nerves and the respiratory system are often involved [11]. With regards to CSF findings, normal white cell count with normal or moderately elevated protein is usually found [11]. Recovery depends on axonal regeneration, occurring at approximately 1 mm daily [11].

Evidence on the effectiveness of i.v.IG in SLE induced neuropathies is limited. Furthermore, it has been reported that i.v.IG imposes a high risk of renal failure [11]. However, it has been reported that in atypical variants such as acute motor-sensory axonal neuropathy i.v.IG administration could be as effective as plasmapheresis [11].

This is a rare case of seronegative, late-onset SLE, initially presented with discoid lupus lesions and subsequently AMSAN. The atypical clinical features combined with negative serological findings led to a ‘troubled’ diagnosis. This case report offers information on the last few weeks’ course of an apparently local disease and its conversion to systemic, through the entire chain of health care delivery (from primary to tertiary). Lupus erythematosus is a potentially life-threatening condition and disease activity or related organ damage cannot be predicted.

### Consent

Written informed consent was obtained from the patient’s next of kin for publication of this manuscript and



accompanying images. A copy of the written consent form is available for review by the Editor-in-Chief of this journal.

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**Conflict of interest** None.

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