Bilateral sudden sensorineural hearing loss as a presenting feature of systemic lupus erythematosus

Case report and brief review of other published cases

Sylvain Chawkia,a,b,c, Jessie Aouizerate, MD,c, Selim Trad, MD,a,b, Jacques Prinseau, MD,a,b, Thomas Hanslik, MD, PhD,a,b,d,e

Abstract

Introduction: Sudden sensorineural hearing loss is an unusual presenting clinical feature of systemic lupus erythematosus.

Case report: We report the case of a young woman who was admitted to hospital for sudden sensorineural hearing loss and hemophagocytic syndrome which was attributed to systemic lupus erythematosus on the basis of specific renal involvement, thrombocytopenia, and consistent autoantibodies. Favorable outcome was obtained on high-dose corticosteroids, and the hearing fully recovered.

Discussion: Sudden sensorineural hearing loss in systemic lupus erythematosus is seemingly more frequently associated with severe systemic involvement and antiphospholipid antibodies may be present. Although management remains empirical, the high risk of permanent hearing impairment seems to justify emergency treatment with high-dose corticosteroids. When the clinical and laboratory criteria of antiphospholipid syndrome are met, antiplatelets agents or anticoagulation therapy shall be considered.

Keywords: autoimmunity, corticosteroids, sensorineural hearing loss, systemic lupus erythematosus

1. Introduction

Sudden sensorineural hearing loss is defined as an acquired hearing deficit of up to 30 dB loss in 3 different frequencies on an audiogram, building up over a few hours to up to 3 days. Five to 20 per 100,000 population are affected, both male and female, typically between 30 and 60 years of age.[1] In the majority of cases, hearing loss is unilateral and associated with vestibular symptoms. The pathophysiology is unclear. Viral, genetic, traumatic, or toxic causes have been discussed. Autoimmune or vascular etiology has been put forward in 10% of cases.[2] Sudden sensorineural hearing loss in systemic lupus erythematosus is seemingly more frequently associated with systemic lupus erythematosus. We reviewed the medical literature indexed in the Medline database (accessed on December 28, 2015). Our search key words were: “hearing OR sensorineural OR deafness AND lupus,” in all fields, only English and French language articles.

2. Case report

A 19-year-old woman was referred to our hospital in December 2006 for a fever, a sudden profound bilateral hearing loss and a malar rash that had appeared 10 days before hospitalization. She had no significant past medical history. Besides hearing loss, physical examination revealed a malar rash, ulcerated stomatitis, enlarged cervical lymph nodes, and subungual hemorrhage. The remainder of the physical examination was normal.

An audiogram showed a hearing threshold of 40 dB in the right ear and 60 dB in the left ear, both in air and bone conduction. Laboratory tests revealed neutropenia (540 neutrophils/μL), thrombocytopenia (125,000/μL), elevated liver enzymes (aspartate aminotransferase 247 IU/L, 8-fold the upper limit of normal range; alanine transaminase 116 IU/L, 3-fold the upper limit of normal range; gamma-glutamyl transferase 166 IU/L, 3-fold the upper limit of normal range; alkaline phosphatase 40 IU/L, normal), hyperferritinemia (10,965 μg/L) and an elevated titer of antidouble stranded DNA (31 IU/L) and anti-Sm antibodies. Antinuclear antibodies were positive (titer 1/2560), with antitriple stranded DNA (31 IU/L) and antihistone antibodies. Antinucleosome and anti-SSA antibodies were present as well.
Coagulation tests disclosed a lupus anticoagulant. Low levels of antiphospholipid antibodies were detected (IgG: 27 µg/L).

Complement was abnormally low with 0.3 g/L C3 (lower limit 0.7 g/L); 0.1 g/L C4 (lower limit 0.1 g/L) and 50% CH50%. Bone marrow aspiration revealed mild hemophagocytosis.

Renal biopsy revealed World Health Organisation class II lupus nephritis with pure mesangial involvement, with IgG, C3, C1q, and IgM deposits on immunofluorescence. There was no alteration of blood vessels (absence of infiltration, necrosis of the vascular wall, or microscopic thromboangiitis), nor proliferation on light microscopy.

Echocardiographic examination was normal, without any valvular abnormality. Cerebral magnetic resonance imaging was normal and displayed no evidence of ischemia.

The patient met the American College of Rheumatology classification criteria for systemic lupus erythematosus. She was treated with high-dose (500mg) intravenous methylprednisolone for 3 days, and clinically improved within a few days. The hearing completely recovered, as assessed by repeated audiograms. The hemophagocytic syndrome, proteinuria, and hematura also improved following corticosteroid therapy.

Long-term treatment with prednisone (1 mg/kg/day with gradual decrease), hydroxychloroquine and aspirin was introduced. Six months later, proteinuria and hematura rebounded and mycophenolate mofetil treatment was introduced. Overall treatment was well tolerated. One year later, clinical examination was normal with a complete remission of systemic lupus erythematosus; mycophenolate mofetil was stopped.

Secondary antiphospholipid syndrome (antiphospholipid syndrome) was excluded on the basis of an uneventful follow-up and the quick fading of anticardiolipin antibodies and lupus anticoagulant that were never detected again over 9 years of follow-up.

A second flare occurred in 2011, with myalgia, arthralgia, fatigue, and hemophagocytic syndrome. This flare was treated by a temporary increase of prednisone dose; no immunosuppressive therapy was necessary. Evolution was unremarkable ever since. When last seen in February 2016, the patient was doing well on 5 mg prednisone and 400 mg hydroxychloroquine daily.

3. Discussion

This patient presented with bilateral sudden sensorineural hearing loss in the context of a hemophagocytic syndrome, revealing systemic lupus erythematosus, and raising questions about pathophysiology and treatment. Sudden sensorineural hearing loss should be clearly distinguished from other sensorineural hearing loss in patients with systemic lupus erythematosus. Indeed, systematic audiometric tests have shown that 20% to 35% of systemic lupus erythematosus patients have chronic sensorineural hearing impairment, often asymptomatic.13-14 Thus, the risk of sensorineural hearing loss seems to be much higher in systemic lupus erythematosus patients compared to healthy age-matched controls, with an odds ratio of 20 (95% CI: 2.93–139.6).4 In contrast, sudden sensorineural hearing loss, which is usually a dramatic condition, has been seldom reported in systemic lupus erythematosus patients (Table 1).

Three pathophysiological hypotheses are proposed for sudden sensorineural hearing loss at the beginning of systemic lupus erythematosus manifestations:9,10,12

- **T-cell autoimmunity:** As shown patients with sudden sensorineural hearing loss presented significant proliferation of T lymphocytes specifically responsive to human inner ear antigens, as well as increased interferon-gamma and other inflammatory intracellular cytokines levels in peripheral blood.
- **Humoral autoimmunity:** Specific autoantibodies directed against inner-ear antigens have been detected in this context and may be involved in sudden hearing loss.17-19
- **Antiphospholipid syndrome:** Case reports have highlighted the possible association of antiphospholipid antibodies with sudden sensorineural hearing loss in systemic lupus erythematosus. Antiphospholipid antibodies (i.e., antiphospholipid antibody, lupus anticoagulant, and anti-β2-GP1) are known to be associated with microcirculation thrombosis and histological proof of microinfarctions has been reported in systemic lupus erythematosus patients with sudden sensorineural hearing loss.20-22 High concentrations of antiphospholipid antibodies have been reported in case reports of lupus-associated sudden sensorineural hearing loss, with satisfying clinical response to anticoagulant therapy.20,22-26 Whether the presence of antiphospholipid antibodies in patients presenting sudden sensorineural hearing loss is sufficient to establish a diagnosis of secondary antiphospholipid syndrome in the absence of other symptoms (i.e., thromboembolic or obstetrical complications) remains to be determined.20,22,24,25

When reviewing the English and French literature in the Medline database, we found 22 documented cases of sudden sensorineural hearing loss in association with systemic lupus erythematosus (Table 1). Patients were between 20 and 50 years old, mostly women (16/22). Hearing loss was unilateral in 14 out of 22 cases. Hearing loss was the first manifestation of systemic lupus erythematosus in four cases. In 11 cases major systemic involvement of systemic lupus erythematosus such as renal, cardiac, or neurological involvement was also reported.

Besides hearing loss, other reported aural symptoms included: middle ear involvement, otitis, and in 9 cases, vestibular symptoms.

When tested, antiphospholipid antibodies, and/or lupus anticoagulant and/or isolated syphilis reaginic antibody proved positive in 11 out of 15 cases. Half of these patients had a past or present medical history of thrombosis. Ten patients had had a brain CT-scan or MRI: among them, 3 had signs of central nervous system ischemia. However, secondary antiphospholipid syndrome was not explicitly considered in several of those cases. Pathological data were available in three cases, showing middle ear lesions such as vasculitis and nonspecific inflammation.

Twelve patients were treated with steroids (0.5–1 mg/kg equivalent prednisone, 1 was treated with 500 mg methylprednisolone on 3 consecutive days), 4 patients were prescribed immunosuppressive therapy with azathioprine or cyclophosphamide, 3 were treated with plasmapheresis and 2 with hydroxychloroquine. Anticoagulation or antiplatelet therapy was prescribed to 4 patients. Clinical outcome was reported for 13 patients: recovery from hearing loss was complete in only 4 patients and partial in 2 other cases. None of the patients treated with anticoagulation or antiplatelet therapy recovered.

A recent publication of a retrospective cohort study from the Taiwan National Health Insurance Research Database reported 27 cases of sudden sensorineural hearing loss associated with systemic lupus erythematosus, but no detail on clinical and biological data was available.47

We conclude that sudden sensorineural hearing loss can be the presenting clinical feature of systemic lupus erythematosus and may be associated with antiphospholipid antibodies. Although...
| Refs. | Age/gender | Time between SLE diagnosis and SSNHL | Unilateral or bilateral SSNHL | Associated SLE symptoms | Laboratory criteria for presence of anti phospholipid | Treatment | Hearing loss recovery |
|-------|------------|--------------------------------------|-----------------------------|------------------------|-----------------------------------------------|-----------|---------------------|
| Hamblin et al\[28\]; case report | 47, F | 6 wk | Bilateral | Rash, arthritis, renal insufficiency | ND | Prednisone 40 mg; plasma exchange | ND |
| Caldarrelli et al\[28\]; Case report | 51, F | 0 | Unilateral | Unsteadiness, arthritis | ND | Prednisone (25 mg × 4); oral cyclophosphamide | No |
| Kobayashi et al\[30\]; case report | 32, F | 2 y | Bilateral | Palmar erythema, arthralgia, myalgia, fever, rash, mitral regurgitation, comlications, lymphadenopathy | Yes | Oral steroids ineffective; plasmapheresis | Yes |
| Hisashi et al\[24\]; case report | 15, F | 2 y | Unilateral | Malar rash, vestibular and cerebellar ataxia, left lateral Homer medullary syndrome, hemiparesis right internuclear ophthalmoplegia | Yes | Prednisone 40 mg | Partial |
| Vyse et al\[31\]; case report | 23, F | 0 | Bilateral | Preeclampsia, feonal vein thrombosis, tinnitus, vertigo | ND | Prednisone; anticoagulation | No |
| Kataoka et al\[32\], case report | 51, F | 0 | Unilateral | Unsteadiness, arthritis | ND | Antibiotics; methylprednisolone; 2 mg/kg prednisone | Partial |
| Naarendrop and Spiera\[22\]; 5 case reports | 26, F | 4 y | Unilateral | Vertigo, aphasis, hipertension, intermittent vision loss, spontaneous aborptions, hyperactivity | Yes | ND | ND |
| 41, M | 0 | Unilateral | Malar rash, proteinuria, pericarditis, neurpathy | Yes | ND | ND |
| 40, M | ND | Unilateral | Chronic sinusitis, asthma, arthralgia, Bell palsy, dizziness, rash | Yes | ND | ND |
| Pain\[33\]; case report | 22, F | ND | Unilateral | Rash, photopsisensitivity, arthritis, alopecia, Raynaud syndrome | No | ND | ND |
| Sone et al\[34\], 2 case reports | 22, F | 13 y | Unilateral | Arthritis, renal insufficiency, otitis media | ND | ND | ND |
| Peena and Barland\[35\], 2 case reports | 47, F | 26 y | Bilateral | Renal insufficiency | ND | ND | ND |
| 45, F | 10 y | Bilateral | Tinnitus, severe aortic insufficiency, photosensitivity, arthralgias, malar rash, fever, pleuritis | Yes | Methylprednisolone 80 mg (3 d) | No |
| 31, F | 9 y | Bilateral | Tinnitus, aortic insufficiency, fever, arthritis, anemia | Yes | Steroids; hydroxychloroquine | No |
| Green and Miller\[36\], case report | 22, M | 0 | Unilateral | Dizziness, arthralgia, left hemiparesis, scotomas, Cohn colitis, otitis media | Yes | Low molecular weight heparin and warfarin; prednisone; 5-methylenaltic acid | No |
| Mora et al\[37\]; case report | 39, M | ND | Unilateral | ND | ND | ND | ND |
| 37, F | 1 y | Unilateral | ND | ND | ND | ND | ND |
| Compadretti et al\[38\]; case report | 22, F | 5 y | Unilateral | Hematologic involvement, arthritis, lupus nephritis | ND | Low molecular weight heparin, prednisone, plasma exchange | ND |
| Sugiura et al\[39\]; case report | 40, M | 7 y | Bilateral | Vestibular syndrome, pleuritis, hemolytic anemia, thrombocytopaenia | Yes | ND | No |
| Khalidi et al\[40\]; case report | 33, F | 9 y | Unilateral | Tinnitus, dizziness, Raynaud phenomenon, pleuritis, polyarthralgia, superior limb venous thrombosis | No | ND | No |
| Lin et al\[41\]; population-based, retrospective cohort study | 27 cases: 25 F, 2 M; 14: 0–34 y; 13 ≥ 35 y | ND | ND | ND | ND | ND | ND |

F = female; M = male; ND = not determined; SLE = systemic lupus erythematosus; SSNHL = sudden sensorineural hearing loss.

*Syphilis reaginic antibody, anticardiolipin antibody, antiphospholipid antibody, or lupus anticoagulant.
management of such cases remains empirical, the high risk of permanent hearing loss seems to justify emergency treatment with high dose corticosteroids. If the laboratory criteria of antiphospholipid syndrome are present, antiplatelets agents or anticoagulation therapy shall be considered.

Informed oral consent was obtained from the patient. All data were strictly obtained from the patient’s medical file.

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