Scientific Research Publishing

Neuroscience & Medicine, 2022, 13, 120-125
https://www.scirp.org/journal/nm
ISSN Online: 2158-2947
ISSN Print: 2158-2912

Peripheral Neuropathies Revealing Gougerot-Sjögren's Syndrome: Description of 3 Cases

Ndiaga Matar Gaye[1], Alassane Mamadou Diop[1,2*], Khalifa Ababacar Mbaye[1], Serigne Abdou Aziz Fall[1], Mamadou Ka[1], Momo Banda Ndiaye[1], Maouly Fall[2], Moustapha Ndiaye[1], Amadou Gallo Diop[1,2]

[1]Neuroscience Department, Fann Hospital, Dakar, Senegal
[2]Neurology Department, Pikine Hospital, Dakar, Senegal
Email: *alassanemamadou@hotmail.fr

How to cite this paper: Gaye, N.M., Diop, A.M., Mbaye, K.A., Fall, S.A.A., Ka, M., Ndiaye, M.B., Fall, M., Ndiaye, M. and Diop, A.G. (2022) Peripheral Neuropathies Revealing Gougerot-Sjögren's Syndrome: Description of 3 Cases. *Neuroscience & Medicine*, **13**, 120-125.
https://doi.org/10.4236/nm.2022.133011

Received: January 28, 2022
Accepted: September 20, 2022
Published: September 23, 2022

Abstract

Introduction: Sjögren's syndrome is an autoimmune epithelitis with various extraglandular signs, among which are neurological, with a variable frequency according to studies. We report three cases of peripheral neuropathy revealing Gougerot-Sjögren's syndrome, collected in the Neurology Department of the Fann University Hospital in Dakar (Senegal). **Observations:** The first patient, aged 48 years, presented with a length-dependent sensitivomotor polyneuropathy associated with retrobulbar optic neuritis, with dry eyes and dry mouth noticed by the patient for several years. The second patient, aged 28 years, was admitted to the hospital with chronic generalized paresthesia in the context of xerostomia and xerophthalmia. The results of the clinical examination and the electroneuromyogram were in favour of pure sensory neuronopathy. The third patient was 32 years old female, with a history of thyroidectomy and acute inflammatory demyelinating polyneuropathy (AIDP), who was seen for acute ascending flaccid tetraplegia with facial diplegia, preceded by diffuse paresthesia. The diagnosis of recurrence of acute demyelinating polyradiculonueropathy was retained in view of the rapidly increasing character of the deficit, the hyperproteinorachy at the lumbar puncture, and the signs of demyelination at the ENMG. The diagnosis of Gougerot-Sjögren's syndrome in our three patients was established on the basis of the 2016 ACR/EULAR criteria. Indeed, the anti-SSA antibodies (Ro) were positive in our 3 patients with a biopsy of the salivary glands which showed stage 3 in the first patient and stage 4 in the two others. Corticosteroid therapy and immunosuppressive treatment resulted in a favourable clinical evolution on the neurological and general levels. **Conclusion:** Gougerot-Sjögren's syndrome is an autoimmune

exocrinopathy that may present with peripheral neuropathy, which may precede the diagnosis of Sjögren's syndrome, be concomitant or occur during the course of the disease.

Keywords

Sjögren's Syndrome, Peripheral Neuropathy, Salivary Gland Biopsy, Senegal

1. Introduction

Gougerot-Sjögren's syndrome (GSS) is an autoimmune exocrinopathy resulting in dry mouth and eyes, associated with multi-systemic involvement in one-third of cases [1]. The frequency of extra-glandular manifestations, particularly neurological, is variable, due to the heterogeneity of recruitment services and inclusion criteria or to the systematic exploration of asymptomatic patients. The neurological manifestations may be central or peripheral and may precede the diagnosis or occur during the course of Gougerot-Sjögren's syndrome.

On average, peripheral neurological manifestations are present in 20% of patients with GSS [2] [3].

We describe the clinical, electrophysiological, and immunological aspects of three cases of peripheral neuropathy revealing an GSS, diagnosed in the Neurology Department of the Fann University Hospital in Dakar, Senegal (see Table 1).

2. Observations

The first patient was a 48-year-old male hospitalised for the exploration of palmo-plantar hyperaesthesia and dysaesthesia associated with bilateral visual acuity impairment. The interrogation revealed distal and symmetrical chronic neuropathic pain, xerophthalmia, and xerostomia. The schirmer test showed insufficient lacrimal secretion. The electroneuromyogram (ENMG) revealed a sensory-motor axonal polyneuropathy, predominantly sensory in the 4 limbs and more marked in the lower limbs. Visual evoked potentials showed bilateral

Table 1. Charactheristics of reported cases.

Case	Gender	Years	History	Neurological signs	Extra-neurological signs	ASGB	Immunology	Treatment
1	M	48	-	Sensorymotor polyneuropathy Retrobulbar optic neuropathy	Dry eyes with dry mouth	Stage III	SSA (Ro)+	Prednisone Methotrexate Pregabalin
2	F	28	-	Sensory neuronopathy	Dry eyes with dry mouth Cheilitis Prurigo, Alopecia Erythematosquamous lesions	Stage IV	SSA (Ro)+	Prednisone Methotrexate
3	F	32	Goiter AIDP	AIDP	Dry eyes with dry mouth	Stage IV	SSA (Ro)+ SSB (La)+	Prednisone

demyelinating optic nerve damage, with no abnormalities on brain MRI. Blood tests showed anti-SSA (Ro) antibodies were positive, and polyclonal hypergammaglobulinemia was noted on serum protein electrophoresis. The dosage of vitamins B12, B1, and B6 was normal. The research on diabetes was negative.

Hepatitis and retroviral serologies were negative. Accessory salivary gland biopsy (ASGB) showed Chisholm and Masson grade III chronic lymphocytic sialitis. Treatment with prednisone, methotrexate and pregabalin resulted in almost complete resolution of sensory signs.

The second patient was 28 years old female admitted to hospital for chronic diffuse paresthesia exploration, in a context of xerostomia and xerophthalmia. The clinical examination revealed hypoesthesia of the right hand and in the median territory of the left hand, dry eyes and dry mouth, impairment in bilateral visual acuity, non-erosive cheilitis, prurigo, non-scarring alopecia, erythematous-squamous lesions of the ears and scalp. The ENMG was in favor of a sensory neuronopathy. Anti-SSA (Ro) antibodies were positive. ANCA and native DNA were negative. BGSA showed Chisholm and Masson stage IV chronic lymphocytic sialitis. The 24-hour proteinuria was 153 mg/24H. There was no vitamin deficiency (B1, B12, and B6) or diabetes.

The remaining biological tests (CRP, muscle enzymes, syphilitic and retroviral serology) were normal. Treatment with prednisone, methotrexate and folic acid resulted in a partial regression of the clinical signs.

The third patient was 32 years old female, with a history of thyroidectomy and acute inflammatory demyelinating polyneuropathy (AIDP), was seen for acute ascending flaccid tetraplegia with facial diplegia, preceded by diffuse paresthesia predominating in the lower limbs. The interrogation revealed the notion of dry eyes and dry mouth. The ENMG showed a demyelinating sensory-motor process in all four limbs with localized conduction pseudo-blocks. The lumbar puncture with analysis of the CSF showed an albuminous-cytological dissociation with no germ found in the culture. The anti-ganglioside antibodies were negative.

The blood count showed a leukopenia of 3490/mm^3. Anti-SSA (Ro) and anti-SSB (La) antibodies were positive. The BGSA showed a chronic sialitis grade IV of Chisholm and Masson. After six months of corticosteroid therapy, the clinical course was favourable with total recovery of motor deficits in the limbs but persistence of facial diparesis.

3. Discussion

The diagnosis of Gougerot-Sjögren's syndrome in our three was based on the 2016 ACR/EULAR criteria [4]. Indeed, the anti-SSA antibodies (Ro) were positive in our 3 patients with a biopsy of the salivary glands which showed a stage 3 in the first patient and a stage 4 in the two others.

Before retaining the diagnosis of Sjögren's syndrome in our 3 patients, the deficiency and metabolic causes were eliminated, namely vitamin deficiencies, diabetes, dysthyroidism as well as hepatitis and HIV retrovirosis. In the third pa-

tient, anti-ganglioside antibodies were negative.

In a cohort of 726 patients followed for systemic disease in Senegal, Kane *et al.* diagnosed Gougerot-Sjögren's syndrome in 32 patients. Half of the cases were of primary etiology [5].

In our series, we collected two men and one woman with fairly young ages of onset (28 and 32 years), which is unusual compared to the literature where there is a female predominance and an age of onset around the fourth or fifth decade [6].

In Senegal, out of 266 patients followed for GSS in the rheumatology department, 56 (21%) of them had central and peripheral neurological manifestations combined [6].

For Garcia-Carrasco *et al.*, peripheral neurological complications were found in only 8% of cases, but asymptomatic cases were not mentioned [3].

The first two observations concern a sensorimotor polyneuropathy and a sensory neuropathy, both axonal, with progressive onset mode over several months. The axonal polyneuropathies are the most frequent type of manifestation and include sensorimotor polyneuropathies and pure sensory polyneuropathy.

From a pathophysiological point of view, axonal polyneuropathies are thought to be caused by ischaemic damage, as vasa nervorum lesions are frequent and described in two forms: vasculitis with an infiltrate of small vessels or necrotizing vasculitis with infiltrates involving vessels of larger diameter, associated with fibrinoid necrosis. This hypothesis could explain their length-dependent character [7].

Depending on the authors, specific immunological markers of B cell activation or monoclonal proliferation may or may not be found between the neuropathy and non-neuropathy groups in patients followed for Sjögren's syndrome [8].

Chronic B-cell activation is characterized by elevated levels of serum gamma-globulins (mainly IgG), presence of other B-cell produced serologic markers (ANA, anti-Ro/SS-A, anti-La/SS-B antibodies, RF), and the formation of ectopic lymphoid tissue with germinal center-like structures. Another immunological sign of primary Sjögren's syndrome is the predisposition to developing oligo- and monoclonal B-cell proliferation, characterized by the presence of mixed cryoglobulinemia, monoclonal gammopathy, and B-cell lymphomas [9].

Sensory neuropathies can be divided into small and large fibers lesions. The latter corresponds to an involvement of the posterior spinal ganglia and is also called ganglionopathy [10].

Indeed, the main differential diagnosis of sensory neuronopathy secondary to GSS is paraneoplastic Denny Brown neuronopathy, which often has a more severe and rapid course. However, the similarities between the sensory neuronopathies of GSS and paraneoplastic neuronopathies suggest a common pathophysiological origin, in the form of antineuronal antibody production [10].

In addition to the sensory disorders already described, small fiber neuropathy may be present, for which the standard ENMG is normal. Specific tests such as

cutaneous sympathetic reflex, laser evoked potentials or skin biopsy with measurement of the intra-epidermal density of nerve fibers are necessary to make the diagnosis [11] [12]. These small fiber neuropathies are generally more disabling and capricious than large-fiber lesions [2].

In the study of Jaskólska, only patients with sensorimotor neuropathy had elevated markers of high B-cell activation as mentioned above. But they also had a significantly longer disease duration compared to other subgroups [9].

The first patient presented with optic nerve damage that could be related to central involvement of the GSS, but brain MRI and visual evoked potentials made it possible to retain the peripheral character. Indeed, the central manifestations appear to be polymorphous, and may be diffuse (cognitive disorder, meningoencephalitis) or focal (spinal cord, encephalic or optic nerve involvement) [2].

The third observation is that of acute polyneuropathy. This involvement during GSS does not seem to be frequent and is clinically, neurophysiologically, and anatomopathologically stackable to idiopathic PRN, making the imputability of GSS uncertain [10].

Only one of our patients had a chest CT scan to look for possible pulmonary complications (interstitial lung disease or fibrosis). They were all referred to an internal medicine consult for continuous follow-up.

The evolution of the patients was favourable, especially in terms of motor function, under corticosteroid therapy. However, it should be noted that immunoglobulins, which are difficult to access in our context, are more indicated, especially in the context of acute PRN.

In fact, the efficacy of immunomodulatory and immunosuppressive therapies in GSS neuropathies is mainly observed when there are necrotizing vasculitis lesions, which are found preferentially in certain clinical forms. This is the case for multiple mononeuropathies or particularly corticosensitive cranial nerve disorders and radiculoneuropathies that respond favourably to immunoglobulins [11].

4. Conclusion

These 3 cases illustrate the polymorphism of peripheral neurological involvement in Gougerot-Sjögren's syndrome. Particular attention must be paid to extra-neurological signs in order to make a precise diagnosis for early and appropriate collegial management.

Consent for Publication

Written informed consent for publication was obtained from the patients.

Funding

The authors declare that they have not received another source of funding.

Conflicts of Interest

The authors declare that they have no competing interests.

References

[1] Vitali, C., Bombardieri, S., Jonsson, R., Moutsopoulos, H., Alexander, E., Carsons, S., *et al.* (2002) Classification Criteria for Sjögren's Syndrome: A Revised Version of the European Criteria Proposed by the American-European Consensus Group. *Annals of the Rheumatic Diseases*, **61**, 554-558. https://doi.org/10.1136/ard.61.6.554

[2] Delalande, S., De Seze, J., Ferriby, D. and Vermersch, P. (2010) Les manifestations neurologiques du syndrome de Gougerot-Sjögren. La Revue de Médecine Interne, **31**, S8-S15. https://doi.org/10.1016/j.revmed.2010.03.006

[3] García-Carrasco, M., Ramos-Casals, M., Rosas, J., Pallarés, L., Calvo-Alen, J., Cervera, R., *et al.* (2002) Primary Sjögren Syndrome: Clinical and Immunologic Disease Patterns in a Cohort of 400 Patients. *Medicine* (*Baltimore*), **81**, 270-280. https://doi.org/10.1097/00005792-200207000-00003

[4] Shiboski, C.H., Shiboski, S.C., Seror, R., Criswell, L.A., Labetoulle, M., Lietman, T.M., *et al.* (2017) 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjögren's Syndrome: A Consensus and Data-Driven Methodology Involving Three International Patient Cohorts. *Annals of the Rheumatic Diseases*, **76**, 9-16. https://doi.org/10.1136/annrheumdis-2016-210571

[5] Kane, B.S., Niasse, M., Ndiaye, A.A., Ndao, A.C., Djiba, B., Diack, N.D., *et al.* (2018) Systemic Diseases in Dakar (Senegal): Spectrum, Epidemiological Aspect and Diagnostic Time-Limit. *Open Journal of Internal Medicine*, **8**, 196-206. https://doi.org/10.4236/ojim.2018.83019

[6] Diallo, S., Niasse, M., Diaw, C.A.B., Diallo, R. and Diouf, C. (2016) PE.Lu-129—Syndrome de Gougerot-Sjogren : Étude préliminaire de 266 observations au Sénégal. *Revue du Rhumatisme*, **83**, A266-A267. https://doi.org/10.1016/S1169-8330(16)30624-X

[7] Carvajal Alegria, G., Guellec, D., Devauchelle-Pensec, V. and Saraux, A. (2015) Existe-il des atteintes neurologiques spécifiques du syndrome de Sjögren primitif? *Revue du Rhumatisme*, **82**, 14-17. https://doi.org/10.1016/j.rhum.2014.03.009

[8] Chen, Y.-M. and Su, K.-Y. (2021) Acute Motor and Sensory Axonal Neuropathy in Association with Primary Sjögren's Syndrome: A Case Report. *BMC Neurology*, **21**, Article No. 161. https://doi.org/10.1186/s12883-021-02190-z

[9] Jaskólska, M., Chylińska, M., Masiak, A., Siemiński, M., Ziętkiewicz, M., Czuszyńska, Z., *et al.* (2020) Neuro-Sjögren: Uncommon or Underestimated Problem? *Brain and Behavior*, **10**, e01665. https://doi.org/10.1002/brb3.1665

[10] De Seze, J., Delalande, S. and Vermersch, P. (2005) Les manifestations neurologiques du Gougerot-Sjögren. *La Revue de Médecine Interne*, **26**, 624-636. https://doi.org/10.1016/j.revmed.2005.02.014

[11] Mori, K., Iijima, M., Koike, H., Hattori, N., Tanaka, F., Watanabe, H., *et al.* (2005) The Wide Spectrum of Clinical Manifestations in Sjögren's Syndrome-Associated Neuropathy. *Brain*, **128**, 2518-2534. https://doi.org/10.1093/brain/awh605

[12] Sène, D. (2018) Neuropathie des petites fibres: mise au point diagnostique, étiologique et thérapeutique. *Revue du Rhumatisme*, **85**, 441-447. https://doi.org/10.1016/j.rhum.2017.10.019