

Neurological Manifestations in the Gougerot Primary Sjogren's Syndrome: About a Study of 25 Cases

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Abstract

Neurological manifestations of primitive Sjogren's syndrome (PSS) are polymorphic and appreciated differently. The aim of our study was to determine the clinical, therapeutic and the evolution of neurological manifestations in patients with the PSS.

Patients and methods

It is a retrospective study of 25 patients followed for a PSS for a period of 10 years (2002-2012). PSS diagnosis was retained according to the criteria of the American-European Consensus Group revised in 2002.

Results

The average age of our patients was 54 years. A female predominance was noted with a sex ratio of 7.33. Neurological manifestations were present in 7 of our patients (28% of cases). They were revealing in one case. Peripheral neurological complications were noted in 6 cases, isolated in 5 cases and associated with central nervous system involvement in one case. The central involvement was observed in 2 cases in the form of encephalitis. In some of our patients, treatment was based on corticosteroids. The evolution was variable.

Conclusion

The absence of homogeneity in the criteria for the diagnosis of neurological manifestations of PSS is due to not only to a limited number of large series but also to clinical diversity of these events.

Keywords: Sjogren's syndrome; Neurological complications; Central nervous system; Peripheral nervous system

Introduction

Neurological manifestations of primary Sjogren's syndrome (UMS) are of variable frequency according to research from 8.5% to 70% with an average between 15 and 25% of cases [1-6]. They are valued differently. It may interest the central nervous system (CNS) and / or peripheral nervous system (PNS), reveal the disease and even precede the dry syndrome [5-9]. The aim of our work was to support clinical, therapeutic and evolutionary aspects of neurological manifestations in the UMS.

Patients and Methods

We performed a retrospective study over a period of ten years (2002-2012). We included 25 patients hospitalized in the internal medicine department of the Tunis military hospital and having a UMS selected according to the criteria of the American-European Consensus (2002), with central nervous system impairment and / or device. The original character was retained on the absence of co morbidities (Table 1).

1.	Eye symptoms : at least one of three criteria:
	Persistent and troublesome daily feeling of dry eyes for more than three months
	Frequent feeling of sand in the eyes
	Use of artificial tears more than three times per day
2.	Oral symptoms : at least one of three criteria:
	Daily feeling of dry mouth for more than three months
	In adulthood, recurrent or persistent swelling of the salivary glands
	Frequent consumption of liquids to swallow dry foods
3.	Eye signs : at least one of the two following tests positive:
	Test de Schirmer \leq 5mm en 5 minutes
	Schirmer test \leq 5mm 5 minutes test Bengal pink or equivalent (Score van Bijsteverd \geq 4)
4.	Histopathologie:
	Sialadenite with a focus score $>$ 1 on biopsy (s) of the salivary glands accessories (defined as the number of lymphocytic foci (containing more than 50 cells and adjacent to mucosal apparently normal acini) by 4 mm ² glandular tissue.
5.	Achievement of salivary glands: at least one of the three following tests positive:
	Abnormal salivary scintigraphy
	Sialographie parotidienne anormale
	Salivary flow without stimulation \leq 1.5 ml in 5 minutes
6.	Autoantibodies:
	Anti SSA and / or anti SSB antibody positive

Table 1: Criteria American-European consensus in 2002 [10].

We excluded from the study patients with other pathology that could explain the neurological. In this sense we sought: a consumer with anti cholinergic drugs (antidepressants, neuroleptics, B blockers), head and neck radiotherapy, pre-existing lymphoma, infection with hepatitis C, HIV infection, sarcoidosis, amyloidosis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, polymyositis, primary biliary cirrhosis, immune thrombocytopenic purpura and other autoimmune disease (thyroiditis, pernicious anaemia).

The collection of epidemiological and clinical data was done in all patients. In some of our patients, additional tests were performed to further confirm the diagnosis of Sjogren’s syndrome, including:

- A test for sugar,
- Break up a time,
- A Schirmer test,
- A rose bengal test,
- An inflammatory balance sedimentation rate, C- reactive protein, protein electrophoresis,
- A blood count,
- A plasma electrolytes,
- Renal balance (urea, creatinine, proteinuria 24 hours)

- Liver function tests
- Immunological balance: anti -nuclear antibodies, anti SSA, SSB antibodies, rheumatoid factor, CCP antibodies,
- A biopsy of the salivary glands (BGSA).

To authenticate the neurological, we realized the appropriate as brain MRI and / or spinal cord and / or electromyography. Other complementary explorations are based on potential breaches extraglandular and clinical orientation.

Some of our patients received oral corticosteroid based treatment. The evolution was judged on the subjective improvement and the clinical examination data. Mean follow-up in our series was 3.7 years with extremes ranging from 1 month to 26 years.

Results

We noted a female predominance with a sex ratio of 7.33 and a mean age at diagnosis of 54 years (31-84 years). The time to diagnosis was 3.89 years on average (1 month- 20 years). The dry syndrome, constituting the circumstance of discovery in 80% of patients, was observed in 92 % of cases (Table 2).

Glandular reached Signs	Number of patients	Frequency (%)
Xerophthalmia	23/25	92
GOAL altered	19/21	90
Schirmer pathological	7/7	100
Rose Bengal test	10/17	59
Xerostomia	23/25	92
Pathological sugar test	12/13	92
BGSA grade III or IV Chisholm	25/25	100
Xerosis	6/25	24
Nasal dryness	4/25	16
Laryngotracheal irritation	3/25	12
Vaginal dryness	2/22	9

Table 2: Glandular Manifestations.

GOAL: Break up time; BGSA biopsy of the salivary glands.

Neurological manifestations were present in 7 of our patients, in 28% cases. They were indicative of UMS in one case (Figure 1). They were peripheral and central type.

Peripheral neuropathies were noted in 4 patients or in 16% of cases. Achieving touched the lower limbs symmetrically in two of these cases. Clinically, pure sensory polyneuropathy was in 3 cases. One patient had sensory polyneuropathy confirmed by electromyography; he showed a myogenic and neurogenic motor impairment. This same patient had a proximal motor deficit of the upper and lower limbs associated with hypoesthesia gloves on both hands. The Brain MRI of this patient revealed a hyper T2 signal and a signal T1 in subcortical hypo. A CNS associated impairment of the SNP in connection with UMS was chosen for this patient given the clinical context.

Cranial nerves were present in 4 cases. A unilateral hearing loss was diagnosed in 2 of our patients and trigeminal neuralgia (V) in two cases.

The central nervous system impairment would be recorded in both cases.

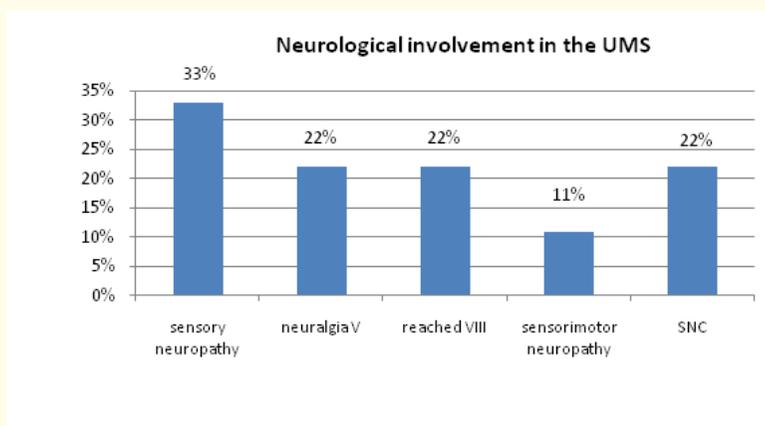


Figure 1: Neurological involvement in the UMS.

In the first case, it was a 65 year old patient complaining of dry syndrome for 6 years. He developed memory problems worsen to become after some months a dementia syndrome. Realized etiologic highlighted on brain MRI in a range T2 signal hyper and hypo T1 signal in the periventricular white matter and in oval centres.

In the second case, there was a patient with peripheral involvement type sensor motor polyneuropathy with brain lesions on MRI without clinical translation.

No nerve biopsy or study of cerebrospinal fluid has been performed in our study.

Patient Number	Symptomatology	MRI	EMG
1	Nensorimotor neuropathy	Hyper Hypo T2 signal in T1 signal in cortical	Myogenic and neurogenic damage
2	Neuralgia intermittent V	No anomaly	NF
3	Neuralgia intermittent V	NF	NF
4	Neuropathie sensitive MI	NF	NF
5	Sensory neuropathy	NF	NF
6	Sensory neuropathy + Hypoacusia left	NF	NF
7	Hearing loss disorder mnesic + Sd dementia	T2 hyper hypo signal T1 signal in the white matter ventricular perished beach	NF

Table 3: Neurological Impairment.

EMG: EMG; MI: Lower limbs; Sd: Syndrome; NF: not done.

Some of our patients received oral corticosteroids at a variable dose depending on neurological involvement, followed by a gradual depression based evolutionary terms. For polyneuropathy, corticosteroid therapy was prescribed in 3 patients with stable symptoms on prednisone 10mg. For CNS, corticosteroid therapy was initiated in attack treatment at a dose of 0.7 mg / kg / day followed by a gradual improvement without depression. Immunosuppressive and immunoglobulins were not used.

Discussion

The frequency of neurological manifestations varies from the studies from 8.5% to 70% with an average between 15 and 25% [1-6]. This variability can be explained by the recruitment service (internal medicine or neurology), by the inclusion criteria or by conducting

systematic complementary examinations in asymptomatic patients. Neurological manifestations can reveal disease and even precede the dry syndrome [5-9]. In this work, the dry syndrome preceded the onset of neurological manifestations in all cases.

Reaching the SNP was more common than CNS in our study results concordant with the literature [4-6]. This disease is slow and insidious course usually involving a clinical syndrome dry and one or more systemic manifestations making diagnosis easier SGS.

Axonal polyneuropathy is the most frequent [4,8,11]. They include the polyneuropathy sensory and sensorimotor polyneuropathy. The clinical attack beginner is symmetrical in most cases by sensory signs predominantly distal affecting the lower limbs. These attacks may be asymptomatic, discovered during the construction of an EMG [4]. In our series, polyneuropathy was observed with 57% of neurological manifestations. They were associated with systemic disease in 75% of cases. The pathophysiological phenomenon of peripheral neurological manifestations would show ischemic injury with lesions of the vasa nervorum found in nerve biopsies [12]. In the literature a combination of these axonal polyneuropathy in cutaneous vasculitis and cryoglobulinemia has been described [4,7].

The cranial nerve has been described with a predominance of the trigeminal nerve (V). It can be seen in 25-45% of cases. This is an often unilateral involvement of sensory and contingent predominant on the lower territory. It would be linked to an infiltration of the trigeminal ganglion [5,7,8,13].

Reaching the cochlea vestibular nerve (VIII), whose frequency is underestimated by Delande, *et al* [4], is responsible for a decrease of hearing or even a sudden deafness [6,14]. In our series, the cranial nerve represented 57% of neurological manifestations with the same frequency for the nerves V and VIII (28% of each). Involvement of the facial nerve (VII) and oculomotor nerves is rare [5,15]. Vincent, *et al* [15] pointed out the possibility of recurrent and multiple cranial nerve palsies.

Sensory neuronopathies are less frequent than axonal polyneuropathy in the UMS. They are characterized by a pure sensory impairment predominantly proximal, affecting all four limbs were described [5,6,13]. Evolution is slowly progressive that can be acute and severe. It may precede the diagnosis of SMS and may be asymptomatic. Sensory evoked potentials would be contributing to the diagnosis. This achievement is due to lymphocytic infiltration of dorsal roots and dorsal root ganglia.

The multiple neuropathies are less frequent during the UMS than they are during other systemic diseases; they are generally faster and more catastrophic evolution. Autonomic nervous system with autonomic symptoms was reported with a variable frequency between 18% and 50% of cases [7,13]. Some observations of sub acute or chronic polyradiculoneuropathy, injury or carpal tunnel of myopathy have been reported [3,16]. These events were not found in our study.

Violations of the CNS associated with Sjogren syndrome are not specific and pose diagnostic difficulties. Their frequency is variable between 1% and 20% of cases [8,17,18]. In our series, 2 patients out of 25 had submitted a CNS 8% of cases and 28% of neurological manifestations. The pathophysiology of these attacks remains poorly understood. Vasculitis is the most often mentioned mechanism, but an autoimmune process has also been proposed [19]. The CNS can be focal or diffuse. According to Lafitte, *et al* [9], the diffuse CNS is the most common, representing 72% of neurological manifestations. By cons, according to Delande, *et al* [4], the focal attacks account for 93% of neurological manifestations.

The encephalic damage may occur from acute, progressive or recurrent. They are reaching the most frequent [4,9]. They are polymorphic, which can be the type of stroke, extra pyramidal syndrome, movement disorders, seizures and may have a table mimicking multiple sclerosis [4]. However, in our study, brain damage was revealed in memory disorders and dementia syndrome in a patient and without clinical in another case.

Spinal cord damage can be acute or chronic; the most table frequent is that of transverse myelitis [19,20] and the achievement is generally intramedullary expanded to more than one metamere. Optic neuropathy may be indicative of the disease, unilateral or bilateral. Meningoencephalitis represent 25% of central neurological complications that are aseptic lymphocytic and it led to the study of cerebrospinal fluid [8].

Radiological abnormalities on brain MRI in neuro- Gougerot are frequent, it is mostly hyper with T2 signal white matter ventricular perished and subcortical. The lesions may be multiple and diffuse. The achievement of the substance gray and basal ganglia are more rare.

It does not seem to be a correlation clinico-radiological. Indeed asymptomatic patients may have damaged radiological MRI, as was the case in our study. Similarly focal encephalic events without abnormalities on MRI have been described by some authors [4]. Accountability of UMS in these radiological abnormalities is discussed.

Radiological abnormalities in spinal MRI are represented by hyper extended intramedullary T2 signal in acute myelopathy kind of transverse myelitis. In chronic myelopathy anomalies in T2 hyper signal type can be small or sometimes be extended to many. It should be noted that a spinal MRI abnormality does not eliminate without spinal cord involvement [4,5].

Recently, an antibody against alpha-fodrin was highlighted in the tissues and sera of patients with Sjogren's syndrome patients. It seems that research of this antibody may have a particular interest in the diagnosis of neuro-Gougerot.

Therapeutically, there is no consensus on the treatment of neurological manifestations and the results are unpredictable in the literature.

Corticosteroid treatment is described as the first line treatment violations CNS. Caselli, *et al* [14] reported a significant improvement from dementia, Alexander, *et al* [8] also reported a stabilization of lesions in 80% of patients with meningoencephalitis corticosteroid. The corticosteroid and boli immunosuppressive drugs are often prescribed for neurological manifestations power stations. Alexander offers monthly cyclophosphamide treatment intravenously for at least a year associated with the treatment of corticosteroids in the beginning [21]. Azathioprine may be an alternative [12,22], although some authors consider it ineffective [21,23]. Methotrexate and cyclosporine are considered ineffective [22]. A dramatic improvement in cyclophosphamide in case of myelopathy was described [6].

For violations of the SNP, corticosteroids appear to be inefficient and some authors [4,6] recommend symptomatic treatment for polyneuropathy. By cons, polyneuropathy associated vasculitis or cryoglobulinemia seem to respond well to corticosteroids. Plasma exchange, intravenous immunoglobulins or biotherapy were also proposed [13].

Conclusion

The neurological damage from UMS is polymorphic and difficult to diagnose. They are valued differently in the absence of homogeneity of diagnostic criteria used and the limited number of large series. There is no consensual treatment but certain proposed treatments seem promising.

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