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Research Article

Neurosyphilis and Intake of Cerebrospinal Fluid (CSF)

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Abstract: The Neurosyphilis is the most severe neurological complication of the active syphilis. It puts real diagnostic problems because of the ascendancy of the atypical forms. Our objective is to analyze the clinical symptoms and to assess the relevance of the different laboratory findings in cerebrospinal fluid (CSF) and serum for the diagnosis and survey of active neurosyphilis. A retrospective study of six hospitalized neurosyphilitic patients at Hospital Moulay Ismail of Meknès from 2003 to 2015 was carried out. Neurosyphilis can be grouped in two categories: early (meningeal and meningovascular neurosyphilis) and late (progressive general paralysis and tabes dorsalis). All patients are HIV negative. All the patients are benefited for an examination cytochimique of the CSF and an examination immunological with the tests VDRL and TPHA for the search for the specific antibodies in the CFS and the serum. The CSF anomalies in neurosyphilis included elevated cell count with lymphocytic-plasmocytic cell reaction, increased protein content, strongly positive blood and CSF serology.

Keywords: neurosyphilis, cerebrospinal fluid, treponema antibodies.

INTRODUCTION

Neurosyphilis is the most severe neurological complication of active syphilis. Although it has become rare, it poses real diagnostic problems because of the predominance of atypical forms [1]. Syphilis is a sexually transmitted infection currently on the rise. The causative agent is a spirochete, Treponema pallidum which in the absence of treatment can invade the nervous system and its envelopes by creating a strong chronic inflammatory reaction. Neurological disorders develop years or even decades after contamination, after a phase of latency clinically mute. It is a serious illness if it is unrecognized or neglected. The term neurosyphilis or nervous syphilis actually groups together several clinical pictures corresponding to stages of the disease more or less advanced. Asymptomatic latent neurosyphilis or syphilitic meningitis is without obvious clinical abnormalities. Neurosyphilis is objectified by cerebrospinal fluid (CSF) analysis. This reveals a chronic inflammation with infiltration of the meninges by a lymphoplasmocytic cellular contingent. Late symptomatic neurosyphilis corresponds to the tertiary stages. General paralysis with diffuse meningoencephalitis and meningovascularitis includes a psychiatric syndrome leading to dementia and a neurological syndrome resulting in physical decline.

MATERIALS AND METHODS

During the period 2003 to 2015, 11 cases of neurosyphilis hospitalized and treated at the HOPITAL MOULAY ISMAIL DE MEKNES were identified in the framework of the serodiagnosis of syphilis in the laboratory. Clinical and biological records were analyzed.

We performed a complete biological and radiological assessment for all patients, including a cytochemical examination of CSF and the detection and titration of anti-treponemal antibodies in CSF and blood.

RESULTS

The majority of patients come from a low socioeconomic level. They are eleven men of average age of 47.4 years with extremes ranging from 35 years to 65 years. (Table 1). Four patients have a previous history of known syphilis treated with penicillin G two years ago. We have observed different neurological tables corresponding to the different evolutionary stages of neurosyphilis:

1) stage of diffuse meningoencephalitis and meningo-vasculitis (n = 6).

The picture is that of a slowly progressive dementia with acute episodes and behavioral disorder.

The average age is 44 years with the extremes 35 and 55 years. Patients are hospitalized in neurology for more or less severe psychiatric disorders.

2) the most late stage of syphilitic dorso-lumbar tabes (n = 4).

It results in an ataxic step quickly becoming impossible leading to general paralysis. Death was observed in 3 patients after 6 years of development. The average age is 48 years with extremes 36 and 65 years. All four patients had a history of previous known syphilis treated with penicillin G two years earlier and meningoencephalitis treated 10 years previously. The clinical improvement in this advanced form is mediocre because the disease progresses despite the numerous intensive treatments.

- A single case with a very atypical clinical picture, in a patient of 54 cases, without antecedent, admitted for management of an isolated attack of the nerve VIII. The lumbar puncture performed during the first inpatient assessment for psychiatric disorders in the 6 patients; the stage of diffuse meningoencephalitis and meningo-vasculitis; Reveals very significant anomalies within the CSF. No history of primary syphilis is known for these six patients. The macroscopic appearance of CSF is clear colorless. The cell reaction is always present. It is moderate, on average at 42.3 elements / mm^3 with extremes ranging from 20 elements to 60 elements / mm^3. The cytological formula on colored smears is lymphocyte. Protein morphology is increased in all our patients with normoglucorachia. The average level of proteinuria is 1.1 g/L, with a minimum of 0.68 g/L, a maximum of 2 g/L (normal <0.40 g/L).

Treponem antibody was positive in CSF and serum by VDRL and TPHA in all 6 patients. (Table 2). Regarding the biological abnormalities found in the four patients admitted to a table of tabes and general paralysis: At this most advanced stage of neurosyphilis, CSF abnormalities are moderate. In two patients; Cellularity of CSF was normal as well as cytology, proteinuria was 0.63 g/L and 1.22 g/L. In the other two cases, CSF cytology was 20 cells / mm^3 and 160 cells / mm^3 predominantly lymphocytic with normoglucorachia and proteinuria at 1.3 g / l and 5.7 g / l. The assay of TPHA and VDRL was positive in CSF and serum. All our patients had negative HIV and hepatitis C serology.

Clinical and biological evolution during the treatment of neurosyphilis:

Six patients were treated with intravenous penicillin G and corticosteroid therapy. They all show both clinical and biological improvement in a few months. However, clinical improvement is partial. The evolution is towards a state of deterioration with neurological sequelae more or less severe.

In the most advanced forms of neurosyphilis, four patients received penicillin G. Despite the treatment, progress was made towards general paralysis with the death of three patients and one case was lost sight of. VDRL-LCRs are sensitive tests in the context of therapeutic follow-up of patients. The negativity of VDRL-LCR is the best marker of therapeutic efficacy. Its quantification is necessary to follow the serological evolution under treatment. Contrary to the interpretation that can be made in serum, the VDRL in the CSF is specific. The LCR TPHA and TPHA indexes decrease under antibiotic therapy without ever normalizing. The improvement at the later stages is always very discreet at both clinical and biological level.

DISCUSSION

Syphilis is a worldwide venereal disease disease (STD) disease by Treponema pallidum. It evolves in 3 phases. The primary phase is characterized by the characteristic inoculation chancre which heals spontaneously in 4 to 6 weeks. The secondary phase corresponds to the dissemination phase of the treponemes. It begins about 2 months after the contagion and is characterized by mucocutaneous lesions that disappear spontaneously in 1 to 2 years. The silent phase, known as latent syphilis, followed after 2 to 10 years and in 20 to 30% of the cases of a tertiary phase, characterized by visceral, cardiovascular, neurological, osseous or cutaneo-mucosal (gums) involvement. The biological diagnosis of syphilis is easy. The biological diagnosis of active neurosyphilis is difficult. It concerns the non specific and specific biological abnormalities observed in the CSF taken by lumbar puncture [2]. Lumbar puncture showed a clear fluid with a cellular reaction of 80 leucocytes per mm3 (normal ≤ 2 cells / mm^3), 124 erythrocytes (normal ≤ 100 / mm^3). The cytological formula established on smears stained with MGG is of the lymphomonocytic type, comprising 98% of lymphocytes, 2% of monocytes and the presence of inflammatory cells, basophilic lymphocytes, lymphoplasmocytes and plasmocytes. CSF also exhibited a hyperprotein- ia of 1.07 g/L (normal <0.40 g/L). Glycorachia is normal. These results are similar to those found in our series as well as in the Caudie series [2]. The immunological assessment makes it possible to investigate an involvement of the CSF / blood exchanges and an intrathecal synthesis of immunoglobulins [3]. He understands:

- assays of albumin and immunoglobulins, IgG and more recently IgA, IgM carried out in the same series on the Immage Coulter Beckman automaton by kinetic immunonephelometry. The albumin quotient is The best marker of the state of exchanges at the level of the blood-brain barrier: Q albumin = albumin LCR / serum albumin X 100 (normal <0.65);
- immunoglobulin indexes are the markers of an intrathecal immune response:

IgG index = IgG ratio (CSF / blood) / albumin ratio (CSF / blood): normal less than 0.70; IgA index = IgA

ratio (CSF / blood) / albumin ratio (CSF / blood): normal less than 0.40; IgM index = IgM ratio (CSF / blood) / albumin ratio (CSF/blood): normal less than 0.20. The electrophoresis of the total proteins on CSF carried out in parallel with the electrophoresis of the serum proteins

- the search for the oligoclonal bands of IgG by isoelectric immunofocalization of CSF and serum [4]. The serology of syphilis is performed in the CSF and serum, in order to compare the titers and to calculate the specific antibody indexes. It includes a non-specific test and a specific test [5, 6]. A confirmation is made by titration in case of positivity. The Venereal Disease Research Laboratory (VDRL) is a non-specific antigene agglutination test for non-treponemal antigen. It is positive and remains positive in the absence of treatment. It becomes negative after an effective treatment. The positive reaction is followed by titration by successive dilutions of serum and CSF. TPHA (Treponema Pallidum Haemagglutination Assay) uses a T. pallidum lysate. This is a simple and inexpensive test. The positivity threshold in the serum is fixed at 80. The positive reaction is followed by a titration by successive dilutions of the serum and the CSF. TPHA is positive 35 to 45 days after infection and rarely normalizes even after a correct treatment. The title does not reflect the activity of the disease and does not make it possible to judge its evolution. A positive test in the CSF does not confirm the diagnosis of active neurosyphilis. To counter this, the Klapper-specific antibody index is calculated. It is the best reflection of an infection of the central nervous system [7]. Since the specific antibody index is greater than 2, the intrathecal synthesis of anti-treponemal antibodies is asserted. Klapper index or TPHA index = TPHA titre ratio (CSF / blood) / albumin ratio (CSF / blood) FTA-Abs (Fluorescent Treponema Antibody Absorbed) is a specific test for indirect immunofluorescence. The FTA-Abs is positive 25 to 30 days after the contamination. This is the earliest test. It is both sensitive and specific. Under treatment it remains positive. FTA-Abs IgM is an indirect immunofluorescence technique for the detection of IgM class anti-serum antibody. Unfortunately, these tests are not performed in our patients.

Table 1: Patient observations at diagnosis Neurosyphilis

PATIENT	AGE	ATCD SYPHILITICS	CLINICAL SIGNS
1	50	Not known	Democratic State
2	44	Not known	Democratic State
3	51	Meningo-encephalitis	Syphilitic Tabes
4	42	Meningo-encephalitis	Syphilitic Tabes
5	65	Meningo-encephalitis	Syphilitic Tabes
6	35	Not known	Behaviour trouble
7	54	Not known	Reaching the nerve VIII
8	55	Not known	Mental confusion
9	36	Meningo-encephalitis	Syphilitic Tabes with General Palsy
10	40	Not known	Democratic State
11	48	Not known	Behaviour trouble

Table 2: CSF profile of patients in the diagnosis of neurosyphilis

PATIENT	GB / mm³	GR / mm³	PROTEINORACHIA	VDRL
1	20	35	2	1 /4
2	55	250	0 ,77	1/4
3	<03	1200	0 ,63	1/8
4	20	700	1, 3	1/8
5	160	130	5,7	1/16
6	47	349	1,5	1/32
7	60	150	0 ,80	1/16
8	40	49	1	1/32
9	9	25	1 ,22	1/8
10	35	120	1,25	1/64
11	60	70	0 ,68	1/64

CONCLUSION

For the current biological diagnosis of syphilis, there are two main groups of indirect serological methods, depending on the origin of the antigen used: 1) non-treponemal antigen reactions to identify patients: VDRD RPR (Rapid plasma reagin test); 2) treponemal antigen reactions to confirm the diagnosis: Treponema pallidum haemagglutination assay (TPHA), FTA (Fluorescent treponemal Antibody test). The latter would be equivalent from the literature to the previous ones. In France, the nomenclature of acts of biology recommends the use of a technique of each of the 2 groups of methods. These serological methods are routinely available in many laboratories. Direct

methods of searching for Treponema pallidum under dark-field microscopy, immunofluorescence, or inoculation to the animal are carried out in specialized structures. Finally, molecular methods are used in applied research.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and / or National Research Committee and the 1964 Helsinki Declaration and its subsequent amendments or comparable ethical standards.

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