

Case Report Of Chronic Meningo Encefalitis By Coccidioides Immitis

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Summary

Chronic meningoencephalitis is a syndrome that corresponds to approximately 10% of meningeal symptoms. It is a disease with various etiologies, which is a true diagnostic challenge. Among the most frequent causes are: infectious, toxic, inflammatory, neoplastic, autoimmune and idiopathic agents. This type of disorder demands a very extensive and expensive study battery, in spite of this; it is not always possible to establish the diagnosis. Cerebral and meningeal biopsies play an important role in the study of these patients. A detailed and careful clinical history is of the utmost importance, together with the study of the CSF to guide the physician towards the etiology of the problem. The different modalities of Neuroimaging have become a useful tool in the search for diagnosis in these cases. The treatment of chronic meningitis depends on the underlying cause. Once a specific cause has been established, case-directed therapy should be initiated. When the cause is unknown, a decision must be made to employ empirical therapy, while the diagnostic evaluation is ongoing. We present the case of the clinical-pathological session in the Hospital Central Militar, about a male patient who was previously healthy and who shows a clinical picture compatible with chronic meningoencephalitis, with a progressive and unfavorable course, in which despite the studies of image, laboratory and CSF, as well as empirical treatment management, it becomes impossible to determine etiology. Finally, postmortem diagnosis of neurococcidioidomycosis is made by means of histopathological study of brain tissue sections. Showing the diagnostic difficulty that these tables represent and the importance of early diagnosis when conditions favor it.

Keywords: Chronic Meningoencephalitis, Coccidioides Immitis and Neurococcidioidomycosis.

Abstract

Chronic meningoencephalitis is a syndrome that corresponds to about 10% of meningeal tables. It is a condition with many causes and therefore constitutes a real diagnostic challenge. Among the most common causes include infectious agents, toxic, inflammatory, neoplastic, autoimmune and idiopathic. These disorders require a battery of extensive and expensive studies, although it is not always possible to establish the diagnosis. Cerebral and meningeal biopsies play an important role in examining these patients.

A detailed and careful history and examination is required along with CSF parameters to guide a clinician towards the etiology of the problem. Neuroimaging modalities have become a useful tool in the quest for a diagnosis in such cases. Treatment of chronic meningitis depends on the underlying cause. Once a specific cause has been established, appropriate targeted therapy is initiated. When the cause is unknown, a decision must be made whether to employ empiric therapy while the diagnostic evaluation is ongoing. We presents a case commented in clinical-pathologic session in Central Military Hospital, about an inmucompetente male patient, previously healthy manifesting clinical signs compatible with chronic meningoencephalitis, with a progressive and unfavorable course, in which, despite the imaging studies, laboratory and CSF, as well as empirical therapy management is becomes impossible to determine etiology. Finally neurococcidioidomycosis performed postmortem diagnosis by means of histopathological examination of brain tissue sections. Demonstrating the diagnostic difficulty that these paintings represent and the importance of early diagnosis when conditions favor it.

Introduction

Meningitis refers to an inflammatory process of leptomeninges and CSF within the subarachnoid space. Meningoencephalitis refers to the inflammation of the meninges and cerebral parenchyma. [1] Chronic meningoencephalitis is a syndrome that corresponds to approximately 10% of meningeal symptoms. They share a clinic of insidious nature such as headache, behavioral alterations, compromise of consciousness, signs of focal neurological compromise and seizures, more encephaliticly than meningitically, associated with moderate CSF pleocytosis composed of mononuclear cells or a mixture of polymorph nuclear cells and cells. Mononuclear; the level of proteins is high, often markedly, and the glucose content is usually reduced or normal, the former in a picture that persists for at least 4 weeks. [2] The etiologies are diverse, both infectious (fungi,

parasites) and bacteria) as non-infectious (chemical exposure), neoplastic, autoimmune and even idiopathic, so their syndromic study merits a series of CSF tests, bounded when possible by the clinic. In the absence of risk factors or clinically orienting in the etiological, in a subacute or chronic meningoencephalitis, evaluation of the CSF whose appearance is clear must include: cytochemical examination, Chinese ink stain and fungal culture, stain and culture for bacillus of koch, tests of cysticercosis, study of syphilis, adenosine deaminase and search for neoplastic cells. The lethality of these pictures will depend on the etiology, but it reaches 30%, además tiene un alto índice de secuelas. En el caso clínico que nos ocupa en esta ocasión, la clínica, laboratorio y paraclínicos nos orientan hacia una meningoencefalitis de origen micótico. En éstas, el cerebro suele estar afectado solo al final de la enfermedad, donde existe una diseminación hematogéna del hongo, la mayor parte de las veces Candida albicans, Mucor, Aspergillus fumigatus y Criptococcus neoformans. En las zonas endémicas patógenos como Histoplasma capsulatum, Coccidioides immitis y Blastomyces dermatidis pueden afectar al SNC tras una infección primaria pulmonar o cutánea. [3] La coccidioidomycosis (CM) es una micosis endémica en algunas regiones de los Estados Unidos, en el Noroeste y Noreste de México y en ciertas áreas en Centroamérica y Sudamérica. [4] La CM extrapulmonar se presenta en 1 de cada 200 sujetos infectados; los sitios más comúnmente afectados son meninges, huesos, articulaciones, [5] piel y tejidos blandos. [6] La CM es la más antigua de las micosis sistémicas, [7] fue descrita por primera vez en un soldado argentino en 1892 reportándose el caso como micosis fungoidea. [8] La meningitis es la complicación más grave de esta infección, sin tratamiento específico el 100% de los pacientes mueren. [9] A continuación se presenta el caso clínico de paciente inmunocompetente, previamente sano, con manifestaciones de meningitis crónica, con cultivos para bacterias y hongos negativos en LCR, en quien a pesar de tratamiento a base de compuestos azólicos, fallece y posterior a esto se realiza diagnóstico histopatológico que revela como agente causal Coccidioides immitis, poniendo de manifiesto la dificultad diagnóstica y la importancia del diagnóstico temprano cuando las condiciones lo favorecen.

It also has a high rate of sequelae. In the clinical case that concerns us on this occasion, the clinical, laboratory and paraclinical lead us to a meningoencephalitis of fungal origin. In these, the brain is usually affected only at the end of the disease, where there is a haematogenous spread of the fungus, most often Candida albicans, Mucor, Aspergillus fumigatus and Cryptococcus neoformans. In pathogenic endemic areas such as Histoplasma capsulatum, Coccidioides immitis and Blastomyces dermatidis can affect the CNS after a primary pulmonary or cutaneous infection. [3] Coccidioidomycosis (CM) is an endemic mycosis in some regions of the United States, in the Northwest and Northeast of Mexico. Mexico and in certain areas in Central and South

America. [4] Extrapulmonary CM occurs in 1 of every 200 infected subjects; the most commonly affected sites are meninges, bones, joints, skin and soft tissues. [6] CM is the oldest systemic mycosis, [7] was first described in an Argentine soldier in 1892, reporting the case as mycosis fungoidea. [8] Meningitis is the most serious complication of this infection, with no specific treatment 100% of patients die. [9] The clinical case of immunocompetent patient, previously healthy, with manifestations of chronic meningitis, with cultures for bacteria and negative fungi is presented below in CSF, who despite treatment with azo compounds, died and after this histopathological diagnosis was made that reveals Coccidioides immitis as a causative agent, highlighting the diagnostic difficulty and the importance of early diagnosis when conditions favor it.

Case Report

It is a male patient, 33 years old, active military, originating and resident of the city of Oaxaca, Oaxaca, in Mexico. He began his illness in November 2009, one month before his admission to the Regional Military Hospital of Puebla (HMRP), with a clinical picture characterized by: intense headache, oppressive, predominantly frontal, which does not yield to the administration of analgesics, accompanied by nausea without reaching vomiting, disturbances of thinking with fluctuations in the course of the day, reduced ability to maintain or direct attention, disorganized thinking, even led to disciplinary problems.

He entered the HMRP on December 23 of the same year where he was approached by the Neurology and Psychiatry services. On admission with few data since indirect interrogation is performed, pathological and non-pathological personal history is unknown, the physical examination reveals: Glasgow 12/15, neck stiffness, kerning and brudzinski (+), fever of 38°C, acute confessional state with Incoherent verbal responses, alteration of critical judgment and reasoning, at 24 hrs generalized tonic-clonic seizures are added.

Table 1.0: Hematic Biometry: Leukocytes 14,690 x103, with neutrophilia, platelets 187,000.

Characteristics	24.12.09	31.12.09	05.01.10
Appearance	Rock wáter	cloudy	Thick
Colour	Colorless	Xanthochromic	Xanthochromic
Pressure			
Glucose	16 mg/dl	27 mg/dl	50 mg/dl
Proteins	158 mg/dl	190.4 mg/dl	
Chlorides		115 mEq/L	
Leukocytes	25	686	34
Polymorphonuclear	60%	85%	60%
Mononuclear	40%	15%	
LDH		105 UI/L	200 UI/L

Serology studies with V.I.H and V.D.R.L negative. Lumbar puncture: Colorless, appearance in rock water, Glucose 16 mg / dl, protein 158mg / dl, leukocytes 25, PMN 60%, mononuclear 40%, negative bacterial cultures. (Table 1.0) Hematic Biometry: Leukocytes 14,690 x10³, with neutrophilia, platelets 187,000. (Table 2.0) Blood chemistry: Glucose 120 mg / dl (Table 3.0). Chest x-ray, EGO and Uroculture without alterations. Cabinet: Skull CAT scan in simple and contrasted phase.

Table 2.0: Blood chemistry: Glucose 120 mg / dl

HEMATIC BIOMETRY		
Parametro	24.12.09	31.12.09
Leucocits	14,690 X10 ³	15,789x10 ³
Neutrofilos	83.90%	95%
Lymphocytes	3.90%	3.40%
Platelets	187,000	92,000

Table 3.0: Chest x-ray, EGO and Uroculture without alterations

BLOOD CHEMISTRY		
Parameter	24.12.09	31.12.09
Glucose	120 mg/dl	127
Creatinin	0.6 mg/dl	
Urea	29 mg/dl	
Sodium	134 mEq/L	155
Potassium	4.2 mEq/L	4.22

(Figure 1) Computed tomography of the skull. A. Simple phase is observed apparently normal. B and C. Phase contrasted with meningeal reinforcement.

Empirical treatment is started with: Meropenem, cefotaxime, rifampin plus isoniazid, acyclovir, dexamethasone, B complex, parenteral fluids. It persists with fever, neurological deterioration and a psychiatric problem is ruled out, so on December 31, 2009, it moves to the 3rd level of care at the Central Military Hospital. It enters with the following clinical data: Disorientation, intense headache, throbbing, holocranana, accompanied by nausea and vomiting, fever of 38 °, confusional state with psychomotor agitation, vague, irrelevant and incoherent language, neck stiffness without finding other meningeal data. The CSF study gives the following data: xanthochromic appearance, thick, glucose 27 mg / dl, proteins 190.4 mg / dl, chlorides 115 mEq / L, leukocytes 686 with 85% PMN. BAAR, GRAM, KOH, Chinese ink and culture for fungi in Sabouraud negative medium. (Table 1.0)

Antifungal treatment is modified by initiating RIFATER, Vancomycin and Acyclovir are added. EEG shows generalized epileptiform discharges, which is why Valpróico Acid is started. January 2, 2010, fluconazole 400mg is added every 12 hrs intravenously. January 5 MRI showed changes compatible with meningoencephalitis, cerebral edema and hydrocephalus

non-communicating, acute ischemic events in ganglia of the base and left side mesencephalon.

(Figure 2) Magnetic resonance image. A is observed. Axial slice in T2 sequence. Sagittal section in T1 sequence. C. Coronal section in T2 sequence. January 7, the Glasgow falls to 8/15,



Figure 1: Computed tomography of the skull



Figure 2: Magnetic resonance image

January 10 was damaged by neurological deterioration and severe respiratory distress and enters intensive therapy, on January 11, ventriculostomy is performed to improve hydrocephalus, however, it occurs with increased pressure intracranial and neurological deterioration, with lethargy and stupor. January 15 falls into cardiorespiratory arrest without success in the resuscitation maneuvers. On January 16, a histopathological study was performed, which reports: Meningitis with basal arachnoiditis, secondary hydrocephalus, vasculitis, multiple infarctions, parenchymal granulomas and thrombosis of the cavernous sinus.

BIOMETRIA HEMATICA		
PARAMETRO	24.12.09	31.12.09
LEUCOCITOS	14,690 X 10 ³	15,789 x10 ³
NEUTROFILOS	83.9%	95%
LINFOCITOS	3.9%	3.4%
PLAQUETAS	187,000	92,000
QUIMICA SANGUINEA		
PARAMETRO	24.12.09	31.12.09
GLUCOSA	120 mg/dl	127
CREATININA	0.6 mg/dl	
UREA	29 mg/dl	
SODIO	134 mEq/L	155
POTASIO	4.2 mEq/L	4.22

Discussion

Coccidioidomycosis or San Joaquin Valley fever is a systemic mycosis caused by the dimorphic fungi *Coccidioides immitis* or *C. Posadasii*, which despite being highly contagious, is not transmitted from person to person and its true incidence and prevalence is unknown because it is not among the pathologies of mandatory reporting. Epidemiology It is an endemic mycosis

in some regions of the United States (California, Arizona, New Mexico and Texas), in the Northwest and Northeast of Mexico and in certain areas in Central and South America, 4 this dimorphic fungus that grows in layers of topsoil in semi-arid zones [10] where a warm climate prevails, low altitude and little rain. Pathophysiological En el hábitat mencionado se desarrolla como un micelio (forma saprófita), éstas células miceliales alternantes sufren un proceso de autólisis y adelgazamiento de sus paredes celulares, las células restantes (artróconidias) desarrollan una capa externa hidrofóbica lo que les confiere la capacidad para mantenerse viables durante periodos largos de tiempo y sus frágiles fijaciones se tornan propensas a la separation by physical rupture or even by some turbulence of air, consequently, they are transmitted by the air in a form apt to be deposited in the lungs if they are inhaled. In the lungs the arthroconidia are remodeled into spherical cells (parasitic form) and lose their hydrophobic outer wall, divide, multiply and as they mature, they break to release viable endospores, which produce a chemotactic effect in neutrophils. The most common route of dissemination to the CNS is hematogenous, and it can also occur by contiguity in cases of cranial or vertebral osteomyelitis. Clinical course The clinical picture is characterized by: Headache, neurological alterations, data of meningeal irritation, signs and constitutional symptoms. The disease can affect individuals at any stage of life and often has an unfavorable evolution. However, males become infected more frequently, probably because of the relationship with occupational exposure to contaminated dust; however, they also have a greater tendency to spread, suggesting a genetic or hormonal component [11]. Laboratory and Cabinet The red and white series do not usually undergo changes, however, in some cases leukocytosis with eosinophilia has been reported. Examination of cerebrospinal fluid usually reveals mononuclear pleocytosis, hypoglucorrhakia, and protein elevation. In some cases, elevated CSF pressure has been reported. Approximately in 33% of the cases it is not possible to identify this agent despite the exhaustive analysis of the CSF and other possible causes outside

the CNS. Some microorganisms that cause chronic meningitis take several weeks to grow in culture. Because extra pulmonary coccidioidomycosis is always secondary to dissemination from a primary pulmonary focus, chest x-rays should be performed, in which it is possible to find a frequently unilateral infiltrate with involvement of the upper lobes [12].

Treatment

Currently, triazole antifungals are the main drugs administered for the treatment of many cases of coccidiomycosis. Fluconazole has been shown to penetrate into the CSF, making it the azole compound most indicated for the treatment of coccidioid meningitis, this should be used with the minimum adult oral dose of 400mg / day that offers a response around the 70%. This is an important difference with the standard treatment of intrathecal Amphotericin B, which was still common until a few years ago [13]. Currently, two new products of this category are posaconazole and voriconazole. However, given the scarce clinical data, the high cost and (especially in the case of voriconazole) the possible toxic effects, the drugs in question are reserved for cases that remain recalcitrant after treatment with fluconazole or itraconazole. The administration of triazoles in high doses can be teratogenic, so we can think of amphotericin B to treat coccidiomycosis in pregnant women [14]. In addition to antifungal therapy to control meningeal inflammation, interventions for other manifestations are needed. Hydrocephalus usually does not respond to antifungal therapy and requires a CSF bypass procedure. Ventriculoperitoneal shunts become a conduit for *C. immitis* from the cerebrospinal space to the peritoneum, but usually do not produce clinically evident abdominal complications. Although the infection predominantly affects the basal meninges, intracerebral abscesses sometimes develop [15]. These lesions may require drainage or resection in addition to systemic mycotic treatment.

Conclusion

The fact that coccidioidomycosis is now a newly emerging disease can be attributed to changes in both demography and contemporary medicine. First, the populations at risk of exposure are very expanded. The regions in which *C. Immitis* is endemic, which were previously sparsely populated, now comprise major metropolitan centers. With this growth, tourism and the movement of people towards infected areas and from them have increased a lot. Second, an important stratum of the population has emerged with compromise of cellular immunity due to underlying diseases or immunosuppressive treatments to control other diseases [16]. However, due to its low frequency in immunocompetent patients, this diagnostic possibility may go unnoticed, and should be considered in endemic areas.

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