

Diagnosis Approach and Management of Rhombencephalitis: Literature Review

Ibrahima Mariam Diallo^{*}, Soumaila Boubacar, Mohamed Lelouma Mansaré, Ousmane Cissé, Japhari Nyassindé, Marie Emilie Yandé Ndong, Mame Maïmouna Diaw Santos, Abou Gueye, Anna Modji Basse, Adjaratou Dieynabou Sow, Marième Soda Diop, Lala Bouna Seck, Kamador Touré, Moustapha Ndiaye, Amadou Gallo Diop, Mouhamadou Mansour Ndiaye

Department of Neurology, Fann National Teaching Hospital, Dakar, Senegal

Email address:

dialloibmcool@yahoo.fr (I. M. Diallo)

^{*}Corresponding author

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Abstract: Rhombencephalitis refers to inflammatory diseases of the rhombencephalon. We present here a literature review of this pathology. It was originally described by Edwin Bickerstaff and Philip Cloake in 1951. The terms Rhombencephalitis and trunk encephalitis are interchangeable. It is a rare disease but potentially serious. The symptomatology is characterized, in some cases, by fever and alteration of consciousness, but also headache, nausea and vomiting sometimes. An involvement of the cranial nerves in the majority of the cases and or affected of the long ways. Paraclinically, cerebrospinal fluid and cerebral imaging can be normal in paraneoplastic causes or, on the other hand, be pathological in infectio-inflammatory causes. The etiologies are mainly distinguished in infectious, autoimmune and paraneoplastic pathologies. Treatment should be etiological by anti-infectives (antibiotics, antivirals, etc.) targeting curable germs such as listeria, mycobacterium tuberculosis or herpes, and/or symptomatic by corticosteroid or immunoglobulin IV. Rhombencephalitis is a rare nosological entity but is subject to severe neurological sequelae with a high mortality rate.

Keywords: Rhombencephalitis, Etiologies, Diagnosis, Management

1. Introduction

The term "rhombencephalitis" refers to inflammatory diseases of the rhombencephalon. The rhombencephalon or posterior brain is composed of the annular protuberance, the spinal bulb and the cerebellum. The term derives from the Greek, with "rhombos" meaning a diamond shaped figure, more "enkephalos", meaning the brain [4]. It is secondary to multiple and varied causes consisting of infections, autoimmune diseases and paraneoplastic syndromes [1, 12].

It was described for the first time by two scientists, Edwin Bickerstaff and Philip Cloake in 1951 [14, 16] to designate inflammatory affections of the rhombencephalon. Then six years later, H. Eck reported the first case of rhombencephalitis related to listeria monocytogenes in 1957

[14]. In addition, the terms "cerebral trunk encephalitis" and rhombencephalitis have often been used interchangeably [4, 12, 14].

It is a rare disease, but with high mortality and morbidity rates [2, 10, 16]. It is sometimes a diagnostic and therapeutic emergency because of the potentially serious and fatal nature of certain causative agents [1, 12].

We present here the epidemiological, clinical, paraclinical and therapeutic aspects of this potentially fatal disease and often few diagnosed in clinical practice.

2. Epidemiology

The Sex-ratio: In the serie of moragaz, Male sex was predominant in the Behcet disease and EBV infection groups.

Some etiologic entities of rhombencephalitis (RH) such as Multiple sclerosis (MS) and Epstein-Barr virus (EBV) appear affected the more young people, while others such as Listeria or paraneoplastic syndromes concern more young adults or elderly subjects [14].

Very little data in Africa, unlike the USA, where cases of Listeria monocytogenes are listed from 2000 to 2014 (Table I)

Listeria is the most common cause of infectious RE (figure

I), and mostly affects young adults. Very little data exist on rhombencephalitis in sub-Saharan Africa. Existing data include cases of listeriosis reported in some countries such as Nigeria, South America, Zambia, etc.) [17, 11].

Enteroviruses are the second most common viral cause and prominently include Enterovirus 71 in the Asian south east. HSV is the third most common infectious cause of RE, and about 80% of cases are caused by HSV1 [3].

Table I. Summary of Listeria monocytogenes-associated food-borne outbreaks in the USA from 2000 to 2014. [13] (From Marler Clark Network, 2014.).

Study period	Total number of cases	Number of hospitalizations	Number of deaths	L. monocytogenes serotype	Food vehicle
2000	13	13	0	4b	Mexican style cheese
	30	29	4	1/2a	Deli meat
2001	28	0	0	1/2a	Deli meat
2002	54	NA*	8	4b	Deli meat
2003	3	NA	NA	4b	Unknown
2005	12	12	1	4b	Mexican style cheese
	6	6	0	4b	Unknown
	3	3	0	1/2b	Grilled chicken
	13	13	1	1/2a	Deli meat
2016	12	12	0	1/2b	Mexican style cheese
	2	1	1	4b	Unknown
	2	0	0	1/2b	Tacho or nacho salad
	3	2	1	4b	Cheese
2007	5	5	3	4b	Milk
2008	5	5	3	1/2a	Tuna salad
	20	2	0	1/2a	Sprouts
2011*	8	4	0	1/2a	Mexican style cheese
	147	147	33	1/2a, 1/2b	Cantaloupes
	22	20	4	NA	Ricotta salata cheese
2012*	6	6	1	NA	Scott ripened cheese
	8	7	1	NA	Sott or semisoft
2013*					Hispanic cheese
2014*					

*NA, Not available

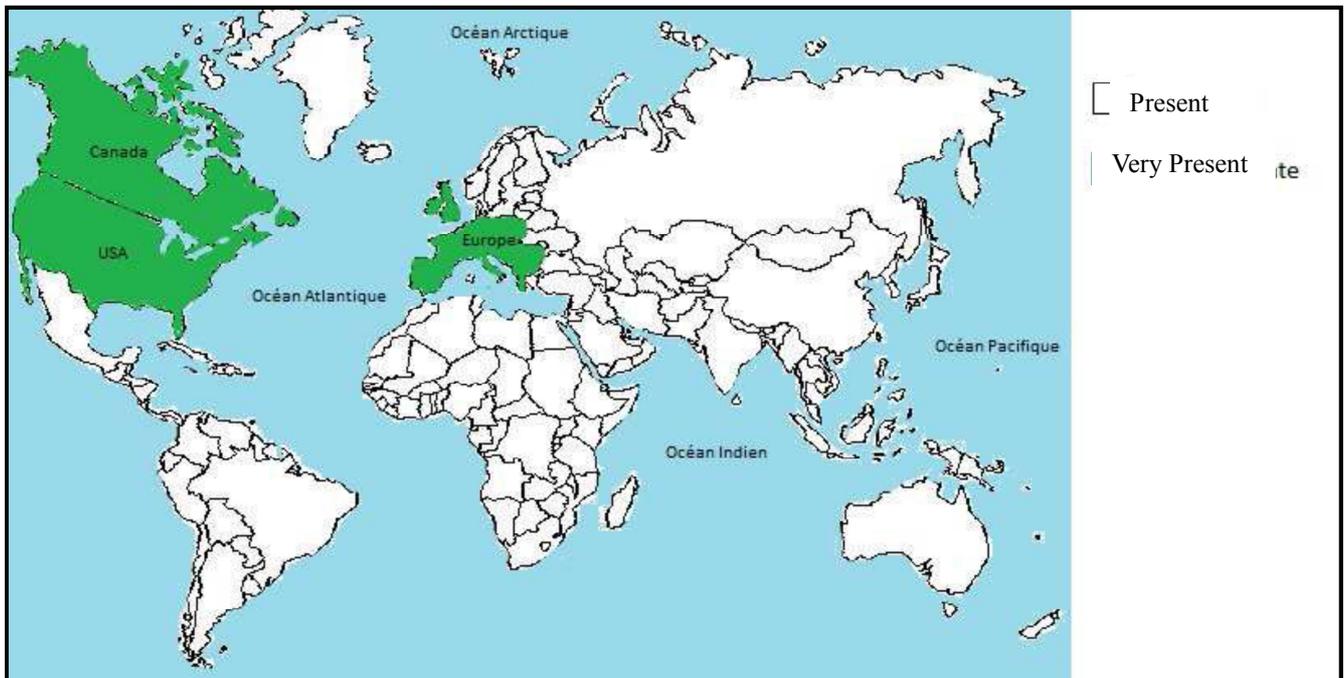


Figure 1. Geographical distribution of listeria monocytogenes in the world [6].

3. Clinical Aspects

The fever and alteration of the initial consciousness are mainly found in infections, coming within the framework of a biphasic symptomatology with headache, nausea, vomiting, malaise followed by a meningeal syndrome [2]. Cranial nerve involvement is one of the most frequent signs (3/4 of the cases). Cerebellar ataxia is also frequently found in infectious and paraneoplastic causes. Longitudinal pathways (pyramidal, sensory and cerebellar) may be alternated and occur predominantly in autoimmune causes such as Behcet's disease [4, 10]. Respiratory and cardiac disorders are the result of the involvement of the last cranial nerves with bulbar-pontic or bulbar cardiorespiratory centers [2, 10]. The clinical picture may evolve unfavorably towards a "locked-in syndrome" made up of a quadriplegia that contrasts with the normality of consciousness or sometimes a deadly coma [10].

Moreover, a particular nosological entity deserves to be known, it is post-infectious rhombencephalitis type Bickerstaff syndrome, which is a diagnosis of elimination which must be evoked before a clinical picture associating ophthalmoplegia, tetraparesis, Pyramid syndrome, and ataxia, and look for the anti-ganglioside antibody GQ1b, which is present in most cases [5, 9].

4. Paraclinic Aspects

The paraclinic assessment is mainly based on cerebral imaging, cerebrospinal fluid (CSF) analysis, blood cultures and in the CSF with polymerase chain reaction (PCR) and the detection of associated antibodies specific to paraneoplastic syndromes.

Cerebro-Spinal fluid may be normal in paraneoplastic causes, or present a pleiocytosis predominantly neutrophilic, or sometimes a lymphocytosis related to infectious causes; High levels of protein are found in most cases [4]. A glucose level may be normal or lowered depending on the etiologies, mainly in the bacterial infectious causes [4].

CT scans: may be normal initially, which does not eliminate the diagnosis of rhombencephalitis or may show foci hypodense brainstem, with or without cerebellar involvement; Or even a diffuse swelling of the rhombencephalon associated with a filling of the peripart cisterns. At a late stage, micro-abscesses or abscesses of greater size may occur in the brainstem or the cerebellum [10].

Magnetic Resonance Imaging (MRI): is usually normal in paraneoplastic syndromes [4, 7, 14], or abnormal in infectious and autoimmune causes [14] by showing hypointense plaques T1, hypersignal T2 and FLAIR (figures 2 and 3), poorly limited, more or less confluent with often a central zone hypointense in T2. The injection of gadolinium often makes it possible to delineate the zone of breach of the blood-brain barrier [10].

The most characteristic result of rhombencephalitis associated with tuberculosis is the involvement of basal

cisterns with enhancement of the leptomeningeal after intravenous contrast injection [12].

The diffusion sequence has a dual interest, not only in the evolutionary determination of the underlying pathology, but also in the distinction between an abscess and a necrotic tumor that usually appears as a hyposignal [10].

Cases of rhombencephalitis caused by paraneoplastic syndromes have been associated with anti-Yo, anti-Tr, anti-Hu, anti-Ri, anti-Ma and anti-amphiphysin antibodies, but we must also know that they are not always present [4, 12]:

Anti-Yo and anti-Tr antibodies in gynecological cancer (ovary, uterus) and breast cancer in relation to paraneoplastic cerebellar degeneration;

Anti-Ri antibody in breast, gynecological and small cell lung cancer is found mainly in paraneoplastic cerebellar degeneration and opsoclonus-myoclonus syndrome;

Anti-Hu and anti-Ma antibodies are related to lung cancer and are detected in paraneoplastic cerebellar degeneration; The anti-amphiphysin antibody is related to small cell lung carcinoma.

The supplementation balance sheet should be supplemented by blood cultures as well as the search for certain germs such as herpes, mycobacterium tuberculosis, after lumbar puncture, polymerase chain reaction (PCR), Gram staining and Ziehl-Neelsen staining in CSF, as well as mycobacterium culture [4].



Figure 2. Cerebrospinal MRI, Hyposignal in T1 extended at the level of the bulb.



Figure 3. Brain MRI, Hypersignal in T2 FLAIR bulbar.

5. Etiological Aspects

The causes of rhombencephalitis can be divided into infectious diseases, autoimmune diseases and paraneoplastic syndromes. The most common infectious causes are *Listeria monocytogene*, enterovirus 71 and herpes viruses. The most common autoimmune cause is Behcet's disease, and the most common paraneoplastic cancer is small cell lung cancer.

Table 2. Possible etiologies of rhombencephalitis (summarized in the following) [4, 7, 12].

Etiologies	Various types
Infections	<i>Bacterial:</i>
	<i>Listeria</i>
	<i>Mycobacterium tuberculosis</i>
	<i>Pneumococcus</i>
	<i>Brucella</i>
	<i>Borrelia</i> (Lyme Disease)
	<i>Salmonella</i>
	<i>Legionella</i>
	<i>Mycoplasma</i>
	<i>Viral:</i>
	Enteroviruses (<i>Enterovirus 71</i> , <i>Bulbar poliomyelitis</i> , <i>Coxsackievirus A16</i> , <i>Echovirus</i>)
	Flaviviruses (<i>Japanese encephalitis</i> , <i>St. Louis encephalitis</i> , <i>West Nile virus</i>)
	Herpes Viruses (<i>HSV</i> , <i>EBV</i> , <i>HH6</i> , <i>CMV</i> , <i>VZV</i>)
	<i>Rabies virus</i>
	<i>Eastern Equine Encephalitis</i>
	<i>Adenovirus</i>
	<i>Influenza A</i>
	<i>Other</i>
	<i>Melioidosis</i>
	<i>Aspergillus</i>
<i>Mucormycosis</i>	
<i>Nocardia</i>	
<i>Cysticercosis</i>	
<i>Toxoplasmosis</i>	
<i>Behcet Disease</i>	
<i>Systemic Lupus Erythematosus</i>	
<i>Relapsing polychondritis</i>	
<i>Sjogren's syndrome</i>	
<i>Sarcoidosis</i>	
<i>Vogt-Koyanagi-Harada</i>	
Paraneoplastic	<i>Cerebellar degeneration</i> , <i>opsoclonus myoclonus</i> , <i>brain stem encephalitis</i> , <i>small cell lung cancer</i>
Other	<i>Lymphoma</i>

6. Management

The treatment of rhombencephalitis should be etiological and/or symptomatic.

In patients with a clinical picture associated with fever, empirical therapy should be initiated with Ampicillin or penicillin G, associated with gentamicin, ceftriaxone, anti-tuberculosis drugs and acyclovir depending on the clinical context [1, 2, 8] for germs potentially serious and / or frequent such as respectively *Listeria*, *Mycobacterium tuberculosis* and herpes.

Corticosteroids are indicated, particularly if rhombencephalitis is linked to a inflammatory or severe infectious causes when there is no improvement in clinical neurological status despite effective and appropriate anti-

infective therapy [2, 15].

Other therapeutic attitudes may be favorably adopted in some forms, including immunoglobulins (Ig) in intravenous in post-infectious rhombencephalitis [9].

The management must be completed by psychotherapy and physiotherapy if the patient presents its indication.

7. Conclusion

Rhombencephalitis is a rare nosological entity but is subjected to severe neurological sequelae with a high mortality rate, hence the interest of early diagnosis and etiological research guaranteeing appropriate treatment in order to minimize neuronal damage for a best prognosis.

Abbreviations

HSV = Herpes Simplex Virus, EBV = Epstein-Barr Virus, HH6= Human Herpes Virus type 6, CMV= Cytomegalovirus, VZV=Varicella zoster virus, CSF=cerebrospinal fluid, MS = multiple sclerosis, PCR = polymerase chain reaction, RE = rhombencephalitis, SLE=systemic lupus erythematosus, TB=tuberculosis, USA= United States of America.

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