CASE REPORT

The Sleeping Sickness Revisited: A Case of Encephalitis Lethargica

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Abstract

The acute phase of Encephalitis Lethargica is usually characterized by fever, ocular movement abnormalities, extreme drowsiness, and erratic neurological signs. The chronic phase manifests months or years later. It is characterized by chorea, orofacial tics, and Parkinsonism with stiffness and delayed movement, which is frequently triggered by stimuli (kinesia paradoxical). There are serious neurological and mental deficits associated with chronic Encephalitis Lethargica. We describe the case of a 9-year-old girl who had been sent to the hospital 15 days before. She had a high-grade fever that started suddenly, was accompanied by three episodes of vomiting, altered consciousness, and, after four days, tremors and dystonia. The patient received treatment in accordance with the MRI diagnosis of Encephalitis Lethargica. The patient's tremors subsided; all limbs were less rigid and dystonic, and limb physiotherapy continued. Encephalitis Lethargica has a very unpredictable outcome. Economo's historical accounts suggested a "rule of thirds": roughly one-third of patients make a full recovery, one-third experience long-lasting behavioral or motor problems, and the other third die from the disease. Children and patients who present primarily with neurological features typically have better outcomes than those who present with persistent psychiatric symptoms.

Keywords: *Encephalitis lethargica, MRI, parkinsonism, oligoclonal, hypersomnia.*

INTRODUCTION

The psychiatrist and neurologist Constantin von Economo first described Encephalitis Lethargica in 1917. He also described von Economo encephalitis, which was an epidemic of brain and brainstem encephalitis that struck North America and Europe between 1916 and 1927. The condition, sometimes referred to as sleeping sickness, is closely associated with postencephalitic Parkinsonism and was first divided into three clinical types [1]. The acute phase of Encephalitis Lethargica is usually characterized by fever, ocular movement abnormalities, extreme drowsiness, and erratic neurological signs. Flu-like symptoms are typical at first, and it quickly develops into one of three forms: somnolent-ophthalmoplegic, hyperkinetic, or amyostatic-akinetic.

The chronic phase manifests months or years later. It is characterized by chorea, orofacial tics, and Parkinsonism with stiffness and delayed movement, which is frequently triggered by stimuli (kinesia paradoxical). Psychiatric symptoms like mood swings, hallucinations, and psychosis are frequent, as are oculogyric crises (involuntary upward eye movements). There are serious neurological and mental deficits associated with chronic Encephalitis Lethargica [2]. Encephalitis Lethargica (EL) can occur at any age, though it is most frequently observed between 10 and 30 years [3].

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CASE REPORT

We describe the case of a 9-year-old girl who had been sent to the hospital 15 days before. She had a high-grade fever that started suddenly, was accompanied by three episodes of vomiting, altered consciousness, and, after four days, tremors and dystonia. She had treatment for meningoencephalitis there. She had injections of Levetiracetam, Meropenum, Vancomycin, Acyclovir, Dexamethasone, and syp. Azithromycin. Her problems were only momentarily alleviated. Blood cultures and sensitivities revealed no growth, and her cerebrospinal fluid and CT brain were unremarkable. The patient was referred to Liaquat National Hospital and Medical College after an MRI revealed acute disseminated encephalomyelitis, most likely as a result of midbrain involvement.

A patient with altered awareness, upper and lower limb tremors and dystonia, a GCS of 8/15, and hypersomnolence arrived at the Paeds Neurology clinic at Liaquat National Hospital and Medical College. She exhibited a masked face, bilateral upper and lower limb rigidity and tremors, hypertonia, brisk reflexes, clonus, and was afebrile on physical examination.

At first, she had an injection of Brivaracetam, Lacosamide, Methylprednisolone in a pulse dose, Diazepam for maintenance, and tablets of Baclofen and Tizanidine. After the recommended initial workup, which included serum electrolytes and LFTs, came back negative, an urgent MRI brain with I/V contrast was performed. MRI findings are described in **Figs. (1** and **2)**.

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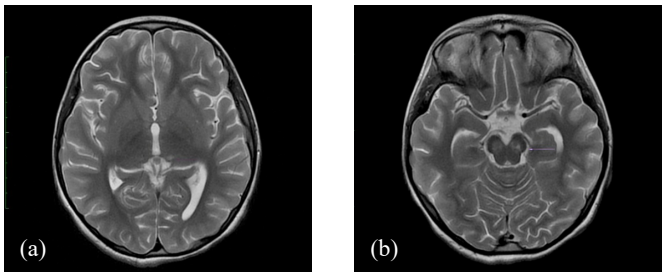

Fig. (1a and b): AX T2 Brain + Gadolinium showing hyperintense signals in the substantia nigra bilaterally and faint high signals in the left thalamus with no post-contrast enhancement.

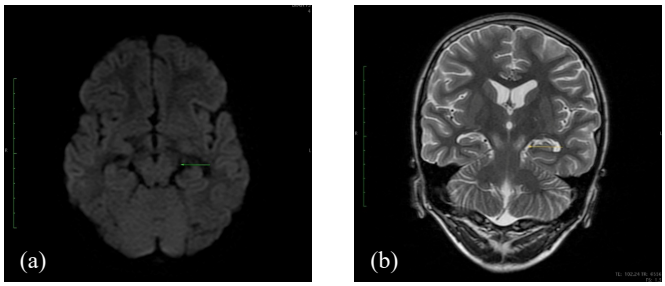

Fig. (2a and b): AX DWI showing hypointense signals in the substantia nigra representing a lack of restricted diffusion (b) COR T2 showing hyperintense signals in the substantia nigra.

Following the diagnosis of Encephalitis Lethargica, methylprednisolone injections were discontinued, carbidopa/levodopa was started eight hours a day, and Diazepam was tapered off. The patient's tremors subsided; all limbs-upper and lower-were less rigid and dystonic, and limb physiotherapy continued. After being released, the patient was monitored in the outpatient department. The patient reported returning to regular life activities at the 15-day follow-up, and speech revealed a slow recovery.

DISCUSSION

Von Economo first defined Encephalitis Lethargica (EL) in 1916. EL is a central nervous system condition that first presents as pharyngitis and then progresses to sleep disturbances, basal ganglia symptoms (particularly Parkinsonism), and neuropsychiatric sequelae. Since the 1916-1927 pandemic, case reports have been sporadic at best.

The acute phase of Encephalitis Lethargica usually starts with flu-like symptoms and quickly develops into one of three forms:

1. Somnolent-ophthalmoplegic: Most common, characterized by sleepiness, disorientation, paralysis of the eye muscles, and a high death rate, but survivors experience fewer long-term consequences.
2. Hyperkinetic: Manic symptoms such as twitches in the muscles, hallucinations, chorea, vocal tics, and irregular sleep patterns.
3. Amyostatic-akinetic: characterized by slow, stiff movements, little emotion, and unharmed mental faculties.

The chronic phase manifests months to years later. It includes movement problems such as chorea and/or orofacial tics, as well as Parkinsonism with stiffness and delayed movement, which is frequently triggered by stimuli (kinesia paradoxical). Psychiatric symptoms like mood swings, hallucinations, and psychosis are frequent, as are oculogyric crises (involuntary upward eye movements). There are serious neurological and mental deficits associated with chronic Encephalitis Lethargica [2].

Sometimes undetected until chronic symptoms emerged, the onset varied from abrupt to moderate. Lethargy affected about one-third of the patients; they were quickly roused from their unexpected sleep. Usually incomplete and asymmetrical, eye abnormalities were widespread, particularly ptosis. Rarely did hemiplegia occur. Postencephalitic Parkinsonism can appear at any moment, usually within five to ten years, but occasionally after twenty years or longer. Neuropsychiatric conditions, Parkinsonism, involuntary movements (chorea, tics, dystonia), oculogyric, and respiratory crises were among the main postencephalitic symptoms. Although illness can occur at any age, Encephalitis Lethargica (EL) is most commonly seen in those aged 10-30. With no known underlying cause, the illness is still classified as an exclusionary diagnosis. Obsessive-compulsive disorder, hypomania, and, less frequently, schizophreniform symptoms were among the personality alterations that adults frequently displayed. Children frequently experienced more severe mental changes, such as serious self-mutilation [2].

Even though it is uncommon, juvenile patients who exhibit unexplained acute or subacute encephalopathy should be evaluated for Encephalitis Lethargica, especially if neuropsychiatric and extrapyramidal symptoms predominate. Early dopaminergic therapy may help alleviate symptoms and promote recovery, even though the exact cause and final treatment remain unknown [3].

The link between acute Encephalitis Lethargica and chronic postencephalitic Parkinsonism is uncertain, as delays of decades occur, some outbreaks lack chronic cases, and many patients do not recall acute illness, suggesting acute infection may be a contributing but not essential factor [2].

According to the diagnostic criteria proposed by Howard and Lees, Encephalitis Lethargica should be diagnosed in

any patient who exhibits at least 3 of the 7 characteristics listed below, together with an acute or subacute encephalitic illness. Obsessive-compulsive behavior, akinetic mutism, central respiratory abnormalities, ocular crises, ophthalmoplegia, involvement of the basal ganglia, and somnolence or inversion of sleep [3].

Since CT scans frequently reveal no abnormalities, neuroimaging particularly MRI is crucial for detecting Encephalitis Lethargica (EL)-like disease [2]. Symmetrical bilateral hyperintensities on T2-weighted and FLAIR images are frequently seen on MRI T2-weighted and FLAIR images in important brain regions such as the midbrain, mesial temporal lobe, and basal ganglia. These hyperintensities correlate to clinical features like hypersomnolence, aberrant behaviors, and Parkinsonian signs.

Studies show laboratory investigations in acute Encephalitis Lethargica were unremarkable. Some patients, but not all, showed a degree of lymphopenia. CSF examination could be normal or show minor lymphocytosis [4]. Some other studies show that Mild lymphocytosis and increased protein levels are typical findings in CSF analysis; oligoclonal bands, which indicate an immunological response in the central nervous system, are seen in about 70-76.5% of patients [5].

In the acute phase, histopathological analyses reveal perivascular inflammation and neuronal necrosis mostly in the midbrain and basal ganglia; in the chronic stages, the substantia nigra is uniformly depigmented. Recent research has failed to detect influenza RNA in brain tissue, indicating that Encephalitis Lethargica is not an invasive form of influenza encephalitis, despite its historical association with the influenza pandemic.

The presence of intrathecal oligoclonal bands and favorable responses to immunomodulatory therapies, such as steroids and intravenous immunoglobulin, further supports an autoimmune etiology. Infections, such as streptococcal and upper respiratory tract infections, frequently precede Encephalitis Lethargica. Other post-infectious neurological syndromes, such as Bickerstaff's brainstem encephalitis, pediatric autoimmune neuropsychiatric diseases associated with streptococcal infections (PANDAS), and Sydenham's chorea, share clinical, radiological, and immunological characteristics with it. Similar MRI abnormalities are present in these illnesses [4].

They share an acute or subacute onset and commonly present with neuropsychiatric or altered mental status features. All three disorders involve motor system abnormalities, though the manifestations differ: Parkinsonism in Encephalitis Lethargica (EL) or choreiform movements in PANDAS, and ataxia in BBE. Pediatric cases are reported in all three, with PANDAS occurring exclusively in children (**Table 1**) [5-9].

Table 1: Comparison between EL, PANDAS and BBE.

Variables	Encephalitis Lethargica (EL)	PANDAS	Bickerstaff Brainstem Encephalitis (BBE)	Ref.
Etiology	Post-infectious; unclear cause (historically influenza-associated)	Autoimmune reaction to Group A β-hemolytic *Streptococcus*	Autoimmune; anti-GQ1b antibody mediated	[7-9]
Typical Age	Children & adults	Children (3-12 years)	Children & young adults	[7-9]
Onset	Subacute	Abrupt, dramatic	Acute	[7-9]
Key Clinical Feature	Profound hypersomnolence	OCD + motor/vocal tics	Ophthalmoplegia + ataxia + encephalopathy	[7-9]
Movement Disorder	Parkinsonism (post-encephalitic)	Tics, choreiform movements	Not typical	[7-9]
Neuropsychiatric Features	Behavioral change, psychosis	OCD, anxiety, emotional lability	Altered consciousness	[7-9]
CNS Target	Basal ganglia, midbrain	Basal ganglia	Brainstem	[7-9]
Ophthalmoplegia	May occur	No	Characteristic feature	[7, 9]
Ataxia	Occasional	Rare	Prominent	[7, 9]
Reflexes	Normal or rigid (Parkinsonian)	Normal	Often hyperreflexia	[7, 9]
CSF Findings	Normal, Mild Lymphocytosis, lymphopenia	Usually normal	Albuminocytologic dissociation	[5-9]
Antibodies	None specific	Anti-basal ganglia antibodies (in some cases)	Anti-GQ1b positive	[8, 9]

Variables	Encephalitis Lethargica (EL)	PANDAS	Bickerstaff Brainstem Encephalitis (BBE)	Ref.
MRI	Midbrain/basal ganglia lesions	Usually normal	Brainstem abnormalities	[7-9]
Course	Acute → chronic Parkinsonism	Episodic; linked to strep infections	Monophasic; usually good recovery	[7-9]
Treatment	Supportive; steroids; L-dopa (chronic phase)	Antibiotics, IVIG, steroids	IVIG or plasmapheresis	[7-9]

Encephalitis Lethargica has a very unpredictable outcome. Economo's historical accounts suggested a "rule of thirds": roughly one-third of patients make a full recovery, one-third experience long-lasting behavioral or motor problems, and the other third die from the disease. Compared to patients with protracted psychiatric symptoms, children and patients who present primarily with neurological aspects typically have better outcomes [3].

CONCLUSION

Encephalitis Lethargica-like illness is a post-infectious neurological syndrome featuring Parkinsonism, hypersomnia, neuropsychiatric symptoms, and ophthalmoplegia. MRI is a valuable tool in diagnosis, along with clinical correlation.

CONSENT FOR PUBLICATION

Written informed consent was taken from the guardian.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Declared none.

AUTHORS' CONTRIBUTION

DF: Studied the case and wrote the case report.

FQ: Managed the patient and helped in writing the case report.

AS: Guided and helped in writing the case report.

BS: Diagnosed the case and reviewed the case report.

RK: Pt's treatment, management, and reviewed the case report.

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