

von Economo Encephalitis

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Abstract :

In April 1917, Dr Constantin von Economo presented his clinical and pathologic findings of a new disease—soon to be part of a worldwide epidemic—before the Vienna Psychiatric Society. He named it encephalitis lethargica. After years of careful observation, he collected and analyzed thousands of cases and classified them into 3 clinical syndromes: somnolentophthalmoplegic, hyperkinetic, and amyostatic-akinetic forms. He described the now legendary post-encephalitic Parkinsonism, noting that symptoms could emerge years after the original infection, often without signs of prodromal "flu." He emphasized the neuropathologic findings: inflammatory changes in the tegmentum of the midbrain accounting for the sleep disturbance and ocular signs. After encountering sporadic cases following the epidemic, he concluded that the somnolentophthalmoplegic syndrome was the primary expression of encephalitis lethargica. This article outlines the observations and conclusions of Dr von Economo during and after the epidemic through seminal quotations primarily from his published works, as well as from more recent reports.

Early observations

The first case of this strange new disease appeared at the end of 1916. Under the careful observation of Dr von Economo, a well-defined syndrome complex began to emerge, characterized by disturbances of sleep and ocular motility as well as ptosis, which he described in his early monograph.

«It seems strange when sleep appears as a symptom of an illness. "Sleeping sickness" where the phenomenon of people falling asleep while eating or working was first described in two cases in our clinic in Vienna in 1916. Usually headache, nausea, and fever were followed, often the next day, by sleeping, frequently in a most uncomfortable position. One can wake them, but in severe cases, coma can rapidly lead to death. Malfunction of eye muscles, especially oculomotor dysfunction, and ptosis, was common.»

In fact, of the 13 reported cases, von Economo described 4 with ptosis, 2 with abducens palsies, and 1 each with supranuclear palsy and medial longitudinal fasciculus syndrome. Only 3 of the 13 had no ocular signs.

Historical background

von Economo may have known of accounts of similar cases—and epidemics—that were reported centuries ago, such as mendocsa in Lisbon in 1521, pestilence soporeuse in Italy in 1561, and lethargy with ocular palsies in Germany in 1605. He was aware of an epidemic in Italy in the late 1800s, which may have given impetus to his major life's work.

«... a half-forgotten memory of childhood came to the fore. In 1890-1891 there occurred in connection with the then pandemic influenza in Italy a peculiar illness associated with stupor called

Nona. von Economo reported that he described his own peculiar cases of stupor to his mother and asked whether she remembered the accounts of the mysterious Nona. She replied that she did»

Neuropathology

Within months of the appearance of the first case, von Economo already had autopsy proven evidence of the neuropathology: notably widespread microscopic inflammatory foci, particularly in the gray substance of the tegmentum of the mid brain. This was presented before the Psychiatric Society in Vienna on April 17, 1917, and named encephalitis lethargica.

«We must assume that it is from the grey matter of this region that the natural sleep function is influenced. This assumption gains all the more probability because Wernicke's encephalitis, in the wake of delirium tremens, eye muscle disturbances and somnolence appear, and hemorrhages are to be found in these same parts of the tegmentum.»

Clinical presentation

Usually associated with the influenza epidemic that claimed more than 30 million lives, tens of thousands of cases of encephalitis were reported during and after the first World War. von Economo was the first to recognize and classify 3 distinct clinical forms.

«Every epidemic of encephalitis lethargica is characterized by the predominance of a certain combination of symptoms.... We are able to distinguish three forms of pathological syndromes which embrace the great majority of cases.... These three syndromes under which encephalitis lethargica has appeared most frequently hitherto are the somnolent-ophthalmoplegic, the hyperkinetic, and the amyostatic-akinetic (the so-called Parkinsonism).»

Somnolent-Ophthalmoplegic

«The prodromal phenomena consists of general discomfort, shivering, headache, and slight pharyngitis. The temperature is generally only a little raised to slightly above 98'C.... Within the next few days, somnolence begins to predominate. The patients left to themselves fall asleep in the act of sitting and standing, and even while walking, or during meals with food in the mouth.... if aroused, they wake up quickly and completely, are oriented and fully conscious ... but soon drop back to sleep. Sleep in this form may last for weeks or even months but frequently deepens to a state of most intense stupor or even a comatose condition which may terminate fatally after some days or weeks.

Generally, during the first days of the illness (cranial nerve) palsies appear. Ptosis is one of the first and most frequent symptoms. The frequent bilateral occurrence of ocular palsies, incomplete usually asymmetrical, suggest that it is, in most cases, a nuclear palsy. Rarely observed are supranuclear paralyzes, paresis of convergence, nystagmus, optic neuritis, papilledema, pupillary

disturbances, and even Argyll Robertson's sign.

Hyperkinetic

In the winter of 1920, there was observed a very large group of hyperkinetic cases, first in Italy then Austria. Chorea and hemichorea as well as myoclonic twitches which were observed may degenerate into wild jactations.

On the other hand, it may find its mental expression in a general, curious restlessness of an anxious or hypomanic type. In most of these cases, there is a very distinct sleep disturbance and generally the condition is one of troublesome sleeplessness.

Amyostatic-Akinetic

Third place in order of frequency, the amyostatic-akinetic form, is characterized by a rigidity, without a real palsy and without symptoms arising from the pyramidal tract. This form of encephalitis lethargica is particularly common in the chronic cases, dominating the clinical picture as Parkinsonism. I reserve the name "Parkinsonism" though symptomatically identical with the amyostatic-akinetic form, rather for the chronic cases. To look at these patients one would suppose them to be in a state of profound secondary dementia. Emotions are scarcely noticeable in the face, but they are mentally intact.»

Writing in 1929, toward the end of the devastating worldwide epidemic, von Economo concluded that the somnolent-ophthalmoplegic form was the primary expression of encephalitis lethargica. If it ever recurred again, be reasoned that it would be in this form.

«Now that the great epidemics of encephalitis lethargica are over, we meet with isolated sporadic acute cases every year. It is interesting to note that these sporadic cases of encephalitis lethargica, occurring at a time when there is no epidemic, are mostly of the somnolent-ophthalmoplegic form. Therefore, it appears probable that the somnolent-ophthalmoplegic form should be regarded as the basic form proper of encephalitic lethargica.»

Geographic-specific syndromes

As the disease ravaged Europe, von Economo recognized particular combinations of symptoms and syndromes, in various countries and cities especially hard-hit by the epidemic and classified them accordingly.

Prognosis

Encephalitis lethargica was quickly recognized as a serious, lethal disease. Aside from a very high mortality rate, many patients were left with significant disabilities.

«The prognosis of clinically welldocumented cases of encephalitis lethargica is: 40% mortality, 14% complete recovery, 26% recovery with defect, but able to work, and 20% chronic invalidity. Encephalitic lethargica must in every case be regarded as a serious and dangerous disease.»

Chronic parkinsonism

As early as 1920 von Economo began observing cases that had apparently recovered fully, only to be stricken with parkinsonian features months, or even years, later.

«Parkinsonism may develop in immediate sequence after the amyostatic form ... as well as 4 or 5 years after an apparently complete recovery from acute encephalitic lethargica. The acute stage may have been slight or serious; it is of no importance in indicating the probable development of later symptoms. Often we see cases where such sequelae develop with no history of a previous acute phase.»

Oculogyric crises

Without doubt, the oculogyric crisis was the one of the outstanding features of postencephalitic parkinsonism, which intrigued clinicians for decades.

«Of particular interest are the visual fits, described by French authors as “crises oculogyres” (van Bogaert, Bing, and Schwartz, Marinesco and Radovici), in English as “tonic eye-fits” or, more commonly, as oculogyric crises. They consist of tonic visual convulsions, occurring in fits and generally lasting only a few minutes, during which the patients as a rule look upwards and sideways.... Frequently, the convulsive twisting of the eyes is also accompanied by other convulsive movements, such as contortion of the head in the direction of vision, tonic stretching of the neck, even of the trunk and extremities...»

Recent observations

While reports of presumed Economo encephalitis or postencephalitic Parkinson disease unrelated to the 1917-1927 pandemic have appeared in the medical literature in the past 30 years, most of them have lacked either an adequate documentation of encephalitis lethargica or a convincing causal relationship between the encephalitis and subsequent neurologic sequelae. In one series, in almost every case, the parkinsonian symptoms and signs first appeared 20 to 40 years after the encephalitis.

Howard and Lees, however, carefully documented 4 cases in 1987. While failing to identify the viral agent, they found positive oligoclonal banding in 3, performed postmortem examinations in 1, and formulated specific diagnostic criteria:

«We propose that a number of clinical features ... as major criteria supporting the diagnosis of encephalitis lethargica. It should comprise an acute or subacute encephalitic illness . . . [with] three of the following major criteria: (1) signs of basal ganglia involvement, (2) oculogyric crises, (3) ophthalmoplegia, (4) obsessive-compulsive behavior, (5) akinetic mutism, (6) central respiratory irregularities and (7) somnolence and/or sleep inversion.»

Duvoisin and Yahr, in 1965, published a review of their patients with postencephalitic parkinsonism. They surveyed the literature for a similar syndrome caused by known viruses and could find no association with any known neurotropic viral agent:

«The rare association of a progressive Parkinsonim syndrome such as is understood by the term Parkinson's Disease with any [known] type of virulencephalitis ... has not be shown to be more than coincidental.»

More than 30 years later, one of the authors again reviewed published reports and concluded that despite the advent of modern virology, the failure to isolate the causative agent continues to cast a shadow of doubt on all reported cases:

«Presumed cases of von Economo's disease parkinsonism have been reported in small numbers since 1970. The clinical and, when available, the pathological data are fairly convincing. However ' lacking a specific confirmation, the doubt will remain concerning the authenticity of the diagnosis.»

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