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History of Neurology

Gayet-Wernicke Syndrome: The eye surgeon in a French neurologic eponym

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INFO ARTICLE

Article history:
Received 30 September 2021
Received in revised form
2 November 2021
Accepted 15 November 2021
Available online 16 February 2022

Keywords:
Gayet-Wernicke encephalopathy
Wernicke Superior Hemorrhagic Polioencephalitis
Wernicke's Encephalopathy
Korsakoff syndrome
Wernicke's Syndrome

ABSTRACT

Gayet-Wernicke syndrome is an eponym mainly used in France. In this article, we revisit Charles Gayet's (1833–1904) speciality and his patient example that gave rise to the eponym. Charles Gayet attributed the anatomical lesions to inflammation. However, they were mainly due to hemorrhage, as Wernicke's term "*polioencéphalite supérieure aiguë hémorragique*" (polio-encephalitis superior haemorrhagica) explicitly indicates. The pathology of Gayet's case did not involve the mamillary bodies, colliculi, or cerebellum. Gayet did not mention abnormal memory functions, which are also cardinal signs of Wernicke-Korsakoff's disease. We argue that the Gayet-Wernicke eponym is not merited and that the more common international term "Wernicke-Korsakoff syndrome" should be used in France as elsewhere in the world.

1. Introduction

Gayet-Wernicke syndrome is an established eponym in France. It is not well known or used elsewhere. It is rarely mentioned in historical works on Wernicke–Korsakoff's syndrome with at least two notable exceptions. Pearce mentioned his name in his historical vignette and had no difficulty identifying Gayet, who described a case 6 years before Wernicke's account, as one of the earlier pioneers of the disease [1]. Victor, Adam and Collins in their classic work mention Gayet but dismiss his contributions: "The case described by Gayet in 1875 was almost certainly not an instance of Wernicke disease" and "it differs from Wernicke disease in essential details, both clinically and pathologically." Based on the available material, they speculated that a necrotic hemorrhagic leukoencephalopathy was a more likely diagnosis [2]. The eponym keeps popping up in the medical literature [3]. We revisited Gayet's work and the facts of his biography that led to his inclusion in the eponym. We critically addressed the need for this rival eponym.

1.1. Who Was Gayet?

Charles Gayet (1833–1904) was born on May 19, 1833, in Saint-Genis Laval, France. After classical studies in a Dominican religious school, he enrolled in the medical school of the Université de Lyon. He did a residency in Lyon's hospitals in 1853, learning the basics of surgery while taking an interest in

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https://doi.org/10.1016/j.neurol.2021.11.012

experimental physiology with his friend Jean-Baptiste Auguste Chauveau (1827–1917), who would go on to become a renowned professor of anatomy and physiology at the Lyon veterinary school. Gayet defended his thesis: *Nouvelles recherches expérimentales sur la cicatrisation des artères après leur ligature* [4] (new experimental research on healing of arteries after ligation) in Paris in 1858. To complete his thesis, he sacrificed no fewer than thirty-four horses and donkeys. In 1862, Gayet became one of the three staff surgeons at Hôtel-Dieu Hospital in Lyon.

During the 1870 Franco-Prussian War, Gayet headed a mobile hospital of the Army Division of Loire and, in the cold and ice of December 1870, treated numerous injured soldiers: ''He performed eighteen amputations in a row in a sheep stable'' [5]. Captured by the Germans, he moved across France with their troops until the Armistice.

Back in 1877, the Lyon Medical School had become a *Faculté de Médecine* and acquired the same status as the Faculty of Medicine in Paris. Initially, Gayet was appointed professor of pathology but later assumed the chair of clinical ophthalmology, the first position of its kind in France, which was created especially for him. In 1893, he published an ophthalmology manual for family physicians, based on his teachings [6]. Within his general surgery department, Gayet developed a specialization in ophthalmological surgery (Fig. 1). In 1911, he published a novel work based on his surgical experiences, and it covered an usual skill at the time: *Iconographie photographique appliquée à l'ophtalmologie* (photographic iconography applied to ophthalmology) [7]. He had numerous students and trained several generations of ophthalmologists, particularly in cataract surgery [5].

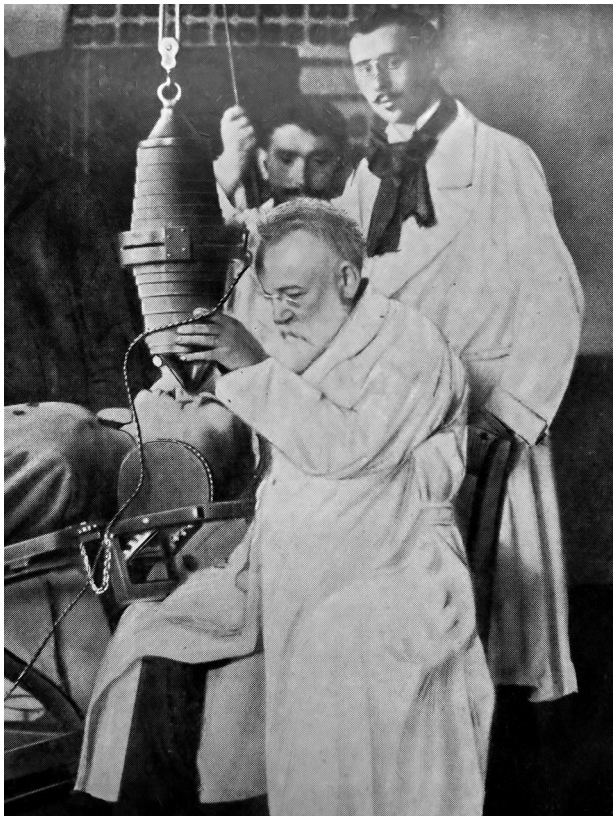

Fig. 1 – A photo of Charles Gayet, from reference 4 (Collection OW).

An active collaborator on the *Dictionnaire des Sciences médicales,* he wrote numerous articles on the following topics: crystalline lens, pathology of the cornea, photophobia, glaucoma, and nyctalopia and predominantly in *Les Archives d'Ophtalmologie*. On 13 July 1904, the pony attached to his cart took fright at the sound of a car's honking horn and ran off, toppling the cart against a sidewalk. Gayet was thrown to the ground. He suffered traumatic head injury and a fractured leg, dying six days later on July 19, 1904, at his home in Lyon [8].

1.2. *Where and why did this eponym originate?*

The case that gave rise to the eponym bearing his name was an observation of diffuse encephalitis, which Gayet linked to sleeping disease [8]. The context and content of this publication are as follows. On November 23, 1874, 28-year-old Eugène Perrot was admitted to Hôtel-Dieu hospital in Lyon. Two months earlier, he witnessed an accident at his workplace that left him badly shaken. He grew very tired and complained of ''an invincible somnolence''. When Perrot was admitted, Gayet noted a pronounced pallor and bilateral ptosis together with divergent strabismus: ''The two upper lids cover three quarters of the ocular globes and cannot be lifted''. The patient's face was immobile but not paralyzed, and he could not perform any task requiring muscular effort. Gayet's diagnosis was bilateral paralysis of the third cranial nerves: ''Each eye engaged separately sees and accommodates very well''. Gayet hypothesized an inflammatory lesion in the cerebral peduncles. For more than a month, the patient remained stuporous, during which time the right hemiplegia worsened. In mid-January 1875, the patient suddenly became more responsive, and the hemiplegia improved. In February, his condition worsened again with bilateral pupillary dilation and deepening coma and died on February 17, 1875 [9]. Gayet never described ataxia, nystagmus, or anterograde amnesia. He mainly focused on a changed level of consciousness that coincided with cranial nerve deficits.

Gayet performed the autopsy of his patient himself. Gross examination of the brain revealed nothing noteworthy. ''I then sectioned the cerebral peduncles just before the pons, continuing to cut to the corpora quadrigemina'' [9]. He noticed that the upper part of the peduncles was an intense red color, more marked on the left side, which he attributed to inflammation. In another section, the pathology extended to ''the posterior part of the optic chiasm''. For Gayet, the floor and lateral walls of the third and fourth ventricles were invaded by the pathological process: ''In addition to the parts already mentioned, the disease has affected the optical layers in their entirety''. In the microscopic examination, he observed ''the presence of a large quantity of nuclear elements coloured red by purpurin within the nervous elements, and within the preparation, very abundant fomentation of the capillary blood vessels''.

In his discussion, Gayet speculated about the pathophysiology of somnolence involving lesions near the optic chiasm: ''Might there by a clue there to understanding the very obscure question of sleep?'' He noted that Marie-Théophile Griffon du Bellay (1829–1908) had observed comparable lesions with the

autopsy of Africans who had died of sleeping sickness [10]. In these cases, like the case he reported, Gayet believed he was encountering some sort of encephalitis.

2. Observations after Gayet

In 1953, Paul F. Girard (1905–1989), Alexandre Garde (1919–2007), and Michel Devic (1919–1987), from Lyon, gathered 18 observations of alcoholic encephalopathy. They published their article in the *Revue Neurologique* to highlight the need for administering vitamin B treatment as soon as possible [11]. They recognized this treatment could favorably influence the course of the disease. The authors questioned the term ''polioencéphalite supérieure aiguë hémorragique de Wernicke'' (Wernicke's hemorrhagic acute upper polioencephalitis) because hemorrhaging occurred inconsistently. They acknowledged the three observations of Carl Wernicke (1848–1905), in his paper entitled ''Die acute, hämorrhagische Polioencephalitis superior'' [12], but emphasized that six years before Wernicke, Gayet had been the first to describe this pathology: ''The color plates that illustrate this article leave no doubt as to the diagnosis of hemorrhagic encephalopathy'' (Fig. 2). Whereas Wernicke had noted Gayet's observation, he omitted it from his discussion and considered it uncharacteristic. However, Girard, Garde, and Devic maintained that ''it would be legitimate to associate Gayet's name with that of Wernicke in the terminology of this encephalopathy'' [11]. The eponym ''Gayet-Wernicke encephalopathy'' did not come into use in France until 1953.

In 1887, Sergei Sergeievich Korsakoff (1853–1900) described a psycho-polyneuritic syndrome, which led to the eponym ''Korsakoff syndrome.'' On August 6, 1889, he presented this pathology to the International Congress of Mental Medicine held in Paris [13]. He emphasized the frequency of this condition, which combined psychic disturbances and ''phenomena of degenerative multiple neuritis''. Alongside the behavioral disturbances, Korsakoff emphasized the ''alteration of the memory of recent events'' with preservation of older memories, leading to ''delirium by fabulation'' [13]. He suggested that the repeated vomiting aggravated the patients' mental state, which he attributed to chronic alcoholism. But addiction was not the only possible cause; he presented 14 cases without intoxication, which occurred during pregnancy, typhus, diabetes, and tuberculosis. He imagined that the nervous system was ''poisoned''; hence, his name for the disease: ''cerebropathia psychica toxœmica'' [13]. We now recognize Korsakoff's syndrome as a prototype of diencephalic amnesia is, which is characterized by both anterograde and retrograde impairments of episodic-autobiographical memory with occasionally impairments of semantic memory, and confabulations.

The clinical and histopathological data and the predisposing factors, most frequently chronic alcoholism, contribute to significant overlap between the two entities described by Wernicke and Korsakoff, and the term ''Wernicke-Korsakoff syndrome'' enjoyed greater use internationally [14]. Both Leo Alexander (1905–1985) in 1940 [15] and Norman Jolliffe (1901–1961) et al. in 1941 [16] demonstrated its pathogenesis and the crucial role of vitamin B1 deficiency treated effectively with thiamine [17].

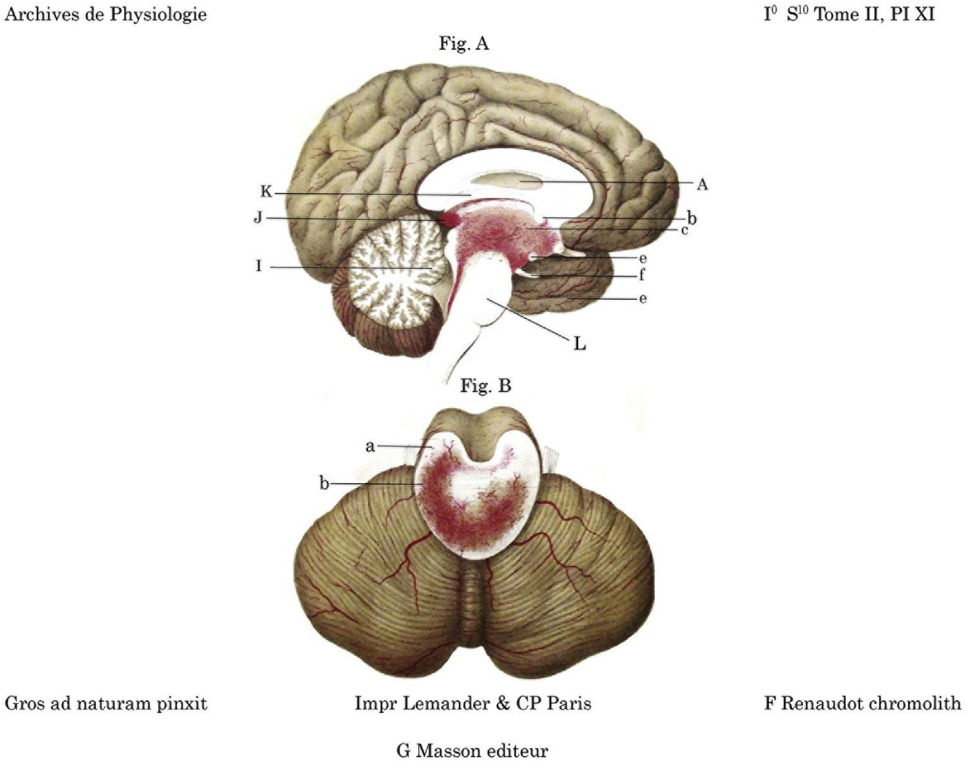

Fig. 2 – Color plate illustrate Gayet's article, from reference 8 (Collection OW).

3. Is there a reason to keep the eponym?

Often thought and unsaid, some eponyms have a disputed attribution. The eponym Gayet-Wernicke is unusual. It does not appear English textbooks on neuropathology and neurology and rarely surfaces in manuscripts. We and others are skeptical that Gayet described that for which he was lauded, and we do not think he deserves eponymous fame. Moreover, there were many others. At the time of the lethargic encephalitis description in the 1920s, Gayet's observation was frequently cited as an example of a case described before the pandemic, as was Charles Achard's (1860–1945), for example [18].

The historical review by Victor, Adams, and Collins [2], which carefully combed through the literature of derangement of memory in alcoholics, documented other physicians with similar observations including Magnus Huss (1807–1890), Jules Voisin (1844–1920), Étienne Lancereaux (1829–1910), Adolf von Strümpell (1853–1925), and even Jean-Martin Charcot (1825–1893).

The crucial question is whether Gayet described the same disease as Wernicke. Oddly, his index patient was relatively young, aged 28 years compared to an average age of 50 years. Gayet perfectly described the ophthalmoplegia related to paralysis of the third cranial nerves. The patient's general condition was profoundly altered, but the progression toward coma and death were non-specific. Second, Gayet did not mention abnormal memory functions, which are cardinal signs of Wernicke's disease (present in 80%). Conversely, Gayet emphasized that "until the end of his life, [the patient's] intelligence remained intact." Nystagmus, which would have been unusual for an ophthalmologist not to notice, was not mentioned, nor was cerebellar ataxia, which could have been missed because the patient was in bed. We acknowledge that the full clinical picture is only seen in approximately 10% of cases; however, Gayet's description lacks too many key symptoms. Third, Gayet attributed the anatomical lesions to inflammation, whereas they were mainly due to hemorrhage, as Wernicke's term "*polioencéphalite supérieure aiguë hémorragique*" (hemorrhagic acute upper polioencephalitis) explicitly indicates. We now know the histopathology well. The abnormalities concentrate in the diencephalon and periaqueductal mesencephalon and affect gray matter. The mamillary bodies and dorsomedian thalamus are affected in patients with memory deficits, but our current understanding is bilateral memory-circuit sites must be affected to cause amnesia [19]. Varying degrees of necrosis are found with astrocytic and microglial proliferation. Hemorrhages are not very common and often petechial in the early stages. Hemosiderin-laden macrophages are common in chronic stages. MRI will identify atrophy of the mamillary bodies and cerebellar vermis and enlargement of third ventricle. Nerve cells in the cranial-nerve nuclei are not destroyed, which allows very rapid improvement after thiamine administration (within a day). In contrast, improvement in the amnestic syndrome may take months, if occurring at all.

Fourth, the Gayet case lacked involvement of the mamillary bodies, colliculi, or cerebellum, which was one of the reasons Wernicke set aside Gayet's observation; the latter did not compile clinical signs of encephalopathy of the so-called "dry" form of beriberi. That link between Wernicke's disease and vitamin B1 (thiamine) deficiency was only recognized in the 1940s.

4. Conclusion

The need to eponymize is generosity. For some it is unmistakably worthy but for others, not truly deserved or misattributed. Victor and Adams suggested combining both names, Wernicke and Korsakoff, because they could rarely find cases without severe amnesia. Others found instances of Wernicke's encephalopathy only, but whether there has been serious attention to the patient deceptive cognitive state, and whether there has been a full appreciation of confabulations cannot be fully ascertained in published reports. (A review of PubMed shows that many papers simply use Wernicke's encephalopathy in their titles.) We submit that the Gayet-Wernicke eponym is not merited and that the international term "Wernicke-Korsakoff syndrome" should be used in France as elsewhere in the world.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure of interest

The authors declare that they have no competing interest.

Acknowledgment

We thank Lea Dacy for careful editing.

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