Recalling the Clinical Diagnosis of Wernicke-Korsakoff Syndrome

Dear Editor,

We read with interest the recent case report by Onuk et al. titled “Wernicke’s encephalopathy: a forgotten disease” (1). We agree with the authors that the phrase “a forgotten disease” aptly describes the subtle aspects of this condition that creates challenges in diagnosis. Herein, we aim to emphasize the salient aspects of this syndrome through a historical and biochemical approach that provides a method for clinicians to perhaps better recall its key clinical features.

It was Carl Wernicke (1848–1905) who published three cases in 1881, two caused by alcoholism and the third by vomiting, in his book titled Lehrbuch der Gehirnkrankheiten für Aerzte und Studirende (Textbook of Brain Disorders for Physicians and Students) (2). In a series of articles published between 1887 and 1891, Sergei Korsakoff (1854–1900) described an amnestic syndrome which he referred to as “psychosis polyneuritica” and recognized by the eponym Korsakoff psychosis (2). It was Murawieff in his paper “Zwei Fälle von polioencephalitis acuta haemorrhagica superior (Wernicke)” published in 1897 who recognized that the clinical features described by Wernicke, conjugated gaze paresis, tachycardia, peripheral neuropathy, nystagmus, as well as the presence of amnesia (psychosis polyneuritica), were caused by the same etiological agent, alcohol:

The etiologic element of all these affections is evidently chiefly protracted alcoholism. Here again we find the fact that one and the same disease affliction simultaneously attacks the peripheral nerves and the central nervous system, thereby producing inflammatory processes besides degenerative ones (3).

Alexander in 1940, recognized that the histopathological findings of thiamine deficiency in humans were similar to those produced experimentally in animals, thus providing the first clinicopathological correlation (4). What makes this disease so difficult to diagnose is that the classic triad of ophthalmoplegia, gait ataxia, and altered mental state is present in only 16% of patients, with one sign found in 37%, two signs in 28%, and no signs in 19% patients (5).

Thiamine is an essential vitamin whose activated form, thiamine pyrophosphate, primarily serves a cofactor in three metabolic pathways involved in glucose metabolism: i. Hexose monophosphate shunt (HMS) or pentose phosphate pathway, required for the production of NADPH, lipid, and nucleic acid synthesis; ii. Pyruvate decarboxylation; and iii. Tricarboxylic acid cycle (TCA cycle) or citric acid cycle, with the latter two involved in ATP production for cellular metabolism, transmission of nerve impulses, and muscle contraction (6). Deficiency of thiamine leads to cell death and clinical manifestations of heart failure and skeletal muscles weakness, central nervous system (confusion, poor memory, and ataxia), ocular opthalmopathy (six cranial nerve palsies with or without palsies of other extraocular muscles, horizontal conjugate gaze paresis, and nystagmus), peripheral neuropathies, as well as the metabolic findings of increased lactic acid levels with anion gap acidosis (6).

Nerve cells surround the cerebral aqueduct (aqueduct of Sylvia), third ventricle, and floor of the fourth ventricle are particularly dependent on TCA and HMS for function and survival. Thus, as found in this and other cases based on both postmortem and brain imaging, thiamine deficiency leads to neuronal cell loss with capillary and blood vessel breakdown and secondary hemorrhage occurring in these brain regions. Diagnosis requires maintaining a high clinical suspicion in at risk patients (e.g. alcoholics, bariatric surgery, hyperalimentation, malnutrition states) and correlating biochemical pathways to structure and function. Early recognition and treatment of this vitamin deficiency is essential to prevent permanent symptoms or death.
Peer-review: Externally peer-reviewed.

Author Contributions: Concept – SHY, HT, ESY; Literature Search – SHY, HT, ESY; Writing – SHY, HT, ESY; Critical Reviews – SHY, HT, ESY.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES