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The PhD Supervisor Letter
in relation to the thesis entitled:

“The medical and organizational aspects of outpatient-management of patients with medical conditions associated with benign focal epileptiform discharges of childhood (BFEDC)”.

As international PhD supervisor I take pleasure in recommendation Olga An, as a PhD candidate submitting her thesis with propositions to be considered for defense.

According to The World Health Organization (WHO), epilepsy accounts for a significant proportion of the world's burden of disease, affecting around 50 million people worldwide including more than 4% of all children. Globally, an estimated 5 million people are diagnosed with epilepsy each year which made it a major public health concern. The self-limited focal epilepsies are the most frequent convulsive disorders in childhood. The incidence of childhood epilepsy with centrotemporal spikes (CECTS), also known as Rolandic epilepsy, is 10 to 20 per 100,000 children up to age 15 years, it makes up 8–25% of all epilepsies in children. Comorbidity is the coincidence of more than one disorder, unrelated in etiology or causality to the principal diagnosis, in the same individual. Cerebral palsy (CP) is the most common motor development disability, occurring in 2–3 children of every 1,000 newborns and about 40% of them have been reported to have seizures. Children with static brain lesions such as cerebral palsy are excluded since the definition of CECTS often includes normal brain imaging. Self-limited focal epilepsies as the most common class of epilepsy syndromes in the pediatric age group would be expected to occur in patients with CP purely by chance and be unrelated to the structural brain imaging abnormalities, causing the motor impairments and there is increasing acceptance of this by the epilepsy community.

It is very important to consider the possibility of dual pathology when clinical pathways are being adopted in health systems around the world. A more favorable prognosis can be predicted in case of medical conditions associated with BFEDC, like self-limited childhood epilepsies where the prognosis would not be expected to be as good in children with epilepsy related to brain lesions. If the prognosis can be correctly identified then some children with CP can avoid prolonged, aggressive and unnecessary medication treatment.

Dr An took on 2 challenges; first she addressed the issue of quality of life and the effect of treatment with antiseizure medications on CETCS which more experts feel does not need to be treated, but is often treated at the insistence of parents who are scared by witnessing epileptic seizures and second whether we could avoid the side effects of medications in patients with dual pathology. She did an excellent job of collecting patients with CETCS, performing QOL studies, and designing a comparison group of patients who under her health system could either be treated or not treated at the parents' choice and comparing their QOL scores. The issues of impaired quality of life and side effects of the medication are important when multiyear


treatment is being followed. Because the quality of pediatric epilepsy management depends not only on the cessation of seizures but also on satisfactory levels of physical, mental, and social well-being, Dr. An used health-related quality of life (HRQOL) to measure the success of the clinical-treatment pathway. The results of the present study have the potential to provide a novel insight into estimation of the ASM treatment burden affecting quality of life in children with conditions associated with BFEDC.

A validated Shortened Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55) meets the requirements for this purpose and could be carried out on a larger scale such as for an entire country and thus help to bring about the optimization of pediatric medical care at the primary health-care level. This prospective clinical research report on the cultural validation of the questionnaire fills a gap in a number of the international studies of health-related well-being in children with epilepsy. Presently, there is a little relevant data on epilepsy in Central Asia (Kazakhstan in particular). Her study provides a framework that could be expanded and have a significant impact on national health systems and their clinical pathways.

I have supervised Olga's research and reviewed the anonymized patient data (history and clinical data, EEGs and MRIs) which was generated by her work. In 2019, she undertook a one-month international scientific internship under my leadership in the Pediatric Neurology Division of the University of Florida. The internship was related to her research topic. She observed inpatient, outpatient and telemedicine consultations at UF Health Shands Children's Hospital. She collaborated with me on a literature-review project relating to Rolandic epilepsy and the preliminary results were reported at a final meeting of the whole department.

During her PhD, Olga confirmed her ability to perform high-quality research. Two abstracts describing the core contribution of the thesis have been accepted by the Scientific Committee for presentation at the International Congresses on Public Health and Neurology. The results from the PhD thesis were of a quality sufficient for publication in two reputable peer-reviewed scientific journals listed in Scopus.

I have read the thesis carefully. In my opinion, the conclusions are correct and I recommend this thesis be accepted for defence. I commend her for her diligence and depth of understanding of this topic

A handwritten signature in black ink, appearing to be 'S.P. Winesett', with a stylized flourish at the end.

International PhD supervisor,
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