Neurocrit Care (2020) 32:86–87
https://doi.org/10.1007/s12028-019-00793-6

NEUROCRITICAL CARE SOCIETY

INVITED EDITORIAL COMMENTARY

Autonomic Dysfunction in Guillain–Barré Syndrome Puts Patients at Risk

Daniel Kondziella[1,2*]

© 2019 Springer Science+Business Media, LLC, part of Springer Nature and Neurocritical Care Society

Chakraborty et al. [1] present a single-center retrospective case series of 187 patients with Guillain–Barré syndrome (GBS) seen at the Mayo Clinic in Rochester, MN, during an 18-year period, emphasizing the high rate of dysautonomia and its association with clinical severity and mortality. Although this is by far not the only case series on this topic, the authors correctly point out that their series reflects the state of the art of GBS care, in contrast to previous case series from the 1980/1990s. Thus, the paper provides clinically meaningful data, and the authors honestly discuss the typical limitations of a retrospective study based on electronic medical records.

For the clinician, there are several key messages here. First, the overall occurrence of any form of autonomic dysfunction in GBS is high, in this case series around 40%. Strikingly, the most common autonomic manifestation was ileus (seen in 42% of all patients with autonomic dysfunction), and not—as most probably would have expected—alterations of blood pressure or cardiac rhythm. I agree with the authors that this is likely due to "different diagnostic criteria for ileus," e.g., ileus being secondary to intensive care unit management and immobility rather than due to primary autonomic dysfunction, but this needs to be addressed by prospective studies. In the same vein, the true incidence of urinary, sudomotor and pupillary dysfunction will likely differ to some degree when examined prospectively with appropriate techniques. For instance, pupillary dysfunction as revealed by clinical examination was noted in the charts in 14% of patients, but automated pupillometry was not employed. Whereas automated pupillometry occasionally misses a pupillary light reflex in very sluggish pupils [2], it does offer a much more objective, reliable and quantitative assessment of pupillary function, including size and constriction/dilation velocities [3, 4]. It seems therefore likely that automated pupillometry would detect an even higher rate of pupillary dysfunction in a prospective setting.

Second, this case series highlights the association of GBS with other syndromes that may not always be suspected at the bedside, notably posterior reversible encephalopathy syndrome (PRES; 6 cases = 3.2%) and the syndrome of inappropriate antidiuretic hormone secretion (SIADH; 27 cases = 14.4%). It seems reasonable to speculate that both these syndromes are even more frequent in reality and that (subclinical) presentations are easily missed, as magnetic resonance imaging of the brain to visualize PRES is not part of the routine workup for GBS and subtle electrolyte alterations as in SIADH are often overlooked. Intriguingly, PRES was the initial clinical presentation prior to the development of neurologic signs of GBS in three of the six patients with PRES. Also, the authors note that two patients had GBS in the setting of a diffuse large B cell lymphoma and that death occurred due to subsequent withdrawal of care. The incidence of GBS appears to be increased in association with lymphoma, particularly Hodgkin's disease [5]. However, it should be noted that neurolymphomatosis (i.e., polyradiculopathy due to lymphomatous infiltration) was not firmly ruled out by autopsy.

Third, patients with dysautonomia tended to be treated more aggressively with plasmapheresis or both intravenous immune globulin (IVIG) and plasmapheresis than patients without autonomic dysfunction. It makes sense that more severe GBS treated with plasmapheresis is associated with more dysautonomia, but could there be an effect in the other direction as well, i.e.,

*Correspondence: daniel_kondziella@yahoo.com
[1] Department of Neurology, Rigshospitalet, Copenhagen University Hospital, Blegdamsvej 9, 2100 Copenhagen, Denmark
Full list of author information is available at the end of the article

This comment refers to the article available at https://doi.org/10.1007/s12028-019-00781-w.

Springer

plasmapheresis, inducing autonomic dysfunction with hypo-/hypertension due to imbalance of fluids and electrolytes? Prospective data are urgently needed to confirm (as is commonly held) that plasmapheresis indeed works better than IVIG in severe GBS and to rule out any overlooked adverse effects. After all, plasmapheresis is a much more invasive and prolonged intervention compared to IVIG, and most experienced clinicians will remember cases of potentially fatal complications associated with plasmapheresis (and the placement of a central vein catheter) such as arterial hypotension, fulminant cerebral edema, septicemia, bleedings and paradoxical air embolism.

Finally, and most importantly, the authors show that autonomic dysfunction in GBS is associated with increased mortality. Although the numbers are way too small to allow for confident statistics, the reported increase in mortality in patients with dysautonomia (6%) as compared to those without (2%) fits well with the clinical gut feeling that mortality should be increased by a factor of 3 (at least). It appears reasonable to suggest that autonomic dysfunction not only is a proxy for severe GBS but is a risk factor for death in its own right. It is likely that dysautonomia is associated with increased morbidity as well, but data on long-term outcome other than survival were not available. Hence, prospective and, preferentially, multicenter studies are needed to quantify the relationship of autonomic dysfunction with mortality and morbidity in GBS.

Author details
[1] Department of Neurology, Rigshospitalet, Copenhagen University Hospital, Blegdamsvej 9, 2100 Copenhagen, Denmark. [2] Faculty of Health and Medical Sciences, Copenhagen University, Copenhagen, Denmark.

Conflicts of interest
The author declares that he has no conflicts of interest.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Published online: 23 July 2019

References

1. Chakraborty T, Kramer C, Wijdicks F, Rabinstein A (2019) Dysautonomia in Guillain–Barré syndrome: prevalence, clinical spectrum, and outcomes. Neurocrit Care (**in press**).
2. Kramer CL, Rabinstein AA, Wijdicks EFM, Hocker SE. Neurologist versus machine: is the pupillometer better than the naked eye in detecting pupillary reactivity. Neurocrit Care. 2014;21:309–11.
3. Peinkhofer C, Martens P, Grand J, Truelsen T, Knudsen GM, Kjaergaard J, Kondziella D. Influence of strategic cortical infarctions on pupillary function. Front Neurol. 2018. https://doi.org/10.3389/fneur.2018.00916.
4. Vassilieva A, Olsen MH, Peinkhofer C, Knudsen GM, Kondziella D. Automated pupillometry to detect command following in neurological patients: a proof-of-concept study. PeerJ. 2019;7:6929. https://doi.org/10.7717/peerj.6929.
5. Hughes RA, Britton T, Richards M. Effects of lymphoma on the peripheral nervous system. J R Soc Med. 1994;87:526–30.