Anticipating the Challenges of Zika Virus and the Incidence of Guillain-Barré Syndrome

Guillain-Barré syndrome (GBS) most commonly presents with acute progressive paralysis with absent deep tendon reflexes. Bacterial and viral infections can precede the onset of this neurological emergency. In recent years, cases of GBS have been associated with arboviral infections including dengue and chikungunya. As of February 2016, 6 countries affected by outbreaks of Zika virus infection have reported an increased incidence of GBS. While some have postulated that concurrent circulation of dengue or other factors could contribute, a case-control study of patients who developed GBS during a Zika outbreak in French Polynesia provides evidence that Zika infection is the culprit. In response, the World Health Organization recently released a statement on GBS aimed at health care professionals and policy makers in countries affected by Zika.

There is concern that the Zika outbreak may soon affect the United States. Aedes aegypti and Aedes albopictus, mosquito vectors of Zika virus, are present in much of the country during the warmer months. Neighboring nations, including Mexico, currently report transmission of Zika. One recent study estimated that 60% of Americans live in regions at risk for the spread of Zika. In the French Polynesia outbreak, 66% of the population was infected with Zika and the incidence of GBS was estimated at 0.24 cases per 1000 infections. Numerous factors will influence the number of cases of GBS in the United States. However, if conditions were to mimic the French Polynesian outbreak, then as many as 30,000 cases of Zika-associated GBS might be expected (population 318 million; 60% of the population at risk for infection; 66% infection rate in those at risk; 0.24 cases/1000 Zika infections), representing a roughly 10-fold increase from the baseline incidence of GBS nationally. As neurohospitalists who frequently care for patients with neuromuscular emergencies, we seek to anticipate challenges that could face our health care system if the incidence of GBS were to sharply rise with the arrival of Zika.

Challenge 1: Diagnosis

Patients with GBS typically report paresthesias, numbness, or pain in the limbs followed by progressive symmetrical bilateral limb weakness. If Zika virus transmission becomes widespread, primary care physicians and emergency department physicians must be attuned to this possibility in patients presenting with new limb weakness and absent deep tendon reflexes. The potential cost of missing the signs and symptoms of early GBS can be serious, as some patients experience rapid worsening within hours to a few days of onset. Perhaps for this reason, the World Health Organization has specifically recommended enhanced training for health care professionals in the evaluation of patients presenting with weakness. At present, there is no roadmap for how this training will be enacted in the United States.

We recommend that primary care professionals and emergency department physicians pursue urgent neurological consultation for patients with suspected GBS. The differential diagnosis of limb weakness is broad and can include diseases affecting all levels of the nervous system. An expert history and examination in such patients can localize the cause of weakness and guide further diagnostic testing and management. Expert evaluation of patients presenting with weakness during an epidemic of GBS may also be important to avoid anchoring on this diagnosis and missing other treatable causes of weakness, such as transverse myelitis. In patients with limb weakness suspected to have GBS, lumbar puncture and electrodiagnostic studies often serve as valuable ancillary tests. Examination of cerebrospinal fluid classically reveals albuminocytologic dissociation, though this finding may be present in only half of patients within the first week of symptoms.

Challenge 2: Triage and Monitoring

It is our experience that the vast majority of patients with suspected or confirmed GBS are hospitalized. Benefits of hospitalization include close monitoring for neurological worsening, trending respiratory function tests, and rapid initiation of acute treatment. In the recent French Polynesia cohort, 38% of patients required intensive care and 29% required ventilatory support for neuromuscular respiratory failure. Another common reason for intensive care unit admission in these patients is autonomic nervous system involvement leading to marked hypotension, hypertension, or cardiac arrhythmia.

Medical complications are common in patients with severe GBS. Venous stasis in paralyzed limbs places patients at risk for deep vein thrombosis. Slow recovery of respiratory muscle function predisposes to prolonged intubation and ventilator-associated pneumonia. Electrolyte disorders such as hyponatremia can occur. The historical mortality rate is 5%, though encouragingly all of the patients in the Zika-associated French Polynesia cohort survived to hospital discharge.

An epidemic of GBS associated with Zika virus would stress hospital and intensive care resources nationally. Each hospital located in an area at risk for transmission of Zika should evaluate its ability to provide optimal monitoring and supportive care for patients with GBS. This may require enhanced education of nurses in the neurological examination.
increased staffing of respiratory therapists, plans for emergency expansion of available intensive care beds, and assessment of available local and regional expertise. A recent disaster preparedness study estimated that US hospitals could absorb 26,200 to 56,300 mechanical ventilators in addition to those already in use, but only with exhaustive planning prior to the pandemic.\(^5\)

**Challenge 3: Acute Treatment**

Intravenous immunoglobulin (IVIg) and plasmapheresis represent the 2 evidence-based acute treatments for GBS. Guidelines developed by the American Academy of Neurology suggest that these 2 therapies have equivalent efficacy, and receiving both does not confer additional benefit.\(^6\)

Careful planning should be pursued to ensure an adequate supply and distribution of IVIg and to maximize plasmapheresis availability. Others have described the scarcity of IVIg and suggested a rational prioritization of distribution, though this has not been formalized at a policy level.\(^7\) Delayed therapy due to inadequate resources can increase morbidity and mortality for patients with GBS. Insufficient availability of IVIg and plasmapheresis in the midst of an epidemic might endanger not just patients with GBS, but other patients reliant on these therapies regularly, including those with primary immunodeficiency disorders, immune thrombocytopenia, chronic forms of demyelinating polyneuropathy, and Kawasaki disease.

**Challenge 4: Rehabilitation**

The vast majority of patients with GBS require physical and occupational therapy in the acute hospital setting as well as after hospital discharge. In cases of severe GBS, recovery of the ability to walk may occur slowly over months. Up to 20% of patients with severe GBS are unable to walk independently 6 months after onset of symptoms.\(^1\) A surge in cases may saturate acute inpatient rehabilitation units, and contingency planning for increasing the number of these programs as well as home-based alternatives should be considered.

**Challenge 5: Managing the Media**

Like Ebola virus before it, Zika virus has become a mainstay in the national news cycle. Unlike Ebola, Zika virus infection itself has been reported to be a mild febrile illness that is not life threatening. With its rapid progression and numerous complications, GBS is likely to be a focal point of media coverage during an epidemic of Zika in addition to the teratogenic effects on the fetus. Efforts to demystify this condition in anticipation of an increased incidence are advisable.

**Conclusion**

While we hope that the ultimate impact of Zika virus nationally is limited, we believe that multidisciplinary planning is essential to mitigating the impact of a steep rise in the incidence of GBS. As neurologists, we pledge to educate other health care professionals and the general public about this important condition.

**REFERENCES**