Clinical Profile

Etiology

The Guillain-Barre Syndrome (GBS) was first described by Landry in 1859 (1), then by Guillain, Barre, and Strohl in 1919 (2). It is also known as acute postinfectious neuritis, acute ascending paralysis and polyradiculoneuritis. The etiology has not been definitively established, although it has been associated with a variety of viral, bacterial, and other infections, as well as endocrine, hematologic, dermatologic, allergic and neuropsychiatric disorders, various toxins and drugs, and with vaccines for rabies, tetanus, typhoid, pertussis, diptheria, smallpox, polio, and influenza (3).

Clinical Manifestations

Although the clinical presentation is fairly uniform, numerous diagnostic criteria have been proposed without universal acceptance. In addition to the original descriptions, detailed criteria have been outlined by Osler and Sidell (4), Marshall (5), Wiedenholt, et al (6), McFarland and Heller (7), Ravn (8) and Masucci and Kurtzke (9). In 50 to 75 percent of nonvaccine-related cases, a history of mild respiratory or gastrointestinal infectious illness, within the preceding 4 weeks, can be elicited. In vaccine associated cases, there is no preceding acute infectious illness in 75 percent of cases (10). There is usually an asymptomatic afebrile period of 1 to 3 weeks, then vague pains or paresthesia of the hands and feet are reported in 75 to 90 percent of cases. The first symptom of prominence is muscle weakness, involving the proximal or distal muscles of the legs, then the arms, but this ascending progression is by no means constant. This involvement is usually bilateral (95 percent) but may be asymmetric. The progression of sensory and other symptoms is gradual and usually complete within 2 weeks, but occasionally can continue for months. Facial weakness and involvement of any or all cranial nerves occur in 50 to 80 percent of cases. Cranial nerves are more often involved in vaccine-associated cases (10). Urinary incontinence or retention may occur in 20 percent but is transient. From 10 to 25 percent of patients may have paralysis of breathing and require artificial respiratory support. Pulmonary complications, anoxia and seizures, and residual neurological deficits may occur, but complete recovery is gradually achieved in one year. Mortality, usually from respiratory involvement, is approximately 5 percent. Residual paralysis occurs in 10 to 30 percent of cases.

Physical examination is marked by bilateral motor weakness of the lower extremities, upper extremities, and trunk. Muscle atrophy and fasciculations may be noted. Sensory deficits may involve position, vibration pain, and light touch. Deep tendon reflexes are depressed or absent; superficial reflexes may be absent, but are usually intact. As noted, cranial nerves may be involved, and papilledema may be found. Some patients, especially children, may have neck stiffness as a sign of meningeal irritation (11). Autonomic dysfunction with hypertension, postural hypotension, facial flushing, and tachycardia may occur.

Laboratory abnormalities are few, but CSF findings are diagnostic. CSF protein should be elevated (above 60 mg/dl), but may be within normal limits early in the illness. The CSF cell count is usually less than 20 WBC/cmm. Peripheral white blood cell count, differential, and erythrocyte sedimentation rates are usually normal. Serum calcium may be elevated in patients immobilized for prolonged periods and electrolyte imbalances with inappropriate secretion of antidiuretic hormone have been reported. Electromyography is usually diagnostic (fasciculations), and motor nerve conduction is delayed.

Epidemiology

In February 1976, an influenza virus was isolated during an epidemic at Fort Dix, N. J., antigenically similar to the virus implicated in the 1918 influenza pandemic. The Federal Government then initiated a
symmetric polyneuropathy with or
December 16, 1976, nearly 43 million doses of killed influenza A/New Jersey/1976 vaccine were adminis-
tered. The program was abruptly halted when an increasing number of reports of GBS (associated with vaccine inoculation) were reported. By January 10, 1977, a total of 581 cases of GBS had been reported, of which 295 had received the vaccine. 11 percent of the patients who received vaccine were less than 3 years of age. Fifty-eight percent were between 30 and 59 years, and 31 percent were 60 years or older. Of 266 unvaccinated patients, 4 percent were less than 30 years, 39 percent between 30 and 59, and 17 per-
cent were 60 or older. There was no differences be-
tween sexes. Cases were noted in 49 of 50 States (12).

The clinical states of vaccinated and non-vacci-
nated patients as reported by the Center for Disease Control were remarkably similar, significantly differ-
ing only in history of previous acute (27 v. 62 per-
cent) or chronic illness (44 v. 27 percent), involve-
ment of cranial nerves (64 v. 47 percent), and sensory symptoms (87 v. 74 percent). Of the vaccinated pa-
tients, there were 41 percent with respiratory in-
volvement, 23 percent placed on a respirator and 5 percent of 299 cases died. Within 8 to 28 days follow-
ing vaccination, 75.2 percent had onset of paralysis, 3.3 percent within 7 days after vaccination, and 21.5 percent more than 28 days following vaccination.

The relative risks of GBS in influenza vaccinated
persons was approximately 12 times greater than in unvaccinated persons (10). The risk was similar for
monovalent or bivalent vaccine. Age-specific attack rates per million population per month were 2.48 for
vaccination v. 0.34 for unvaccinated in ages O to 17
years, 3.45 and 0.70 for ages 18 to 24, 9.21 and 0.56
for ages 25 to 44, 6.49 and 0.81 for ages 45 to 64, 7.22
and 0.76 for over 65, and 6.99 and 0.58 for all ages.
Thus, all ages were at risk.

Pathology
Pathological examination varies with the stage of
disease progression. There are no significant path-
ologic changes in the cerebrum, brain stem, or spinal
cord, except for severe changes in the anterior horn
cells and motor nuclei of the brain stem. Acutely,
there is marked edema of the spinal roots and cranial
nerves. Later, demyelination and degeneration of the
spinal and cranial nerve axons are seen. Lymphocytic
inflammatory cells invade the myelin sheath and
Schwann cell proliferation follows. Chromatolysis of
dorsal root ganglia and anterior horn cells may be
observed (13).

Diagnosis
Diagnostic criteria are those outlined under clinical
manifestations and include:
1. acute or subacute onset of muscle weakness
   and/or sensory symptoms (i.e., paresthesia,
numbness or pain);
2. usually ascending spread (may be descending,
   or variable) with progression over 1 to 2 weeks
   (up to 2 months);
3. bilateral (may be asymmetric) muscle involve-
   ment;
4. deep tendon reflexes absent or diminished;
5. cranial nerves may be involved; and
6. CSF protein elevated (>60 mg/dl), CSF WBC
   count < 20/cmm.

Differential Diagnosis
The differential diagnosis of influenza-vaccine-
associated GBS includes:
1. GBS secondary to other causes, including viral
   infections (infectious mononucleosis, measles,
   hepatitis, upper respiratory and gastrointestinal
   infections, etc.), bacterial infections (streptococ-
   cal, etc.), other vaccinations, (rabies, tetanus
   toxoid, etc.), autoimmune disorders (lupus ery-
   thematosis, polyarteritis nodosa, etc.) malig-
   nant diseases (Hodgkin’s disease, etc.), endo-
   crine disorders (diabetes mellitus, etc.), poisons
   and toxins and antibiotic therapy (penicillin,
   etc.). Only a complete history, appropriate viral
cultures and serologies, toxic screens, and
search for underlying disease can implicate these
disease etiologies.
2. Poliomyelitis, which is differentiated by epi-
demic occurrence, meningeal symptoms, bi-
phasic course (aseptic meningitis then paralysis),
fever, asymmetric muscle involve-
ment, CSF pleocytosis without cytoalbumin dis-
association and positive viral cultures.
3. Acute myelitis, which is marked by sensori-
motor paralysis below a specific spinal level.
4. Diphtheric polyneuropathy characterized by
   weakness or paralysis of limbs and muscles in-
ervated by cranial nerves associated with loss of
   position and vibratory sensation. This can be
   easily diagnosed by the obvious symptoms of
   laryngeal, pharyngeal or nasal diptheria, i.e.,
   fever, pseudomembrane, proteinuria and posi-
tive culture for Corynebacteria diptheriae.
5. Porphyric polyneuropathy, a rapidly advancing
   severe, symmetric polyneuropathy with or
   without psychosis or convulsions. Diagnosis of
   underlying porphyria is accomplished by usual
   serum and/or urine tests.
Outcomes

Few prognostic data are available regarding influenza vaccine associated cases of GBS. Prognosis of other cases is usually good. Death occurs in approximately 5 percent of cases (5, 6, 10, 14).

In vaccine associated cases, 3 to 4 extremities are involved in 85 percent of cases, cranial nerves in 47 percent, respiratory impairment occurs in 41 percent, and ventilator assistance is required in 25 percent (10).

The duration of hospitalization ranges from weeks to years depending upon the eventual outcome. Of 97 patients from the Mayo Clinic (6), 50 made complete recovery with a year, 7 more in 2 years, and 4 more after 2 years. Twelve patients made incomplete recovery, five had moderate incapacity, four marked incapacity, and three respiratory insufficiency. Fifteen patients were improved when last seen, four unchanged 3 or more years after diagnosis, and five dead. From Columbia Presbyterian Medical Center, 49 of 81 patients were reexamined at least 2 years after onset of GBS. Of these, 8 had marked distal weakness, and 8 mild distal weakness (14).

Impairment may range from mild weakness of one or more extremities to marked paralysis and respiratory insufficiency requiring ventilator assistance, and constant nursing care. Relapses may occur weeks or years after resolution of symptoms (14, 15). Influenza vaccination of persons who have previously suffered from GBS may precipitate a second attack (16). From 50 to 60 percent of patients should be able to return to their normal routine within 1 year of onset. Approximately 15 percent will be completely disabled (6, 14).

Appendix D References