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Title Page

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Abstract

We describe the inpatient clinical rehabilitation course of three patients with neuromyelitis optica (NMO; Devic's Syndrome). These patients had varying functional deficits. Each patient improved in several functional independence measures (FIM domains), but had minimal to no progress in other domains after acute rehabilitation stays between 1 to 1.5 months. NMO is a severe central nervous system demyelinating syndrome distinct from MS, characterized by optic neuritis, myelitis, and at least two of three criteria: longitudinally extensive cord lesion, MRI nondiagnostic for multiple sclerosis, or NMO-IgG seropositivity. Persons with NMO may demonstrate improved function with rehabilitation efforts; though gains may be lost to relapse Future immunomodulatory intervention may augment the benefits of rehabilitation.

Key Words

Neuromyelitis Optica, Devic's Syndrome, Multiple Sclerosis, Rehabilitation

Text

Neuromyelitis optica (NMO, Devic Syndrome, Devic's Syndrome) is a demyelinating disorder distinguished by the combination of optic neuritis (ON) and myelitis. These symptoms can be mischaracterized as multiple sclerosis (MS). NMO has a more acute and severe course. Although NMO is closely associated with MS, it has specific diagnostic criteria, and unique pathological features compared to prototypic MS.[1,2,3,4]

History

In 1870, Sir Thomas Clifford Allbutt first described an association between myelitis and optic nerve disease.[5] The myelitis followed optic nerve changes by approximately 3 months. In 1879, Erb reported a 52 year old man who developed recurrent optic neuritis followed by subacute myelitis.[6] In 1880, Sequin reported that the associations in the literature, including Erbs's were accidental.[7] In 1882, Dreschfeld performed a pathologic exam in a case of optic neuritis and myelitis, reporting inflammation in both the spinal cord and optic nerves.[8] In 1888, Gower's textbook recognizes that they are of a common cause.[9] In 1894, Devic and his student Gault reviewed 16 previous cases, as well as another case, for Gault's doctoral thesis and concluded that optic neuritis and myelitis constituted a distinct clinical entity.[10,11] In the early to mid-1900's Beck and Stansbury reported more cases but were unable to conclude whether this was a distinct entity from acute disseminated encephalomyelitis or MS.[12,13]

Classification

Even recent texts have classified NMO as a variant of MS. In the Far East, NMO was characterized as the optico-spinal variant of MS. MS is characterized by two or more occurrences of central nervous system symptoms and signs separated in time and space. The McDonald criteria represent the currents standards in diagnosis for MS.[14] Since the late 1800's there have been several sets of the diagnostic criteria that have attempted to clarify the controversy of NMO as a distinct entity.[9,10,15,16] . The distinction between MS and NMO is necessary, particularly for the relapsing form, because of the significant difference in morbidity and mortality.[17] Furthermore drugs useful for MS may not be appropriate for NMO. In 1999, Wingerchuck et al proposed diagnostic criteria with 85% sensitivity and 48 % specificity.[18] In 2006, his group revised the criteria to define the syndrome, reporting an impressive 99% sensitivity and 90% specificity. The diagnostic criteria characterize NMO by optic neuritis, myelitis, and at least two of three criteria: longitudinally extensive cord lesion, MRI nondiagnostic for MS, or NMO-IgG seropositivity.[4]

Demographics

Like MS, NMO predominantly affects women. The median age of onset for NMO is in the late 30's as compared to the late 20's for MS. MS most commonly affects people of Northern European/Caucasian ancestry. NMO comprises a relatively greater proportion of a non-Caucasian background. The occurrence of ON or severe myelitis in a non-Caucasian ancestry should increase diagnostic suspicion for NMO.[19]

Clinical Course

Wingerchuk et al. characterized the clinical course as either monophasic or relapsing.[18] The time course of presentation is usually characteristic for each type. Patients with a monophasic course usually present with rapidly sequential presentation of myelitis and ON within a median of 5 days, while the relapsing course has an extended interval between the presentation of the myelitis and ON with a median of 166 days and occasionally 2 years between initial events.

The initial presentation of monophasic NMO is more severe but recovery is better. Functionally, the monophasic patients are able to maintain some degree of independence despite moderate visual and motor deficits. The relapsing disease may present with less initial severity and better recovery, but recurrent episodes diminish recovery gains.[20] The relapsing course has a poor prognosis with more than half developing severe visual loss and an inability to ambulate without modification within 5 years of the disease onset. Furthermore, the patients are at high risk for high cervical myelitis causing respiratory failure and death.[21]

Therapy

Acute medical therapeutic recommendations in the literature are beyond the scope of this report. In a rehabilitation setting, a patient may be admitted on azathioprine in combination with prednisone[22] or rituximab[23] as a measure to prevent recurrence. Just as the diagnostic criteria continue to be refined, the medical treatments for acute episodes as well as prophylactic therapy are a work in progress. The mainstay of rehabilitative therapy is to prevent complications, treat symptoms, and optimize recovery of function in

order to reduce disability, handicap and improve well-being. We present three patients stricken with relapsing NMO who under went a comprehensive inpatient rehabilitation program and their functionality at discharge.

Case Reports

Case 1

A 49 year-old woman initially presented with fatigue and chest discomfort. Five months later, she developed left leg numbness, inability to urinate, bilateral ascending sensory deficits to the level of T6, and unsteadiness with gait. She was diagnosed with MS, and experienced nine episodes of recurring thoracic myelitis over four years. These flares were treated with the standard MS therapies and rehabilitation. She was independent in activities of daily living (ADLs) with modified independent mobility using a rolling walker. After further work-up, she was diagnosed with NMO. Her 10^{th} episode began with neck pain and rapidly progressed to obtundation, flaccid tetraparesis, a C2 sensory level and ventilator dependent respiratory failure. After receiving acute medical therapy, she started to improve.

On admission to an inpatient rehabilitation facility, physical examination revealed monocular blindness on the left, cognitive impairment, anxiety, and marked global weakness in manual muscle testing with right-side 0-1/5 and left-sided 2-3/5. Absence of sensation to light touch and pinprick was noted from the level of T4. Spasticity was generalized at 1/4 Ashworth scale. She required a foley catheter and bowel program. She exhibited maximum deficits in many areas of function. She was dependent for transfers, feeding, grooming, dressing, bathing, toileting (Table 1). Several barriers in her function were high levels of anxiety accompanied by poor endurance and impaired concentration.

Over a 1.5 month period of inpatient rehabilitation, her cognitive function and anxiety improved, and she was able to focus and make functional gains. Her endurance improved and she was able to actively participate in her program. Her manual muscle testing improved to grades 3+/5 in her right upper limb, 4/5 in her left upper limb, and 1-2/5 in her lower limbs. Sensation was intact to the level of T4 dermatome with partial preservation to T10. Spasticity was 1/4 in the upper limbs and 2/4 in the lower limbs. Cystometrogram (CMG) revealed an insensate dyssynergic hyperreflexic bladder that requires a constant foley catheter. She was continent with a bowel program. Functional gains were made in feeding, grooming, and upper extremity dressing. Many areas such as lower extremity dressing, toileting, and transferring had minimal improvement (Table 1). She was discharged home with plans for outpatient rehabilitation.

Case 2

A 43 year-old woman was initially diagnosed with multiple sclerosis then shortly afterwards developed right eye blindness. Functionally, she was independent in ADLs and required a cane for modified independent mobility. Two years later, she developed lower extremity weakness with an inability to urinate which was later complicated by urosepsis. Neurologic work-up concluded that she had NMO.

On admission to our inpatient rehabilitation facility, physical examination revealed a female patient blind in the right eye with impaired vision in left eye. Her upper extremity strength was 4/5 and lower extremity 0/5. Sensation was decreased to light touch and pinprick, without a clear sensory level. She had flaccid paraplegia and bilateral ankle

contractures. She required a foley catheter and bowel program. She exhibited deficits in many areas of function. Specifically, she was dependent in lower extremity dressing, toileting, bathing, and toilet/tub transfers (Table 1).

Her flaccid paraplegia persisted after one month of rehabilitation. CMG revealed an areflexic neurogenic bladder with some preservation of bladder sensation, which she managed by intermittent catheterization. She also required a bowel program. Functional gains were made in lower extremity dressing, bathing, and toilet transfers. Areas such as toileting and tub transfers had minimal improvement (Table 1). She was discharged to a skilled nursing facility.

Case 3

A 41 year-old women initially developed transient bilateral blindness, with left eye vision return. Two years later, she developed chest discomfort accompanied by loss of sensation and movement below the level of T3. Extensive work-up revealed cervical and thoracic myelitis and she eventually was diagnosed with NMO. Prior to the presentation of weakness, she was independent in ADLs and ambulation.

On admission our inpatient rehabilitation facility, physical examination revealed a female patient blind in the right eye. Her upper extremity strength was graded 4/5 and lower extremity 0/5. Sensation was decreased to light touch and pinprick below the level of C6 with dysesthesias in her right upper extremity. She had flaccid paraplegia. She required a foley catheter and bowel program. She exhibited deficits in many areas of function.

Specifically, she was dependent in bathing, lower extremity dressing and toilet/tub transfers (Table 1).

Her course of rehabilitation was complicated by urosepsis and pulmonary embolism. Eventually, she was able to complete 1 month of uninterrupted rehabilitation. Her physical exam revealed persistent paraplegia with right upper extremity weakness and dysesthesia. CMG revealed an areflexic neurogenic bladder without detrusor contraction or sensation. She required a foley catheter and bowel program. Functional gains were made in feeding, lower extremity dressing, and bathing. Areas such as toileting and tub transfers had no improvement (Table 1). She was discharged home.

Discussion

NMO is a severe central nervous system demyelinating syndrome distinct from MS; characterized by optic neuritis, myelitis, and at least two of three criteria: longitudinally extensive cord lesion, MRI nondiagnostic for MS, or NMO-IgG seropositivity. Literature search reveals that NMO is poorly described in the physiatric literature. This is most likely due to the low incidence and prevalence as well as an evolving understanding of the clinicopathological features that set it apart from MS.

There are a myriad of symptoms and signs of NMO, which must be addressed in a rehabilitation setting to maximize functional recovery. *Fatigue* can be treated with a planned regiment of rest between therapies, focused energy efficient compensatory strategies, and psychostimulant medications. *Spasticity* can be treated with frequent stretching of spastic muscles. Incorporation of spasmolytic medications with close monitoring for enhancement of function versus hindering function may assist in overall functional improvement. Other useful modalities are localized nonsystemic blocks and baclofen pumps. *Weakness* may improve with progressive resistance exercises which may improve function. Care must be taken not to overfatigue the muscles. *Neurogenic bladder* must also be addressed to prevent long term complications of infection, hydronephrosis, stone formal, vesicouretal reflux, and renal failure. CMG can establish the presence of sphincter dyssyngergia, detrusor hyperreflexia, or detrusor areflexia. Depending upon the severity of the bladder dysfunction, the patient's mental status and upper limb dexterity, medications, indwelling catheterization or intermittent catheterization may be implemented in an acute rehabilitation setting. *Anxiety and*

depression are common. The utilization of a psychologist, group meetings and medications can help make the patient a more active participant in a program. Interventions *for memory impairments* include the use of a memory books (which must be appropriate for the patient's visual deficits and possible loss of hand dexterity), a structured environment, and consideration of medications such as donezepil.

Physiatrists need to focus on optimizing acute rehabilitation in order to treat symptoms, minimize complications and improve the quality of life. This is even more pertinent with NMO versus MS because of the severe sequalae that occur after an acute episode. Rehabilitation planning must consider the progressive nature of the disease and risk of relapse. Kraft says, "…We need to adapt rehabilitation strategies to a progressive neurologic disease with an uncertain course.[24]" Although he was referring to MS, this concept applies to NMO as well.

Each of these three patients was not able to return to baseline ADL and ambulatory function after relapse. However, they were able to improve in several domains of function from their initial assessment on admission to a rehabilitation facility. Our first patient was significantly hindered by cognitive impairment, anxiety and fatigue, which improved during her stay. Consequently, she was able to improve her function and had less apprehension when she returned to the community. Our second patient was admitted with a much stronger functional profile and was able to become much less dependent after her rehabilitation. Our third patient provides an example of how medical complications, just as with MS, spinal cord injury, stroke, and traumatic brain injury, can

interrupt rehabilitation. The patient and her rehabilitation team persevered so that her quality of life was improved. In turn, the period between discharge and her next relapse, she will have improved function.

All three patients benefited from acute rehabilitation. Although they did not return to prior functional levels, they were able to improve. Functional gains can be expected, with attention to treating symptoms and preventing complications, through a comprehensive rehabilitation program.

Conclusion

Although rehabilitation strategies for MS are well reported in the literature, those for NMO are not. This may be due to a historical confounding of rehabilitation modalities for NMO with MS. The neurological literature now shows that there are unique clinical characteristics[22, 23, 25] and pathological processes that distinguish MS from NMO. These differences may affect the neurological therapy and acute management of the disease. Thus, as newer treatments become available, it will be necessary to modify and optimize rehabilitation strategies to treat symptoms and prevent complications to maximize recovery of function. Just as controlled clinical trials will need to be developed to identify the best acute care neurological treatments; controlled trials will need to be developed to assess recovery of function in the acute care and long term rehabilitation settings. In order to do this we will need to determine the best set of outcomes measures for comparison of inpatient rehabilitation treatments. As documented in our patient series, functional gains can be made by a comprehensive rehabilitation program.

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