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Title Page

Rehabilitation of Neuromyelitis Optica (Devic's Syndrome): 3 Case Reports

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20

Text

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

26

History

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

40

Classification

41

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

56

57 **Demographics**

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

63

64 **Clinical Course**

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

71

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

80

81 **Therapy**

82 Acute medical therapeutic recommendations in the literature are beyond the scope of this
83 report. In a rehabilitation setting, a patient may be admitted on azathioprine in
84 combination with prednisone²² or rituximab²³ as a measure to prevent recurrence. Just as
85 the diagnostic criteria continue to be refined, the medical treatments for acute episodes as
86 well as prophylactic therapy are a work in progress. The mainstay of rehabilitative
87 therapy is to prevent complications, treat symptoms, and optimize recovery of function in

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

Case Reports

91

Case 1

92

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

103

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

112

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

124

125 **Case 2**

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

131

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

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

139

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

146

147 **Case 3**

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

153

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

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

161

162 Her course of rehabilitation was complicated by urosepsis and pulmonary embolism.

163 Eventually, she was able to complete 1 month of uninterrupted rehabilitation. Her

164 physical exam revealed persistent paraplegia with right upper extremity weakness and

165 dysesthesia. CMG revealed an areflexic neurogenic bladder without detrusor contraction

166 or sensation. She required a foley catheter and bowel program. Functional gains were

167 made in feeding, lower extremity dressing, and bathing. Areas such as toileting and tub

168 transfers had no improvement (Table 1). She was discharged home.

169

170

Discussion

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

177

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

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

198

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

206

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

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

219

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

224

225 **Conclusion**

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

239

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240

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