Severe Acute Axonal Polyneuropathy in the Setting of Nutritional Deficiency

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Introduction

- Acute axonal neuropathy presenting with a Guillain–Barré syndrome (GBS) like pattern has been described in patients with alcohol abuse[1], after bariatric surgery (BS)[2] and in anorexia[3].
- Patients present with numbness > weakness, acute to subacutely (<4-12 weeks)
- CSF protein is normal
- Nerve conduction studies (NCS) show an axonal pattern
- Vomiting and weight loss have been described as risk factors
- The etiology has remained unclear, but multifactorial nutritional deficiencies have been postulated.
- Differentiation from acute (sensory) motor axonal neuropathy (AM(S)AN), Miller-Fisher variant, toxic (arsenic, direct alcohol effect) or metabolic neuropathies (porphyria) is important, as treatment differs: While early vitamin supplementation may be critical, immunotherapy may be unnecessary.
- Here we present a retrospective case series of 10 patients, elucidating clinical features and demonstrating diagnostic challenges

Methods

- Computerized search of our EMG clinical database including 44000 patients previously evaluated through our department at the University of Rochester between August 1999 to December 2015
- Search terms: "vomiting", and/or "alcoholism" and "axonal neuropathy"
- Retrospective review of the patients clinical charts

Results

- 10 patients were identified: 100% women, average age 35.6 years, with ascending acute to subacute numbness (100%) and weakness (80%), preceded by weight loss (100%) and vomiting (90%), requiring hospital admission for gait impairment and pain control but no involvement of respiratory muscles
- No ophthalmoplegia, but areflexia in the lower extremities and gait ataxia

Table 1. Clinical characteristics of patients 1-10. neg=negative, na=not available

Patients #	1	2	3	4	5	6	7	8	9	10
Age	41	29	54	30	34	22	51	16	32	47
Time to nadir (weeks)	2-3	3	4-12	3	8	12	8	6	8	4
Vomiting	✔	✔	✔	✔	✔	✔	✔	✔	neg	✔
Diarrhea	neg	neg	✔	✔	✔	✔	neg	neg	neg	✔
Weight loss	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
in #/time (kg/months)	11/3	22/4	9/na	na/na	42/5	10/na	na/na	24/5	27/na	15/na
Alcohol (A)/ Bariatric Surgery (BS)/ other	**A**	**A**	**A**	**A**	BS	Bulimia	**A**	abd. pain/ anorexia	**A**	**A**
Pain/ Sensory loss	✔/✔	✔/✔	✔/✔	✔/✔	✔/✔	✔/✔	✔/✔	✔/✔	✔/✔	✔/✔
Limb ataxia	✔	✔	✔	✔	neg	✔	neg	neg	neg	✔
Areflexia (legs)	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Tachcardia (bpm)	105	90-105	110	115	122	115	126	93	na	100
Gait/ assistance devices	ataxic/ walker	ataxic/ walker	ataxic/ wheel-chair	ataxic/ walker	ataxic/na	ataxic wheel-chair	ataxic/ cane	na/wheel-chair	na/walker	wide based/ walker
Treatment	B1, folate, MVA	IVIG, MVA, B1, B6, folate	B6, MVA	MVI, folate B1, E	steroids weekly x6, copper, MVA, B1	B1, folate	B1, folate, B12	B-complex	B1, B12 injection	IVIG, B6, B12, B1, folate

Table 2. Laboratory characteristics of patients 1-10. Abnormal findings marked in red. nl=normal

	reference range	1	2	3	4	5	6	7	8	9	10
Vitamin B1	70-180 nmol/l	160 *	107 *	78 *	nl *	198 *	133 *	13.6 (4-15)	0.5 (0.2-2)	low	48
Vitamin B6	20-125 nmol/l	19	10	13.4	34	7.3	31	na	nl	na	<2
Vitamin B12	211-946 pg/ml	810	393	nl	910	774	1414	203	790	low	305
Albumin	3.5-5.2 g/dl	2.7	3.1	3.8	2.8	3.1	3.1	na	na	na	3.6
Prealbumin	20-40 mg/dl	7	9	na	12	14	15	na	na	na	na
MCV	79-95 fL	108	106	na	105	97	102	na	nl	na	101
ESR/CRP	0-20mm/hr/0-10 mg/l	6 / 7	na/5	na/1	54/7	23/6	10/5	na/na	nl	na/na	56/19
SSA/SSB	0-0.9 AI	neg/neg	neg/neg	neg/neg	neg/neg	neg/neg	neg/2.9	neg/neg	na/na	na/na	neg/neg
AST/ALT	0-35 U/L	41/25	142/77	90/30	84/35	16/38	63/29	308/53	18/22	na	87/28
K	3.3-5.1 mmol/l	3.1	2.7	na	low	3.1	2.2	na	na	low	2.6
*** B1 iv/po before lab**	# days	4	3	3 months	treated	1	7 months	na	na	na	0

Table 3. Electrophysiological characteristics of patients 1-10.
Nerve conduction studies showed moderate to severe axonal sensory > motor polyneuropathy

Nerve affected	Reference range	1	2	3	4	5	6	7	8	9	10
SENSORY		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
sural	SNAP µV () CV m/s (>41)	absent	5.6 (>8) 52.8	absent	absent	6.4 (>8) 46	absent	0.8 (>5) 37	absent	absent	absent
radial	15 µV 50 m/s	8.8 53	6.6 62.5	absent	absent	na	absent	14.6 55	nl	absent	absent
ulnar	>13 µV 50 m/s	6 44.2	4.6 51.8	absent	absent	nl	absent	11.6 58	na	absent	absent
MOTOR		✔	neg	✔	neg	✔	✔	✔	✔	neg	✔
Peroneal EDB ankle/ fibula head/ popl. fossa	2 mV / 41 m/s	0.78 0.81 / 46.5 0.86 / 46.4	nl	0.99 1.06 / 40 1.02 / 42	nl	0.54 0.38 / 40 0.34 / 37	0.13 0.13 / 49 absent	1.4 1.17 / 39 1.17 / 45	absent	na	absent
ulnar wrist/ below elbow/ above elbow	6 mV / 49 m/s	nl	nl	5.05 4.35 / 52 3.33 / 50	nl	nl	nl	nl	nl	nl	8.73 8.26 / 41 8.17 / 40
EMG – active denervation?		✔	neg	✔	neg	✔	neg	neg	✔	neg	✔
IMPRESSION NEUROPATHY		axonal sensori-motor with de-nervation	axonal sen-sory	axonal sensori-motor with de-nervation	axonal sensory	axonal sensori-motor with de-nervation	axonal sensori-motor	axonal sensori-motor	axonal sensori-motor with de-nervation	axonal sensory	axonal sensori-motor with de-nervation

- Available laboratory data available was incomplete
- Low albumin, prealbumin and potassium in all patients (when available)
- Vitamin B 1 normal in all but 2 patients, but samples were obtained after thiamin treatment
- Vitamin B 6 low in 50 % of patients
- CSF obtained in 7/10 patients with normal protein
- Ganglioside antibodies obtained and negative in 3 patients
- Porphobilinogen negative in 4 patients (porphyria)
- Heavy metals negative in 3 patients (arsenic poisoning)
- Copper and folate normal
- Absence of sicca symptoms and negative serologies (Sjoegren's)

Conclusion

- We suggest that acute axonal neuropathy in patients with severe vomiting and weight loss previously described in the setting of alcohol abuse, gastric bypass or bulimia is one syndrome, likely caused by nutritional deficiencies.
- We were unable to determine a single nutritional deficit in this retrospective study.
- Prospective comprehensive nutritional laboratory analysis of similar patients prior to receiving supplements, may be informative.
- Awareness of this syndrome will reduce delay in targeted treatment of nutritional deficiencies (e.g., vitamin supplementation), and avoid immunotherapies when not indicated.

Discussion

- 10 cases with acute axonal sensory or sensorimotor neuropathy preceded by weight loss, vomiting and metabolic derangements, associated with significant disability: marked sensory loss, limb and gait ataxia, variable muscle weakness, and neuropathic pain, requiring hospitalization.
- Vomiting and weight loss prior to symptom onset and laboratory evidence of malnutrition in all our patients suggests a nutritional etiology.
- A single vitamin or nutrient deficiency was not identified.
- B6 levels were low in a number of our patients, and could play some role, but B6 was normal in several patients.
- Vitamin B1 (thiamine) deficiency[4] remains a hypothetical cause for this neuropathy, but B1 levels were generally tested after supplementation.
- Beriberi[5] (thiamine deficiency) remains a possibility, but none of our patients had other features such as ophthalmoplegia or encephalopathy.
- Absence of albuminocytologic dissociation in CSF, absence of cranial nerve or respiratory compromise, and negative ganglioside antibody testing, argues against "axonal" variants of GBS.
- 3 patients presented without alcohol exposure but with alternate causes for weight loss and vomiting, which suggests that alcohol toxicity is not the only / critical causal agent.

References

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