

Electrophysiological profile in arsenic neuropathy

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Abstract
Comprehensive electrophysiological studies were performed on 13 patients with arsenic neuropathy. The most prominent finding was a marked abnormality in sensory nerve conduction in the presence of moderate abnormalities in motor nerve conduction. The motor nerve conduction studies and needle EMG were typical of those seen in axonal degeneration which was confirmed by sural nerve biopsy.

Arсенic neuropathy is an age old condition. As yet, however, there has been no comprehensive study describing the electrophysiological features in a substantial number of patients.

Methods and materials

This study was based on 13 patients (10 males and three females, aged from 19 to 48 years) with arsenic neuropathy who were observed in our department over a 17 year period from 1972-89. In all cases, arsenic neuropathy was clinically characterised by a subacutely developing symmetrical sensory-motor polyneuropathy with more distal impairment (table 1). In 12 cases there was a single episode of arsenic poisoning and in one case

there was multiple episodes of poisoning. Attempted homicide was clearly documented in six cases and suspected in five cases. In two cases, pesticide was presumed to be the source of arsenic poisoning. Invariably, sensory symptoms appeared first and were followed by motor weakness. A history of gastrointestinal upset, multiple organ failure, dermatological lesions and Mee's line, characteristic of arsenic intoxication, were common findings. Arsenic intoxication was confirmed by detection of excessive amounts of arsenic in the urine ($>100 \mu\text{g/L}$) in 12 cases and in the hair ($>65 \mu\text{g}/100 \text{ gm}$) and fingers ($>100 \mu\text{g}/100 \text{ gm}$ of nail) in the remaining patient. Sural nerve biopsy showed a definite reduction of myelinated fibres and active axonal degeneration (myelin ovoids or myelin digestion chambers) as the most prominent finding in all the nine cases studied.

Nerve conduction studies were performed using surface recording electrodes following the standard methods, for sensory nerve conduction of the median, ulnar, and sural nerves, for mixed nerve conduction of the median and ulnar nerves, and for motor nerve conduction of the median, ulnar, peroneal, and posterior tibial nerves.¹ For measurement of the amplitude of compound muscle action potentials (CMAP) and of compound nerve action potentials (CNAP), the peak-to-peak amplitude was measured. For calculation of

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Table 1 Clinical and laboratory features

Case	1	2	3	4	5	6	7	8	9	10	11	12	13
Sex/age	F/19	M/46	M/33	M/40	M/40	M/48	F/42	M/43	M/37	M/31	M/37	M/34	F/28
Symptoms													
Duration	16 w	3 w	4 w	4 d	4 w	1 w	6 w	12 w	12 w	4 w	6 w	3 w	5 w
G-I symptoms	+		+	+	+		+	+	+	+	+	+	+
Findings													
Neuropathy	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM	SM
Cranial nerve													
Encephalopathy				+		+							
Respiratory failure			+			+							
Mee's line	+	+		+	+	+	+	+	+		+	+	
Skin lesion	+					+	+	+					
Other organ failure			+ ¹			+ ²				+ ³	+ ⁴	+ ⁵	
Disability score ⁶	9	16	12	16	10	20	4	12	12	4	4	12	8
Arsenic													
Exposure	1*	1	1	1	1	1	1	1	1	Multiple	1	1	1
Urine	1.5†	1.4	24	46	+	47	4	3	2		25	87	1.7
Hair		113†			+	+		62		32	5	5	19
Finger		1.7**			++	-				28	6	11	18
Spinal fluid													
Cell/ml ⁷	0			1	2	0	0	0	0	0	0	0	0
Protein (mg/dl)	37			34	90	216	53	70	36	35	39		18
Outcome				Dead‡									

¹Anemia, arrhythmia, pleural effusion, pulmonary edema. ²Bone marrow suppression, liver. ³Bone marrow suppression, liver and pancreas. ⁴Bone marrow suppression. ⁵Arrhythmia, malabsorption, and splenomegaly. ⁶Disability score of peripheral neuropathy is calculated following the previously described guideline. ⁷Two sensory and two motor functions in the lower and upper extremities are graded. In this scoring system, 20 represents maximal disability and 0 normal functions.

*1, one time exposure.

†1.5, 1.5 times normal value. +: higher than normal value for arsenic but no quantitative data were given. -: negative for arsenic.

‡All other cases showed slow recovery.

F, female; M, male; d, days; w, weeks; y, years; G-I, gastro-intestinal symptoms; SM, sensory-motor.

Table 2 Nerve conduction data¹

	Absent potentials	Low potentials	Prolonged L/slow NCV	Normal ²
<i>Sensory nerve conduction</i>				
Median	11 ³	2	2	0
Ulnar	11	2	1	0
Sural	12	1	0	0
Radial (N = 5) ⁴	5	0	0	0
<i>Mixed nerve conduction (N = 12)</i>				
Median: W-E	11	1	1	0
E-Ax	8	2	3	0
Ulnar: W-E	6	5	5	1
E-Ax	6	4	6	0
<i>Motor nerve conduction</i>				
Median: CMAP (N = 12)	1	9		2
TL	1		9	3
E-W	2		9	2
Ax-E	2		9	2
FW (N = 5)	3		1	1
Ulnar: CMAP (N = 12)	1	8		3
TL	1		8	4
E-W	1		8	4
Ax-E	1		8	4
FW (N = 5)	2		1	2
Peroneal: CMAP (N = 12)	5	6		1
TL	5		4	4
K-A	5		6	2
FW (N = 5)	3		1	1
Post tibial: CMAP (N = 12)	3	7		2
TL	3		7	3
K-A	3		9	1
FW (N = 5)	3		1	1

¹Data is based on 13 cases unless stated. ²Normal values from Oh's data. ³Number of cases. ⁴N = Number of tested cases. NP—no potentials. TL—terminal latency. W—wrist. E—elbow. Ax—axilla. A—ankle. K—knee. FW—F wave latency. L—latency. CMAP—compound muscle potential.

the sensory and mixed nerve conduction velocity (NCV), the distance is divided by the latency to the negative peak of CNAP.¹

Needle EMG studies were performed following standard methods using a monopolar needle in the involved distal muscles.

Results

Nerve conduction findings

A marked abnormality was observed in sensory and mixed nerve conduction in all cases (table 2). In sensory nerve conduction, CNAPs were not obtainable in median and ulnar nerves in 11 cases and in sural nerve in 12 cases. In mixed nerve conduction, CNAPs were not obtainable in eight cases in median nerves and in six cases in ulnar nerves. In the remaining cases, NCVs were either slow or CNAP amplitudes were low in almost all segments of nerves.

Motor nerve conduction was abnormal in all cases but less severely affected than sensory nerve conduction. The most prominent abnormality among motor nerve conduction parameters was abnormal compound muscle action potential (CMAP): either absent or low amplitude in 11 cases in peroneal nerve and in 10 cases in posterior tibial and in 10 cases in median and in nine cases in ulnar nerves. This is also confirmed in mean CMAP amplitudes. Mean terminal latencies were mildly prolonged by 29–44% of normal means, and prolonged terminal latencies were observed in 50–67% of cases. Mean motor NCVs were reduced minimally by 22–35% of normal means and motor NCVs were slow in all cases in the peroneal and posterior tibial nerves and in 67–78% of cases in median and ulnar nerves. F-waves were absent in three cases, prolonged in latency in one, and normal in one. In four cases, there was conduction block: in median nerve in one case

and in posterior tibial nerve in three cases. Temporal dispersion was also present in the posterior tibial nerve in two cases.

In case 6, three serial nerve conduction tests were performed over a six week period as polyneuropathy progressed. There was a steady worsening of nerve conduction abnormalities, and after six weeks, there was no motor or sensory response in any tested nerves. There was a conduction block in median and ulnar nerves in the second test.

Needle EMG findings

Distal muscles were examined in 12 cases. Prominent fibrillation and positive sharp waves were observed in 11 cases. Normal motor unit potentials (MUP) were observed in nine cases while long-duration MUPs were noted in two and high-amplitude MUP in one case. Polyphasic MUPs were increased in seven cases. A reduction in interference pattern was observed in all cases.

Discussion

All our cases had the classic clinical features of arsenic neuropathy: subacute mixed sensory-motor polyneuropathy and other systemic features of arsenic intoxication: a history of severe gastrointestinal upsets, multiple organ failure, dermatological lesions, and Mee's line.^{2–4} The most helpful diagnostic finding of arsenic polyneuropathy was the presence of Mee's line in the fingernails and toenails as observed in 80% of our cases.^{3–5}

The most prominent electrophysiological finding was the marked abnormality in the sensory and mixed nerve conduction in the presence of moderate abnormality in motor conduction. In almost all cases, the CNAPs were not unobtainable. We believe the mixed nerve conduction abnormalities were due to sensory nerve conduction abnormalities since motor conduction abnormalities were minimal in the median and ulnar nerves. This prominent finding was seen in the early stage as well as in the recovery stage of neuropathy. In one of our cases, sensory nerve conduction was still abnormal even nine years after exposure. This finding has been consistent in all studies.^{4–8} Generally, sensory or mixed nerve conduction shows more abnormalities than motor nerve conduction in peripheral neuropathy,¹ but this degree of dissociation between sensory and motor nerve conduction is unusual. There are two possible explanations. It may be a distinct finding in arsenic neuropathy due to the more severe involvement of sensory fibres or it may represent simply a severe degree of axonal neuropathy. We favour the former explanation, because sensory CNAP was absent in the presence of relatively normal motor nerve conduction in median and ulnar nerves in three cases. A further comparison with other axonal neuropathies, however, is needed to settle this issue.

In contrast to the marked sensory nerve conduction abnormalities, motor conduction abnormalities were moderate. The most prominent abnormalities in motor nerve con-

duction parameters were abnormal CMAP amplitude and mild slowing in NCV, which are typical of axonal neuropathy.¹ Needle EMG findings were also typical of axonal neuropathy. These electrophysiological findings were well supported by the histological observation of axonal degeneration as the predominant process in the sural nerve biopsy.

Conduction block, an electrophysiological marker of demyelinating neuropathy, was not a prominent feature in our series since we observed it in only one of six tested nerves in four cases. Conduction block was documented eight to 10 weeks after exposure in two of Le Quesne's cases and two to five weeks after the appearance of sensory complaints in four of Donofrio's cases.^{6,7} In three of Donofrio's cases, conduction block was transient as earlier and later tests did not show any features of it.⁷ We observed a transient conduction block in one case (case 6) during a worsening period of neuropathy. We believe that this is an incidental finding since segmental demyelination was not observed in any of the teased nerve preparations in our cases (unpublished data). In practice, however, it is important to remember that conduction block, though transient, may be observed rarely in a few nerves in arsenic neuropathy. This, together with elevated spinal fluid protein in some patients with arsenic neuropathy, may lead clinicians to the diagnosis of Guillain-Barré syndrome in otherwise classic cases of arsenic neuropathy.^{7,9}

Serial studies in one case showed a steady deterioration of nerve conduction over a six weeks period. This is typically seen in toxic neuropathies and has been observed in Murphy's cases.¹⁰

Needle EMG study showed active denervation process in all tested cases. Prominent fibrillation and positive sharp waves in the presence of normal or long-duration MUPs were indicative of axonal degeneration. This was confirmed by predominant axonal degeneration in the sural nerve biopsy.

In summary, our study showed that arsenic neuropathy is characterised electrophysiologically by the findings typical of axonal degeneration and the most prominent finding in arsenic neuropathy is a marked abnormality in the sensory nerve conduction in the presence of moderate abnormality in motor conduction. Axonal degeneration was histologically confirmed by the sural nerve biopsy.

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