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Complete List of Authors:	Alam, Taimour; Leeds Teaching Hospitals NHS Trust, Clinical Neurophysiology Alix, James; Royal Hallamshire Hospital, Clinical Neurophysiology Rao, D; The Royal Hallamshire Hospital, Neurophysiology Hadjivassiliou, Marios; Royal Hallamshire Hospital, Neurology
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Anti-MAG negative distal acquired demyelinating symmetric neuropathy in association with a neuroendocrine tumor

*Taimour Alam MRCP[3]

*James J.P. Alix MRCP, PhD[1,2]

D. Ganesh Rao MD FRCP[2]

Marios Hadjivassiliou MD FRCP[4]

[1]Sheffield Institute for Translational Neuroscience, University of Sheffield, Sheffield, England

[2]Department of Clinical Neurophysiology, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, England

[3]Department of Clinical Neurophysiology, Leeds General Hospital, Leeds Teaching Hospitals NHS Trust, Leeds, England

[4]Department of Neurology, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, England

*Contributed equally

Address for correspondence:

Department of Clinical Neurophysiology, Brotherton Wing, Leeds General Infirmary, Great George Street, Leeds. LS1 3EX

We followed with interest the fascinating cases of anti-MAG positive Distal Acquired Demyelinating Symmetric (DADS) neuropathy by Ayyappan et al.,[1] and Galassi and Luppi[2]. We would like to take this opportunity to add to this stimulating debate on the relationship between neoplasia and DADS neuropathy.

A 75 year old woman was referred to our Neurology service with a 4 month history of paresthesia affecting the hands and feet. She had a 2 year history of metastatic neuroendocrine tumor following an abdominal lymph node biopsy strongly positive for CD56 and chromogranin. Cauda equina syndrome occurred shortly after diagnosis due to a metastatic deposit at S2. Neurological examination at this time revealed saddle anesthesia, lower limb weakness, and absent lower limb reflexes. A course of radiotherapy, steroids, and somatostatin analog treatment improved leg strength sufficiently for mobilization with a walking stick.

Examination revealed no upper limb ataxia but mild lower limb heel-shin ataxia. Tandem walking was difficult. Speech was normal. There was a loss of vibration sensation up to the knees bilaterally, but joint position sense was preserved. Tendon stretch reflexes were absent throughout; power was normal in the arms and reduced proximally in the legs. Nerve conduction studies demonstrated unrecordable sensory nerve action potentials in upper and lower limbs with markedly prolonged distal motor latencies with reduced terminal latency indices, particularly in the upper limbs (table 1). Blood tests, including anti-MAG/IgM, anti-glutamic acid decarboxylase, anti-neuronal nuclei, anti-Hu, anti-Yo, anti-Purkinje cell, anti-CV2/CRMP-5, anti-PNMA2(Ma/Ta), anti-Tr, voltage gated Ca channel, and anti-ganglioside antibodies were all negative. Celiac serology was also negative. MR spectroscopy showed significant reduction of the NAA/Cr ratio from the vermis and right hemisphere but without cerebellar atrophy.

Treatment with intravenous immunoglobulin produced no improvement, and her symptoms progressed. Treatment with 10mg of prednisolone led to symptomatic stabilization. Unfortunately

she died approximately 2 years after her neuropathy diagnosis due to metastatic disease, with no significant change in her neurological condition.

Our conclusion at the time of diagnosis was that the anti-MAG negative DADS neuropathy was paraneoplastic in nature. A third of DADS cases may be negative for anti-MAG antibodies[3], suggesting the antibody is a marker for disease, rather than being pathognomonic. Larue et al., reported 10 cases of anti-MAG negative DADS neuropathy, 9 of whom had an associated hematological condition[4].

While the lack of paraneoplastic antibodies makes our association less firm, this may help explain the plateau in symptoms[5]. It is also worth noting that antibodies are only present in around 50% of patients with paraneoplastic syndromes[6]. Unfortunately, the palliative nature of our case also precludes association by improvement after cancer treatment; by the criteria of Graus et al., our case would be considered “possible paraneoplastic”[6].

Stabilization of the patient’s condition despite continuing malignant disease, raises the possibility of the pathological process leading to the neuropathy being transient in nature. Overall, our experience leads to us to agree with Ayyappan et al., in their conclusion of DADS associated with malignancy, and also with Galassi and Luppi in their assertion that clinicians should maintain vigilance in neuropathies with a possible paraneoplastic association, including the DADS variant.

Abbreviations

MAG: Myelin Associated Glycoprotein

DADS: Distal Acquired Demyelinating Symmetric

References

1. Ayyappan S, Day T, Kiers L. Distal acquired demyelinating symmetric (DADS) neuropathy associated with colorectal adenocarcinoma. Muscle Nerve 2015;51(6):928-931.

2. Galassi G, Luppi G. Distal acquired demyelinating symmetric neuropathy associated with colorectal adenocarcinoma: Should it be termed paraneoplastic? Muscle Nerve 2015.

3. Katz JS, Saperstein DS, Gronseth G, Amato AA, Barohn RJ. Distal acquired demyelinating symmetric neuropathy. Neurology 2000;54(3):615-620.

4. Larue S, Bombelli F, Viala K, Neil J, Maisonobe T, Bouche P et al. Non-anti-MAG DADS neuropathy as a variant of CIDP: clinical, electrophysiological, laboratory features and response to treatment in 10 cases. Eur J Neurol 2011;18(6):899-905.

5. Tschernatsch M, Stolz E, Strittmatter M, Kaps M, Blaes F. Antinuclear antibodies define a subgroup of paraneoplastic neuropathies: clinical and immunological data. J Neurol Neurosurg Psychiatry 2005;76(12):1702-1706.

6. Graus F, Delattre JY, Antoine JC, Dalmau J, Giometto B, Grisold W et al. Recommended diagnostic criteria for paraneoplastic neurological syndromes. J Neurol Neurosurg Psychiatry 2004;75(8):1135-1140.

Table 1

Motor nerve conduction studies in the upper and lower limbs. Temperature was monitored and maintained at or above 34°C in the upper limbs and 32°C in the lower limbs

Nerve	Site	Amplitude (mV)	Distal motor latency (ms)	Conduction velocity (m/s)	F wave latency (ms)	Terminal latency index
R. Median	Wrist	6.1	14.4	-	48.2	0.10
	Elbow	5.5	-	42	-	-
L. Median	Wrist	5.9	12.9	-	40.9	0.10
	Elbow	4.9	-	48	-	-
R. Ulnar	Wrist	4.0	9.1	-	49.0	0.19
	B. Elbow	3.7	-	34	-	-
	A. Elbow	3.4	-	31	-	-
L. Ulnar	Wrist	3.8	6.1	-	40.9	0.25
	B. Elbow	3.5	-	40	-	-
	A. Elbow	3.4	-	43	-	-
R. Peroneal	Ankle	1.5	15.9	-	NR	0.14
	Fibula head	1.3	-	35	-	-
	Pop fossa	1.0	-	36	-	-
L. Peroneal	Ankle	0.9	14.9	-	-	0.22
	Fibula head	0.6	-	24	-	-
R. Tibial	M. Malleolus	NR	NR	-	-	-
L. Tibial	M. Malleolus	NR	NR	-	-	-

Normal values: Upper limb motor amplitudes >5mV, conduction velocity >48m/s, DML <4.5ms in median and <3.5ms in ulnar nerve, F wave latency <30ms (adjusted for height).