Dropped head with positive intravenous edrophonium, progressing to myasthenia gravis

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SUMMARY

'Dropped head syndrome' (DHS) may be associated with a variety of neurological diseases. The absence of neurological clues to the underlying cause of DHS can make management particularly challenging. We review six patients who presented with only DHS, responded to intravenous edrophonium and turned out to have myasthenia gravis (MG) including similar patients who were previously documented. Six patients presented with neck weakness and three had bulbar symptoms. Acetylcholine receptor (AChR) was positive in four patients. One patient had thymoma. The interval from the onset of DH to the presentation of typical MG features was shorter in patients who tested positive for anti-Ach antibody (1–2 months) than in patients who tested negative for anti-AchR antibody (13 months, 4 years). Our results suggest that patients with DHS responding to intravenous edrophonium might turn out to have MG and such patients might respond to a combination of anticholinesterase agents and steroids.

BACKGROUND

Restricted weakness of the extensor muscles of the neck is a relatively rare condition, designated as 'dropped head syndrome' (DHS) and DHS may be associated with a variety of neurological diseases, including neuromuscular, motor-neuron and neurodegenerative disorders.¹ When DHS is accompanied by neurological features of such disorders, potential causes, such as myositis and dystonia can be confirmed, facilitating the selection of treatment. However, the absence of neurological clues to the underlying cause of DHS can make management particularly challenging. We review six patients who presented with only DHS, responded to intravenous edrophonium and turned out to have myasthenia gravis (MG) including similar patients who were previously documented.^{2–5}

CASE PRESENTATION

Our subjects were two Japanese patients who presented with DH that responded to intravenous edrophonium (table 1). No subject had functionally significant weakness or wasting of the limbs, ocular, respiratory or bulbar musculature before presentation of DH; bladder or bowel dysfunction; or other neurological deficits, except for MG manifestations, such as extrapyramidal signs or ataxia. The response of intravenous edrophonium to DH was defined as positive when the inclination of the head was apparently reduced in association with increased muscle power of the neck extensor muscles on the Manual Muscle Test, as evaluated by at least two experienced neurologists. This test was performed under cardiac monitoring and

informed consent was obtained from all patients. Cranial MRI showed no evidence of a mass lesion, inflammation, major vessel disease or multiple infarcts in any patient. Binding antibodies to acetylcholine receptor (AChR) were measured in all patients before immunosuppressive therapy or thymectomy.

INVESTIGATIONS

Six patients presented with neck weakness and three had bulbar symptoms (table 1). Binding antibodies to AChR was positive in four patients. The interval from the onset of DH to the presentation of typical MG features was shorter in patients who tested positive for anti-Ach antibody (1–2 months) than in patients who tested negative for anti-AchR antibody (13 months, 4 years). Waning on repetitive nerve stimulation tests was evident in four patients. Creatine kinase levels were normal in all. One patient had thymoma.

OUTCOME AND FOLLOW-UP

The severity of DH was reduced in all patients by treatment with prednisolone or anticholinesterase drugs.

DISCUSSION

DH responding to edrophonium responded to steroids or anticholinesterase agents and typical MG features developed. MG can present with DH, and neck weakness is the initial manifestation in 3% of patients with MG.⁶ MG is known to affect the neck muscles, predominantly the neck flexors and DH has developed along with ocular, bulbar or limb involvement late in the course.^{4–7} However, about 20% of patients with MG have no anti-AchR antibody,⁸ which often creates difficulty in diagnosing MG when only DH is present. This responsiveness to edrophonium suggests that a neuromuscular junction disorder probably caused DH.

The interval from the onset of DH to the presentation of typical MG features differed between patients with and those without anti-AchR antibody. Two patients with antibodies to muscle-specific tyrosine kinase (MuSK) antibody who presented with DH as the initial manifestation had long periods of DH without typical MG symptoms (3 years, 4 years) but DH in one patient showed no responsiveness to edrophonium.^{5–9} The apparent relation between these antibodies and the interval remains uncertain, but may be attributed to different inhibitory mechanisms of AChR. For example, anti-AchR antibody directly blocks the receptor, whereas other antibodies such as anti-MuSK antibody inhibit muscle cell proliferation.¹⁰

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Table 1 Clinical characteristics of patients with only dropped head responding to edrophonium who turned out to have myasthenia gravis

	Patient 1	Patient 2	Patient 3 ref. ²	Patient 4 ref. ³	Patient 5 ref. ⁴	Patient 6 ref. ⁵
Sex/age (at initial examination)	80/F	66/F	55/M	61/F	78/M	46/F
Family history of neuromuscular or neurodegenerative disease	—	—	—	NA	NA	NA
Duration of only DH	2 months	1 months	2 months	13 months	2 months	4 years
<i>Neurological examinations</i>						
Response of edrophonium to DH	+	+	+	+	+	+
Neck weakness	+	+	+	+	+	+
Bulbar symptom	+	+	—	—	+	—
Ptosis	+	—	—	—	+	—
Limb weakness	—	+	—	—	+	—
Fatigability	—	+	NA	—	NA	+
<i>Work-up</i>						
Anti-Ach-R antibody (nmol/l)	37	132	1.9	—	6.5	—
MuSK antibody (nM)	ND	ND	NA	NA	NA	10
Waning on repetitive nerve stimulation test	+	+	—	+	NA	+
Thymoma present	—	—	—	+	NA	—
CK	55	58	normal	normal	NA	NA
<i>Outcomes</i>						
Treatments	cho, ST	ST	cho	cho, ST	cho, ST	cho, ST
DH	reduced	reduced	improved	improved	improved	improved
MG symptoms	reduced	reduced	no appeared	no appeared	improved	no appeared

cho, anticholinesterase; CK, creatine kinase; DH, dropped head; MG, myasthenia gravis; m, months; NA, not available; ND, not done; MuSK, muscle-specific tyrosine kinase; ST, steroid.

Our results suggest that patients with DHS responding to intravenous edrophonium may turn out to have MG and such patients might respond to a combination of anticholinesterase agents and steroids.

Competing interests None.

Patient consent Obtained.

Learning points

- Patients with DHS responding to edrophonium may turn out to have myasthenia gravis (MG).
- Patients with dropped head syndrome responding to edrophonium might respond to a combination of anticholinesterase agents and steroids.
- The interval from the onset of dropped head to the presentation of typical MG features was shorter in patients who tested positive for anti-acetylcholine (Ach) antibody than in patients who tested negative for anti-AchR antibody.

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