

# A Case of Hepatocellular Carcinoma Presenting with Myasthenia Gravis

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## Introduction

The association of Myasthenia Gravis (MG) with thymomas and thymic hyperplasia is well known. However, MG with extrathymic malignancy is much less common; cases of MG associated with hepatocellular carcinoma (HCC) are even more rare. Here we report another rare case of HCC presenting with MG.

## History of Present Illness

A 73-year-old right handed male with a past medical history of psoriasis, type 2 diabetes mellitus and hypertension who presented to regional academic center with five months of progressive dysphagia, dysarthria, and 40-pound weight loss.

Initial outside hospital evaluation was remarkable for negative endoscopy and fiberoptic laryngoscopy. MRI brain without contrast was only remarkable for an incidental frontal dural based lesion.

Review of systems negative for double vision, neck muscles and extremity weakness, dyspnea and preceding respiratory or diarrheal infections.

He was found to have multiple large hypodense hepatic lesions with variable enhancement.

## Physical Examination

General	No acute distress
Mental Status	Alert and oriented to person, place and time. Language intact. <b>Moderate labial and lingual dysarthria which became severe with prolonged speech.</b>
Cranial Nerves	<b>Moderate bilateral ptosis which improved with ice pack test. Bilateral orbicularis oris and oculi weakness.</b>
Motor	Tone normal. Strength 5/5 throughout, no fatigability.
Sensory	Intact to light touch, temperature and vibration.
Reflexes	1+ throughout, absent Babinski and Hoffman.
Other	No dysmetria with finger to nose. Normal based gait.

## Laboratory Data

CSF	WBC 2, 70% lymphocytes Protein 53, Glucose 82 Cytology and Mayo paraneoplastic panel negative Oligoclonal bands present in CSF and serum
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Liver Function Test	<b>AST 60, ALT 40, Alkaline phosphatase 184, GGT 119, Total bilirubin 1.3</b> Hepatitis A, B, C negative
Cancer screening	<b>Alpha fetoprotein 640.1 (ref &lt;10.0)</b> CA 19-9, CEA negative
Autoimmune	<b>ANA 1:640 with speckled pattern</b>
MG testing	<b>Acetylcholine receptor (AChR) binding antibodies 21.50</b> (ref <0.03 neg, 0.31-0.49 equivocal) <b>AChR blocking antibodies 69 (ref &lt;15% inhibition)</b> <b>AChR modulating antibodies 87 (ref &lt;30% inhibition)</b> Anti-MuSK antibodies were negative

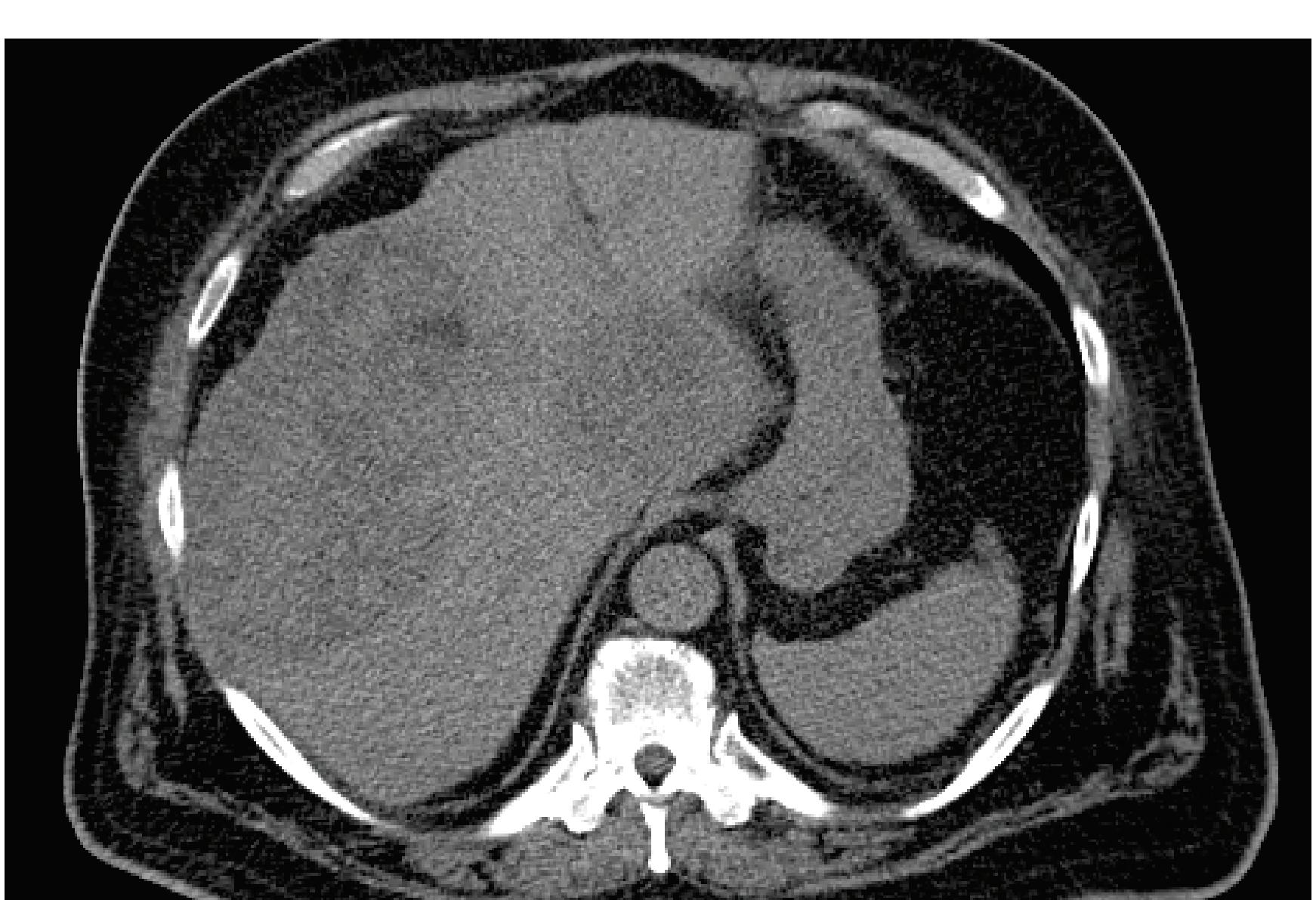
## Diagnostic Testing

**Table 1:** Nerve conduction study (NCS) data showing positive decrement in compound muscle action potential (CMAP) amplitudes with 2 Hz repetitive stimulation before and after exercise in the right trapezius.

### Repetitive Nerve Stimulation Accessory (Spinal).R

Baseline	Potential Number	Amplitude		Baseline	Potential Number	Amplitude	
		Val. (mV)	Decr. (%)			Val. (mV)	Decr. (%)
Baseline	1	2.01	0	1 Min. Post Exercise	1	2.23	0
	2	2.05	-2		2	2.19	2
	3	2.06	-2		3	2.19	2
	4	2.03	-1		4	2.15	4
	5	2.02	0		5	2.14	4
	6	2.04	-1		6	1.88	16
	7	2.04	-1		7	2.08	7
Immediately Post Exercise	1	1.14	0	3 Min. Post Exercise	1	2.19	0
	2	0.84	29		2	2.18	0
	3	0.84	29		3	2.14	2
	4	0.75	34		4	1.91	13
	5	0.56	50		5	2.14	2
	6	0.63	46		6	2.10	4
	7	0.63	43		7	2.08	5

## Imaging



**Figure 1:** Axial CT abdomen with contrast showing multiple hypodense heterogeneously enhancing masses within the liver. The largest measured 14 cm x 11.5 cm x 6.4 cm.

## Hospital Course

Ultrasound guided biopsy of hepatic mass showed foci of necrosis with a tiny focus of perivascular atypical cells which were positive for Hepar-1, CAM5.2, and Glyican and negative for PAX-8, GATA 3, pankeratin, vimentin, CK7, WT-1, and RCC suggestive of HCC. Surgical biopsy confirmed moderate to poorly differentiated HCC. He was not a candidate for Y-90 radioembolization. CT Chest did not show thymoma or thymic hyperplasia. Given the clinical history and EMG/NCS findings, he was started on IVIG 400 mg/kg/day for five days and pyridostigmine 60 mg TID with clinical improvement. He was eventually transitioned to Mycophenolate Mofetil 500 mg BID and Prednisone 60 mg daily.

He continued to have poor oral intake requiring PEG tube placement. He was then discharged home with plan to follow up with regional cancer center for second opinion and treatment.

## Literature Review

Only two other cases of MG and HCC have been reported previously to the best of our knowledge.

**Case 1**<sup>1</sup> A 55-year-old male diagnosed with MG (based on symptoms, EMG and lab workup findings) on pyridostigmine had an incidental finding of liver mass on CT scan which was found to be biopsy proven HCC.

MG symptoms improved after 4 cycles of chemoembolization and left hepatectomy and he was taken off pyridostigmine.

No thymoma was found.

**Case 2**<sup>2</sup> A 60-year-old with coexisting pemphigus vulgaris (biopsy proven) and HCC (diagnosed with angiography, no biopsy performed) developed ptosis of the upper lids and weakness in his arms. He was diagnosed with MG (positive anti-AChR antibodies).

He had symptomatic response to neostigmine administration.

No thymoma was found.

## Discussion

The pathophysiology behind MG associated with extrathymic malignancies is not well defined; especially when antibodies are directed at normally expressed proteins. However, CD8+ T-lymphocytes have been shown to mount immune response to normal protein when expressed in cancer cells, possibly related to abnormal antigen presentation.<sup>8</sup>

AChR are expressed in hepatocellular carcinoma and increased acetylcholine signaling appears to be a poor prognostic factor, partly through associated increased androgen mediated promotion of cell migration, invasion and decreased apoptosis.<sup>6,7</sup>

Another hypothesis presents MG as a paraneoplastic syndrome in which autoantibody production is associated with an immune response against tumor cells.<sup>1</sup>

Further understanding of the pathophysiology is important to help guide treatment options in such cases.

## Conclusion

While MG associated with extrathymic malignancies is not uncommon, its association with HCC is infrequent and may be suggestive of an alternative immune-mediated pathophysiology.

Further studies are needed to assess if all patients diagnosed with MG should get CT abdomen and pelvis along with CT chest as part of screening for extrathymic malignancies.

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