Chemical Shift and Fat Suppression Magnetic Resonance Imaging of Thymus in Myasthenia Gravis

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Myasthenia gravis (MG) is an autoimmune neuromuscular disease leading to fluctuating muscle weakness. Approximately 70% of patients with MG have thymic hyperplasia, and 10–20% of them have thymoma. In MG patients without thymoma, thymectomy should be performed only in selected patients. In contrast, thymectomy should be performed in all patients with thymoma. In addition, thoracoscopic thymectomy can be used in non-thymomatous MG but not in MG with thymoma, since it has limited exposure. Therefore, it is essential to differentiate thymic hyperplasia from thymoma in MG patients so that physicians can determine the need for thymectomy together with the best approach[1] to use.

In most previous studies, imaging characteristics of thymic hyperplasia and thymoma overlapped considerably on both computed tomogram (CT) and conventional magnetic resonance imaging (MRI).[2] However, by incorporating new sequences, MRI has shown recent promise. Inaoka et al. found that chemical shift MRI could reliably differentiate thymic hyperplasia from thymus gland tumors.[3] Furthermore, Popa and colleagues confirmed the ability of chemical shift technique in differentiating thymic hyperplasia from thymoma in MG.[4] In addition, Kuhnt et al. suggested that MRI with fat suppression sequences was superior to CT in thymic imaging.[5]

Although the above studies are valuable for the application of MRI in MG, they did not use chemical shift and fat suppression techniques together and directly compare their performance. Moreover they did not consider the influence of age. The proportion of fat tissue in thymus changes significantly over a lifetime; after 40 years-of-age it is predominantly replaced by fat. On the other hand, chemical shift and fat suppression techniques performed differently according to the ratio of fat in the tissue.[3,6] The performance of these MRI techniques on thymus imaging may change across different age groups as the ratio of fat in thymus changes. The purpose of this study was to assess the role of chemical shift and fat suppression MRI techniques in thymic imaging of patients with MG and to determine whether their performance changes with age.

Methods

Subjects

The institutional review board of our hospital approved the study protocol. We retrospectively reviewed the medical records, CT and MRI images of consecutive MG patients treated at our hospital from 2009 to 2011, and found seven MG patients who had undergone both CT and MRI (including chemical shift and fat suppression MRI) studies of the thymus, with known histological results. The diagnosis of MG was based on their history, neurological examinations, neostigmine test and electrophysiological studies (including single fiber electromyography and repetitive nerve stimulation). A summary of their demographic and clinical characteristics is shown in the Table. Only Case 2 had received small dose corticosteroid treatment before the imaging studies; none of the other patients had received immunosuppressants, including corticosteroids, before CT and MRI scanning.

Imaging Study

All MRI was performed using a 1.5 T unit (Signa; General Electric Medical Systems, Milwaukee, WI, USA) and a torso coil. Chemical shift images were obtained by using both in-phase and opposed-phase T1-weighted gradient-echo sequences in all subjects. These images were acquired using fast multiplanar spoiled gradient-echo sequences with a flip angle of 90°, 5 mm section thickness, 1 mm intersection gap, 340-380 mm field of view, 288 × 180 image matrix, one signal acquisition, and a bandwidth of ± 62.5 kHz in a single breath-hold of 20 seconds. Repetition time (TR) was 220 msec on each image. Echo time (TE) for the in-phase image was 4.9 msec and that for the opposed-phase image was 2.3 msec. We also obtained T2-weighted spin-echo axial images with and without fat suppression in all subjects. The T2-weighted spin-echo imaging was obtained using a single shot fast spin-echo sequence with the following parameters: TR range/TE range, 2000-2333.33/79.65-86.51; section thickness, 5 mm with a 1 mm intersection gap; and matrix, 288 × 180.

All patients underwent CT scan using a 16-slice scanner (Brightspeed; General Electric Medical Systems, Milwaukee, WI) without contrast. Helical CT was performed from the lung apices to the middle portion of both kidneys with 4-mm collimation and a pitch of 1.3. The image data were reconstructed using 5-mm thickness. Scanning parameters were 120 kVp and auto-mA by keeping

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Table: Summary of demographic, clinical, CT, and MR characteristics

Case	Gender	Age	Osserman's grading	Muscle groups involved	Thymic histology	Shape on CT	CT attenuation (HU)	Shape on MRI	Opposed-phase imaging	CSR	Fat suppression
1	Female	30	IIa	Ocular and limbs	LFH	Triangular	27	Convex	Signal decreased	0.16	Signal slightly decreased
2	Male	30	IIb	Ocular, facial, bulbar, axial and limbs	LFH	Convex	9	Convex	Signal decreased	0.78	Signal slightly decreased
3	Female	60	IIb	Ocular, facial, bulbar, axial and limbs	LFH	Convex	−107	Convex	No change	1.02	Signal decreased
4	Female	34	IIa	Ocular and limbs	Type B1 thymoma	Irregular	36	Irregular	No change	0.98	No change
5	Female	32	IIa	Ocular and limbs	Type B2 thymoma	Round	29	Round	No change	0.96	No change
6	Female	33	IIa	Ocular, facial, bulbar, axial and limbs	Type B1 thymoma	Irregular	33	Irregular	No change	1.12	No change
7	Female	51	IV	Ocular, facial, bulbar, axial, limbs, and respiratory	Type B2 thymoma	Irregular	26	Irregular	No change	1.06	No change

CSR = chemical shift ratio; LFH = lymphoid follicular hyperplasia

the noise index below 11. The lung (window width, 1500 Hounsfield units(HU); window level, -600 HU) and mediastinal (window width, 400 HU; window level, 35 HU) windows were reconstructed using the bone algorithm and soft tissue algorithm, respectively.

Image Analysis

The CT and MRI images were independently assessed by two professional radiologists, who were blinded to patients' clinical information. Final decisions were reached by consensus.

Both the CT and MRI images were assessed for the shape of the thymuses, their relationship with adjacent structures and the signal homogeneity; the CT attenuation value and MRI signal intensity of the thymuses (or thymoma) were evaluated on CT and MRI, respectively. The chemical shift ratio (CSR) was determined by comparing the relative change of the signal intensity of the thymic tissue (or thymoma) (tSI) to that of the paraspinal muscle (mSI) for the in (in) and opposed (op) phases. A circular region of interest (ROI) was placed within the thymus (or thymoma) and the paraspinal muscle at a slice level of the maximum axial surface of the thymus (or thymoma) when the lesion was homogeneous. If the lesion had heterogeneous signal intensity, its signal intensity was determined by the dominant signal intensity. The CT attenuation values of the thymus (or thymoma) were measured on the way similar to MRI signal intensity measurements. The area of the ROI ranged from 66 to 194 mm^2. The following equation was adopted: CSR = (tSIop/mSIop)/(tSIin/mSIin).[3]

Thymectomy and Pathologic Examination

Thymectomy was performed through median sternotomy in all patients by thoracic surgeons in our hospital. Operation records were reviewed. Thymic pathology was determined by clinical pathologists in our hospital. The diagnosis of thymic hyperplasia was established by the presence of several lymphoid follicles with germinal centers. Thymoma was diagnosed and classified according to the latest World Health Organization classification.

Results

Thymic hyperplasia Group

The findings of CT and MRI are summarized in the Table. There was no compression to surrounding structures by the thymuses on both imaging modalities. In Case 1 and Case 2, the thymuses were soft tissue density structures on CT. On MRI examination, the thymuses of these two cases were of intermediate signal intensity between muscle and fat on T1 and T2 imaging. After fat suppression their signal intensity was only slightly reduced and was higher than both muscle and subcutaneous fat. However, on chemical shift imaging of Case 1 and Case 2, there was significant signal intensity loss on the opposed-phase images relative to the in-phase images and the CSRs were 0.16 and 0.78 respectively (Figure 1 for Case 1). In Case 3, an elderly patient, there were few micronodularities and linear strands in the thymus on both CT and MRI (Figure 2). The thymus showed predominant fat attenuation on CT, while on MRI the signal intensity of the thymus was similar to subcutaneous fat and much higher than muscle on T1 and T2. After fat suppression, its signal intensity was significantly reduced, which was similar to subcutaneous fat. However, on chemical shift imaging, there was no signal loss on the opposed-phase image; its CSR was 1.02.

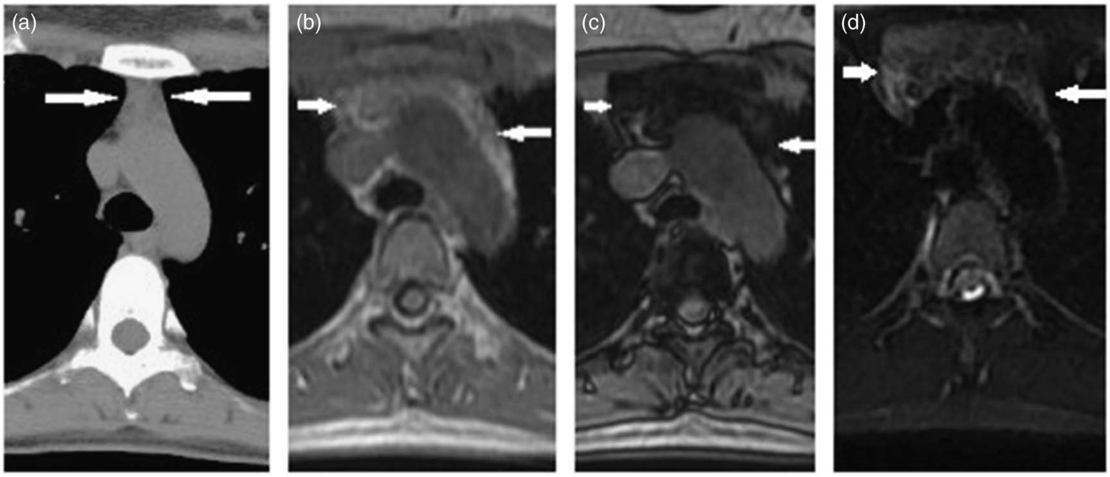

Figure 1: *30-year-old woman (case 1) with MG and thymic LFH.*
A. Un-enhanced CT scan shows soft tissue of triangular shape (arrows) in anterior mediastinum.
B. In-phase gradient-echo MR image shows the signal intensity of the thymus (arrows) is greater than that of muscle and less than that of fat.
C. Opposed-phase gradient-echo MR image demonstrates significant signal intensity loss of the thymus (arrows) relative to that in the in-phase image.
D. Fat suppression using the fat saturation technique shows the signal intensity of the thymus (arrows) is greater than that of both muscle and fat.

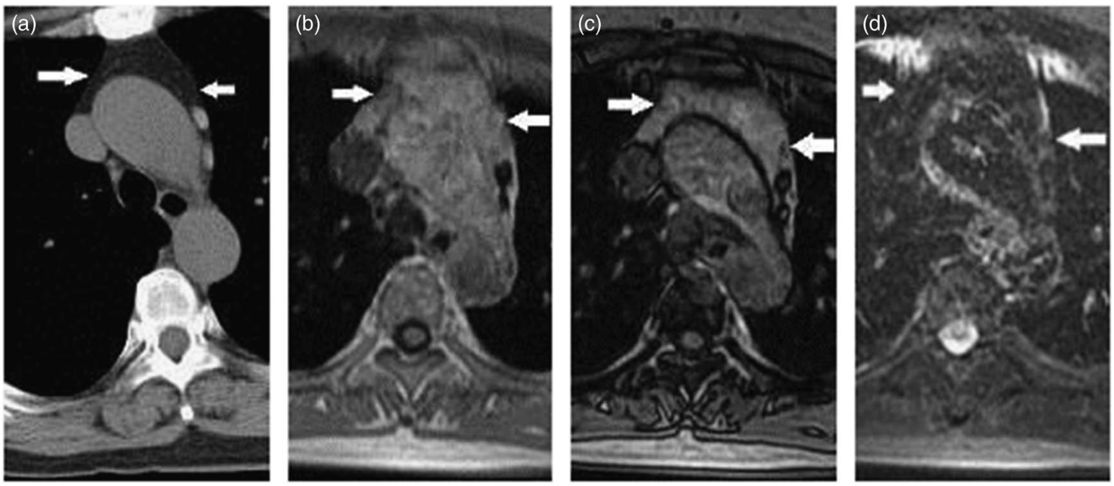

Figure 2: *60-year-old woman (case 3) with MG and thymic LFH.*
A. Un-enhanced CT scan shows the thymus (arrows) predominantly composed of fat.
B. In-phase gradient-echo MR image shows that the high signal intensity of the thymus (arrows) is similar to subcutaneous fat.
C. Opposed-phase gradient-echo MR image also demonstrates that the high signal intensity of the thymus (arrows) is similar to that of subcutaneous fat.
D. Fat suppression using the fat saturation technique shows the signal intensity of the thymus (arrows) is significantly reduced and similar to that of subcutaneous fat.

Thymoma Group

There was compression to the surrounding structures in Case 7 but not in other patients. All the thymomas showed soft tissue density on CT and homogenous signal intensity between that of muscle and subcutaneous fat on T1 and T2 imaging. After fat suppression, there was no significant signal intensity loss of the tumors and the signal intensity of these thymomas also showed no reduction in the opposed-phase image when compared with the in-phase image. The CSR ranged from 0.96 to 1.12 (mean 1.03). Compared with other MRI sequences and CT, the performance for delineating the margin of the tumors and their relationship with surrounding tissues was better on chemical shift imaging in Case 4, 5 and 6 (Figure 3 for Case 4), while was better on fat suppression imaging in Case 7, who was much older (Figure 4).

Discussion

In the present study, by incorporating chemical shift and fat suppression techniques, MRI could demonstrate the composition

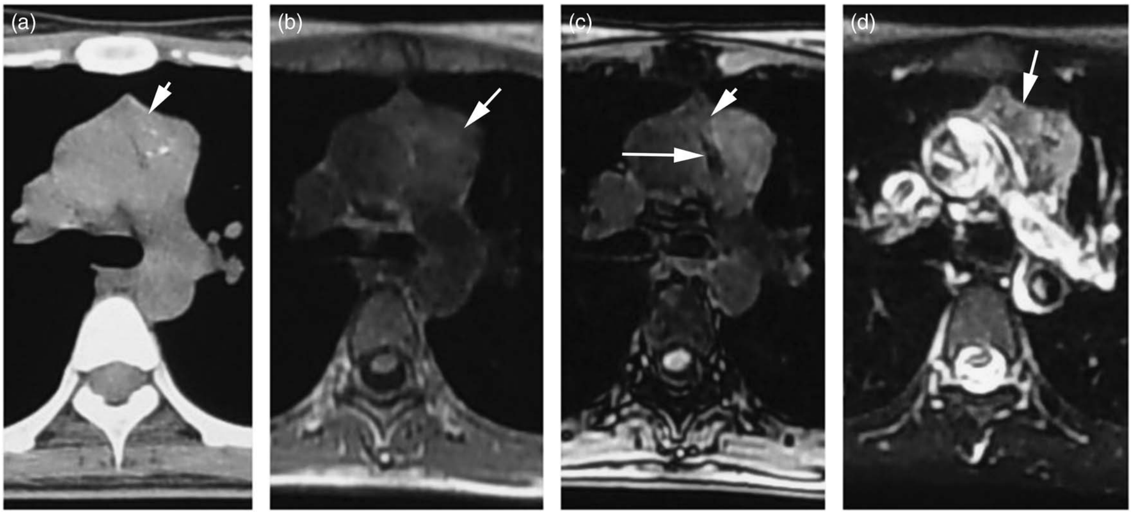

Figure 3: *34-year-old woman (case 4) with MG and thymoma.*
A. Un-enhanced CT scan shows an irregular mass lesion (arrow) in the left anterior mediastinum, its signal intensity is similar to the large vessels, and its demarcation is poorly displayed.
B. In-phase gradient-echo MR image shows the signal intensity of the thymoma (arrow) is higher than the vessels, which provides better contrast resolution than CT.
C. Opposed-phase gradient-echo MR image demonstrates the signal intensity loss of the tissue around the thymoma, especially the right anterior (short arrow) and the right border (long arrow) of the thymoma, which are much clearer than them on CT and In-phase.
D. Fat suppression using the fat saturation technique does not provide more details about the tumor.

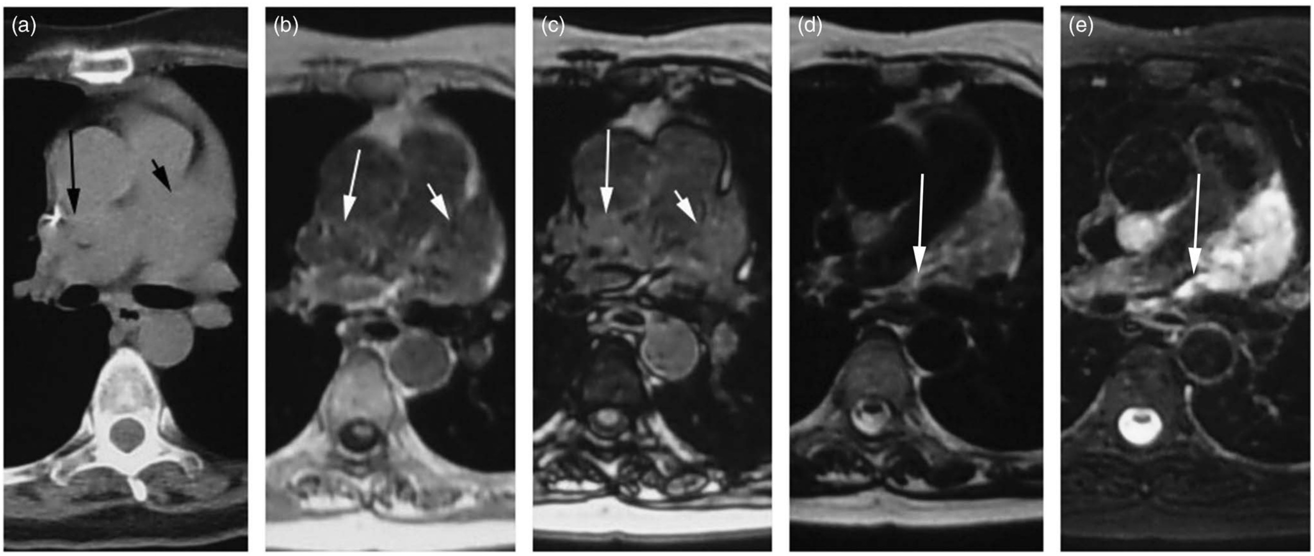

Figure 4: *51-year-old woman (case 7) with MG and thymoma.*
A. Un-enhanced CT, the mass lesions (short and long arrows) are hardly distinguished from the vessels.
B. In-phase gradient-echo MR shows the thymoma (short and long arrows), and there are some fat tissue around the tumor.
C. Opposed-phase gradient-echo MR image, the border of the tumor is poorly displayed.
D. T2WI does not make a distinction between the tumor and surrounding fat tissue (arrow).
E. Fat suppression using the fat saturation technique gives a much better delineation of the demarcation of the tumor (arrow).

of the thymuses, thus differentiating thymic hyperplasia from thymoma. In addition, these techniques helped delineate the margin of thymoma and its relationship with surrounding tissues. Furthermore, chemical shift and fat suppression MRI performed differently in young and older patients.

Chemical shift imaging is based on the resonance frequency differences of protons in water and fat and is best suited for tissue mixed with fat and water. It has been widely used in radiological diagnosis of adrenal adenoma and fatty liver.[7] Fat suppression techniques such as fat saturation and inversion-recovery imaging were based on the property of fat tissue itself and perform best in tissues that contain predominantly fat tissue, such as subcutaneous fat.[5]

Although Cases 1, 2 and 3 all had thymic hyperplasia, the signal intensity changes of their thymuses on chemical shift and fat suppression imaging were different. We suppose it is determined by their age difference. It is well known that the thymus attains its largest size at puberty and then gradually involutes and become replaced by fat.[7] A hyperplastic thymus of young patients may look like a soft tissue mass, which is difficult to distinguish from thymoma on CT and conventional MRI.[2] For example, CT attenuation of the thymus of Case 1 is 27, which is in the range of the thymoma group. Because the hyperplastic thymus in this age group is mixed with fat and water, while thymoma contains no fat, chemical shift imaging is able to reliably differentiate thymic hyperplasia from thymoma. This is consistent with the study led by Popa et al.[4] On the contrary, in older patients, aged more than 40 years, the thymus is mostly replaced by fat, so fat suppression technique is easily capable of showing its fat dominance. This phenomenon can be seen in Case 3 (Figure 2).

Age related changes of the thymus also have an impact on thymoma imaging. In young patients, the thymus is only partially replaced by fat, so the thymus tissue that surrounds thymoma will resemble soft tissue on conventional CT and MRI scanning, and makes the tumor margin and extension ambiguous. However, due to its composition of mixed fat and water, thymus tissue surrounding the tumor shows signal intensity loss on opposed-phase imaging, so chemical shift imaging will help in depicting the tumor margin and invasiveness in young patients (Cases 4, 5, and 6). In older patients, the thymus tissue has already almost completely been replaced by fat, so fat suppression technique is able to show the tumor's margin and its relationship with contiguous structures better than other MRI sequences and CT, such as Case 7. In the initial CT report of Case 7, by consensus of two experienced radiologists, the tumor was neglected.

There were two main limitations of our study. First, the sample size was small, because it was difficult to satisfy all the criteria when selecting MG patients who had undergone all the imaging studies and thymic pathologic examination. Systematic analyses of the effects of age need to be carried out in larger sample studies. Second, all of the patients only had CT scans without contrast. Considering that iodinated contrast agents might cause allergy or disease exacerbation, contrast enhanced CT scans are only done in few selected MG patients at our hospital.

Chemical shift and fat suppression MRI have remarkable advantages in differentiating thymic hyperplasia and thymoma in MG. In clinical practice and future research, attention should be paid to the age of the patients in thymus imaging. In young patients, chemical shift MRI is better than CT, conventional MRI sequences, and fat suppression in both differentiating thymus hyperplasia from thymoma, and depicting the tumor margin and its relationship with surrounding tissues in thymoma. In elderly patients, fat suppression should be preferred, especially in patients with thymoma, for it proved better than CT and other MRI sequences in our study in depicting tumor margin and its relationship with surrounding tissue. These results show promise and warrant further investigation.

Statement of Authorship

Kai Li and Da-Wei Yang contributed equally to this study.

Disclosures

The study was not funded by any grant. Hai-Bo Chen does not have anything to disclose.

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