

6 Multiple System Atrophy Update

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Multiple system atrophy (MSA) is a sporadic adult-onset neurodegenerative disease. It is characterised clinically by parkinsonism, cerebellar features and autonomic failure in varying combinations, and pathologically by the presence of neuronal loss, gliosis and α -synuclein positive oligodendroglial cytoplasmic inclusions (GCIs)^{1,2} in a selection of structures. These include supratentorially the striatum (particularly posterior putamen) and substantia nigra, infratentorially the inferior olives, pons and cerebellum, and the intermediolateral cell columns and Onuf's nucleus in the spinal cord.

Clinical Features and Diagnosis

Correct diagnosis of multiple system atrophy (MSA) is important in terms of patient management and prognosis, and for research to provide better understanding of the nature and cause of the disease, leading hopefully to better treatment or even prevention. Prior to 1989 there was really no framework of diagnostic criteria for MSA. In that year GCIs were first described¹ as a pathological hallmark of MSA regardless of whether patients were predominantly parkinsonian, and labelled as striatonigral degeneration (SND), predominantly cerebellar, and labelled as sporadic olivopontocerebellar atrophy (sOPCA), or were predominantly autonomic, and labelled as the Shy-Drager syndrome (SDS). In the same year Quinn³ suggested some preliminary diagnostic criteria, dividing cases of MSA according to their predominant motor disorder into SND-type (the majority), and OPCA-type (the minority). These criteria were subsequently slightly modified in 1994⁴ and later, in 1998, broadly similar criteria were operationalised in the Gilman et al consensus criteria,⁵ which have since been revised in 2008.^{5a} In parallel, SND- and OPCA- type MSA are now called MSA-P and MSA-C respectively.

Prior to the 2008 update, none of the previous sets of diagnostic criteria included ancillary investigations, with the exception of the inclusion of an abnormal sphincter EMG in the 1994 version of the Quinn criteria, and the use of imaging to exclude other conditions, rather than to positively diagnose MSA. The diagnosis remains largely clinical. However, in the latest set of criteria there is more scope for investigations to support a clinical diagnosis. Simpler diagnostic criteria were used in the NNIPPS study.^{15a}

Differential Diagnosis

The differential diagnosis of MSA covers a number of other conditions. The commonest diagnostic error is for patients with MSA-P to remain misdiagnosed in life as idiopathic Parkinson's disease (IPD). An autonomic presentation of MSA may be confused with pure autonomic failure (PAF), which usually has Lewy body pathology, or with some cases of PD presenting with autonomic failure. Most cases of MSA presenting with autonomic failure develop other neurological features within 5 years, but in rare cases the interval can be longer (up to 8 years in my experience). Progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) also enter into the differential diagnosis of MSA-P, as does (rarely) primary lateral sclerosis (PLS), or the PLS presentation of amyotrophic lateral sclerosis (ALS), where pyramidal slowing and spasticity together with pyramidal signs can be misinterpreted as a levodopa-unresponsive akinetic-rigid syndrome with pyramidal signs. Cerebrovascular disease may give rise to a mixed picture mimicking MSA. On the cerebellar side, about 21-33% of patients with idiopathic late onset cerebellar ataxia (ILOCA) will ultimately turn out to have MSA.⁶⁻⁸ Sometimes late onset atypical Friedreich's ataxia may be misdiagnosed as MSA-C, as may SCAs 2 and 3⁷, which may present with a combination of cerebellar and parkinsonian features, the latter sometimes levodopa-responsive,^{9,10} but one would expect a positive family history. Later onset cases of a pure cerebellar syndrome due to the SCA 6 mutation may lack an obvious family history.⁷ Occasional patients with primary progressive multiple sclerosis, may also cause confusion, as can subjects with fragile X tremor ataxia syndrome (FXTAS).^{7a} A large study^{7b} found premutations in 4 of 626 cases of clinical MSA. Most of the remaining cases of ILOCA, or sporadic adult onset

ataxia (SAOA), probably have sporadic cerebellar-olivary atrophy (see excellent recent review by Klockgether).^{7c}

It is more common for patients with MSA to die with another diagnosis (most commonly IPD, in anything up to 55% of cases), than for patients dying with a clinical diagnosis of MSA to have a different disease at autopsy (one recent study¹¹ found a false positive rate of 14%, again the commonest cause being IPD).

Exclusion Criteria

Before considering positive diagnostic pointers, it is worth considering the exclusion criteria that are usually applied. There has never been a pathologically proven case of MSA starting before age 30. The incidence rises thereafter, appearing to peak in the late 50's, and to decline thereafter. A marked frontal lobe picture, or frank dementia, can rarely be seen in MSA, sometimes due to superadded Alzheimer change, but is so uncommon in MSA, and so common in progressive supranuclear palsy (PSP) and in patients with Lewy body disease with cortical involvement, that dementia is usually considered an exclusion criterion (even though some patients with pathologically proven MSA may develop marked cortical atrophy on imaging,¹² but again this is unusual). To date, there has not been a single instance of familial MSA with pathological proof of diagnosis in more than one individual, apart from a pathological paper containing 2 first cousins. Therefore, although a relative with typical Parkinson's disease would be acceptable by chance, the presence of atypical parkinsonism in a first degree relative should still cast doubt on a diagnosis of MSA. No causative mutations in the alpha-synuclein (SNCA) gene have been isolated, but recently two groups^{12a,b} have identified single nucleotide polymorphisms (SNPs) at the SNCA locus associated with increased risk of developing MSA. Because PSP and corticobasal degeneration (CBD), as poorly levodopa-responsive causes of atypical parkinsonism, enter into the differential diagnosis, and have characteristic eye movement disorders, certain oculomotor features should exclude the diagnosis of MSA. Eye movement abnormalities that are acceptable include excessive square wave jerks, mild to moderate hypometria of saccades (but with normal velocity, and latency to onset), spontaneous nystagmus or positioning downbeat nystagmus^{12c}. Definitely slow saccades would suggest PSP or SCA 2, limitation of downward gaze PSP or, less likely, CBD, and difficulty with initiating saccades, with delayed latency to onset, would suggest CBD.

In most case series, cases of MSA-P outnumber MSA-C by between 2 and 4 to 1. Cerebellar clinics, not surprisingly, have a preponderance of MSA-C cases, which also seem to predominate generally in Japan¹³ as opposed to other countries.

“Core” Diagnostic Features

The overall theme in terms of major diagnostic criteria is that MSA-P cases present with parkinsonism that is usually non- or poorly-levodopa responsive (although up to 30% may have a good response at some stage,¹⁴ usually waning thereafter), with additional features of cardiovascular autonomic or urogenital dysfunction, with or without cerebellar features or pyramidal signs. Along the cerebellar route, the main requirement is to have an ILOCA syndrome with additional cardiovascular autonomic or urogenital disturbance, with or without pyramidal signs or parkinsonism. However, particularly early in the disease, the cardinal core diagnostic criteria may not be fulfilled. In such cases, although current diagnostic criteria do not include them, certain clinical “red flags” may, especially when multiple, point strongly to the diagnosis.

Clinical “Red Flags”

Two thirds of MSA patients have a tremor of the upper extremities. In contrast to IPD, this is only rarely (less than 10% of cases) of a classical pill-rolling nature.¹⁴ Instead it is usually an irregular jerky postural and action tremor, and close inspection may reveal that the jerkiness is due to myoclonic jerks (polyminimyoclonus), which are sometimes touch- or stretch- sensitive,¹⁵ and not seen in uncomplicated IPD, or in PSP, but are seen in CBD. A marked tremor, the presence of titubation, or slow progression, should raise the possibility of FXTAS.

Rapid disease progression with early instability and falls are common to MSA, PSP and CBD relative to IPD. However, falls as a presenting feature, or within the first year of the disease, would be more in favour of PSP than MSA.^{15a}

Otherwise unexplained cardiovascular autonomic failure occurs commonly in MSA, invariably in PAF, and in a minority of patients with IPD. It is uncommon in PSP or CBD. Urinary frequency and urgency are common in IPD and PSP as well as in MSA. However, incontinence not due to severe motor slowing, and incomplete bladder emptying, would not be expected in IPD, but occur in most patients with MSA¹⁶ and a substantial minority of those with PSP. Male erectile dysfunction is virtually universal and early in patients with MSA, who are also relatively young, but can be more difficult to interpret in older patients with PSP and IPD. A majority of MSA patients also display abnormalities of the microcirculation with cold, dusky, violaceous extremities¹⁷ which blanch on pressure, with poor circulatory return. Peripheral oedema not accounted for by drugs is relatively common in MSA, as is Raynaud's phenomenon,¹⁸ which may be particularly provoked by ergoline agonists.

Abnormalities of sleep and breathing are common in MSA. At least two thirds of patients have rapid eye movement (REM) sleep behaviour disorder (RBD),¹⁹ in which the usual limb atony in REM sleep is lost, so that patients act out frightening dreams which they may recall if woken. They may talk or shout in their sleep, strike out at their bed partner, and even fall out of bed. This is commonly a very early, if not the earliest, symptom and, curiously, usually improves as the disease progresses. It is not specific to MSA, and can be seen in a third or more of patients with IPD, and may be a feature common to alpha synucleinopathies,²⁰ as it appears to be relatively uncommon in PSP. Patients with MSA may also experience nocturnal or diurnal stridor, worsening or new onset of severe snoring, and involuntary inspiratory sighs or gasps during the day, all of which are uncommon in IPD, PSP and CBD.

The speech of patients with MSA may be almost diagnostic. Patients with MSA-P, in addition to the hypophonic monotony of parkinsonian speech, usually have an increase in pitch, and a quivery croaky strained element to their speech, with sometimes an element reminiscent of myoclonic speech. On the other hand, patients with MSA-C may have a more typical slurring cerebellar dysarthria. In contrast, patients with PSP usually have a lower pitched, growling dysarthria that terminates in groaning noises in the advanced stages. Significant dysphagia is a prominent feature of both MSA and PSP, more so in the latter, and an uncommon and late feature in IPD.

The new development of emotional incontinence with weeping or, less commonly, laughing, when moved by an event, or music, or something on the television, is very common in PSP but also common in MSA, whereas it is uncommon in IPD.

Over time, most patients with IPD develop typical mobile dystonic or choreo-dystonic movements of the extremities on chronic levodopa treatment. In contrast, patients with MSA frequently have more sustained dystonic dyskinesias, sometimes unilateral, often involving the face and neck,²¹ sometimes mimicking a 'risus sardonius',²² and patients with PSP may have levodopa-induced oromandibular dystonia. Dystonia is also common in untreated MSA patients.^{21,22} Other postural abnormalities that are more common in MSA relative to other parkinsonian disorders are disproportionate antecollis, camptocormia, and lateral deviation of the trunk ("Pisa syndrome").²³ Contractures of the extremities are very common in CBD, relatively common in MSA, and uncommon in PSP and IPD.

If there is any suspicion of atypical parkinsonism (and one should always be suspicious of the diagnosis, not only that made by others but also continually reviewing one's own diagnosis), all of the above should be enquired about. To an astute clinician multiple clinical "red flags" can indicate a diagnosis of MSA with a high probability even if full core criteria are not satisfied. A recent study^{23a} comparing "red flags" between IPD and MSA-P cases looked at 6 categories: early instability, rapid progression, abnormal postures, bulbar dysfunction, respiratory dysfunction and emotional incontinence and found that when 2 or more were positive the specificity for predicting probable MSA was 98% and the sensitivity 84%.

Investigations

Many different investigations have been explored in MSA, but they are only beginning to feature in accepted diagnostic criteria. The utility of the various investigations depends on the question that is being asked. In patients with predominant parkinsonism, the most common diagnostic question that investigations are called upon to resolve are:

- Does the patient have IPD or not?
- If it is clear that the patient does not have IPD, do they have PSP or do they have MSA?

Some investigations can help answer question 1 but not 2, and others vice versa. In the examples given below, a notation such as IPD versus MSA signifies that the technique has some ability to discriminate between IPD and MSA. IPD versus MSA/PSP indicates that the technique can help differentiate between IPD and [MSA/PSP], but not necessarily between MSA and PSP.

For patients with a cerebellar presentation, the main question, after excluding known genetic causes, or secondary causes of a sporadic presentation, is whether the patient has ILOCA that will not turn out to be MSA-C, or whether the patient has, or will turn out to have, MSA-C.

The most useful investigation in routine clinical practice is probably standard MRI. In selected centres, cardiac MIBG SPECT scanning and sphincter EMG can also be helpful.

Structural Brain Imaging

MRI

Routine 1.5 Tesla MRI may demonstrate a linear hyperintense rim at the lateral border of the putamen, putaminal atrophy or, on T₂-weighted images, posterior putaminal hypointensity relative to globus pallidus.^{24,25} The most helpful of these is the first. Specificity is good, relative to IPD and to PSP, but sensitivity is low. However this can be improved (for IPD versus MSA-P) by using thin (3 mm thick) sections.²⁶ Infratentorially one may see cerebellar atrophy, atrophy and a “hot cross bun” appearance in the pons (not specific to MSA), and hyperintensity of the middle cerebellar peduncles (also seen in many cases of FXTAS).

Other MR methods that have so far only been applied in research settings are magnetisation transfer imaging²⁷ (MTI—MSA versus controls), diffusion weighted imaging (DWI—MSA versus IPD²⁸, but not MSA versus PSP),²⁹ and T₂* weighted MRI³⁰ (MSA versus IPD). 3-dimensional MRI-based volumetry can often discriminate between IPD and MSA/PSP (but not necessarily between MSA-P and PSP),³¹ and shows more pronounced brainstem atrophy in MSA-C versus ILOCA patients.³² Voxel-based morphometry can detect cortical and basal ganglia (versus IPD)³³ atrophy in MSA-P and intratentorial abnormalities in MSA-C (versus controls).³⁴ Fluid-registered MRI is also being used to better delineate the sites and progression of atrophy in MSA.³⁵ Recent diffusion tensor imaging (DTI) and tractography (DTT) studies have elegantly shown atrophy of middle cerebellar peduncles in MSA as opposed to atrophy of superior cerebellar peduncles in PSP.^{35a} Brooks and Seppi^{35b} have recently published a review of neuroimaging in the diagnosis of MSA, and Hotter et al^{35c} a review of MR imaging in the differential diagnosis of parkinsonism.

Transcranial Sonography

There are recent claims that transcranial sonography, or brain parenchyma sonography (BPS), shows abnormalities in substantia nigra in IPD that are not detected by MRI,³⁶ and also that the nigral signal may distinguish IPD from MSA/PSP,³⁷ but these need replication.

MR Spectroscopy (MRS)

MRS may show reduced N-acetyl aspartate (NAA) concentrations relative to choline or creatine in lentiform nucleus in parkinsonian disorders. However, so far the heterogeneity of results precludes its use to differentiate between PD, MSA and PSP.³⁸

Functional Brain Imaging (PET/SPECT)

Facilities for functional imaging studies are less widely available, although SPECT is more accessible than PET. ¹⁸F-dopa PET scans cannot reliably differentiate between IPD and PSP/MSA,³⁹ nor, not

surprisingly, can dopamine transporter SPECT scans (“DaT scans”).⁴⁰ IBZM-SPECT demonstration of reduced D2 receptor binding in striatum has some usefulness in de novo (L-dopa-naïve) patients. Generally, reduced binding is a reasonable predictor of subsequent poor responsiveness to L-dopa treatment, with many of these subjects also developing additional features incompatible with IPD.⁴¹ However, it does not distinguish between MSA-P and PSP. Moreover, it is less useful in patients already on chronic L-dopa treatment, since this down-regulates post-synaptic striatal D2 receptors, and therefore diminishes the difference between IPD and MSA/PSP cases.

One study has shown impaired striatal ¹¹C-diprenorphine binding in MSA versus IPD.⁴²

¹⁸F-deoxyglucose (FDG) PET scans are probably the most useful brain functional imaging modality for differentiating between IPD, MSA and PSP.⁴³

“Autonomic” Investigations

The principal “autonomic” symptoms in MSA are cardiovascular and urogenital, although strictly speaking most of the latter symptoms are not “autonomic” in origin.

Cardiovascular

Clinical tests The single most important cardiovascular symptom/sign in MSA is postural faintness/orthostatic hypotension (OH). The single most useful measure is an otherwise unexplained drop in systolic blood pressure by ≥ 20 or 30 mmHg, depending on criteria used, in systolic BP three minutes after assuming the erect position.⁵ Unfortunately, dopaminergic drugs can cause OH, which makes results difficult to interpret. OH is a feature of both IPD and MSA, although usually later, and less common, in the former. The presence of OH or the demonstration of more widespread abnormalities on a battery of cardiovascular autonomic function tests can tell you that a patient has autonomic failure, but not whether this is due to IPD or MSA-P.⁴⁴ However, they may help to distinguish between MSA-P and PSP. They may be more useful in cerebellar patients, since cardiovascular autonomic failure is common in MSA-C, but rare in ILOCA and inherited SCAs.

Functional cardiac imaging The origin of the sympathetic autonomic deficits in IPD (or other forms of Lewy body disease) is principally post-synaptic, due to pathology in the sympathetic autonomic ganglia, whereas in MSA it is pre-synaptic. Cardiac ¹³¹I-MIBG SPECT or 6-[¹⁸F]-fluorodopamine PET^{45,46} scans can differentiate between pre- and post-synaptic sympathetic denervation. In MSA, the post-synaptic element is usually (but not always, especially in advanced cases) intact, giving normal results. In PAF, and in IPD with AF, there is impaired uptake of tracer over the heart. Some IPD patients without AF have normal, and most have abnormal, scans. This technique may also help differentiate between patients with Alzheimer’s disease (AD) and patients with dementia with Lewy bodies (DLB).⁴⁷ MIBG SPECT or F-dopamine PET may well emerge as one of the most useful investigations to distinguish between post-ganglionic (= Lewy body) and pre-ganglionic (= MSA) sympathetic autonomic failure. Results are typically normal in PSP.

Urogenital

Onuf’s nucleus in the sacral spinal cord is a specialised group of anterior horn cells supplying the nerves to the striated external anal and urethral sphincters. It is involved pathologically in both MSA and PSP, and sometimes in PD. As with somatic anterior horn cell dropout elsewhere, for example in ALS, sprouting occurs to re-innervate denervated muscle fibres, resulting in combinations of increased voltage, increased duration and polyphasia of motor unit potentials. **Sphincter EMG** must be undertaken by an expert, since there are many pitfalls. Technically, automated EMG machines may miss delayed “satellite” potentials. The interpretation of the result is also crucial.^{48,49} Multiple or traumatic childbirth, lower abdominal surgery, including retropubic (but not trans-urethral) prostatectomy, haemorrhoidectomy, and chronic constipation⁵⁰ may all produce an abnormal urethral or anal sphincter result. A recent retrospective study in pathologically proven cases⁵¹ indicates that abnormal results are not diagnostically useful, since they can be seen in many cases of PD as well as in almost all cases of MSA. However, a normal result would make MSA very unlikely. The test cannot distinguish between MSA-P and PSP.⁵² It might help differentiate between ILOCA and MSA-C, but this has not yet been established.

Other Investigations

Growth Hormone (GH) Response to Clonidine Infusion.

The normal GH response to clonidine infusion is typically lost in patients with MSA-P and MSA-C.⁵³ However, it is also lost in a proportion of patients with IPD.⁵⁴ Therefore, in a parkinsonian patient, it may only be useful when it is normal, which makes MSA unlikely. This response has not been studied in PSP. A more reliable test seems to be the arginine GH stimulation test, which can apparently distinguish between MSA-P and both IPD and PSP.^{54a}

Polysomnography

REM sleep behaviour disorder (RBD) appears to be a “marker” for α -synucleinopathies (IPD, DLB, MSA), in contrast to tauopathies (PSP, CBD) and amyloidopathies (AD). A good clinical history is suggestive, but definite confirmation can be given by polysomnography (PSG) which, in selected cases, may be helpful.²⁰

Sleep apnoea is common in MSA, less so in IPD and PSP. Documentation of sleep apnoea may therefore be helpful in the differential diagnosis (and management) of MSA patients.

Sweating

Hyper- and hypo-hydrosis occur, and have been investigated, in both IPD and MSA. Quantitative sudomotor tests may show group differences between IPD and MSA patients, but may not be significantly robust to prove whether a given abnormality in an individual subject is due to IPD or MSA.

Conclusions on Investigations

No single investigation is diagnostic. Combinations of investigations⁵⁵⁻⁶ may be more helpful than the results of a single “test”. Moreover, some of these investigations are only available in specialised centres, and for many of them their ability to differentiate between MSA and, particularly, PSP and IPD, has only been studied in relatively advanced cases with clinically established diagnoses. For many of them, their predictive utility early in the disease process remains to be established. They must be used intelligently, according to what question the clinician is trying to answer. Moreover, they are often expensive – the (relatively cheap) skills of an informed clinician are still more important than spending a large amount of money on, for example, a dopamine transporter SPECT scan that will not answer the question being asked.

Treatment

Currently, not only is there no treatment known to influence the underlying disease course, but also the efficacy of symptomatic treatments of MSA is limited. Patients’ clinical state will therefore continue to progressively worsen, with steadily increasing disability and handicap, leading ultimately to premature death, most commonly from bronchopneumonia. Against this background, an honest, sympathetic and supportive approach by a healthcare team knowledgeable about the condition is the cornerstone of management. Nevertheless, there are many other ways in which patients can be helped, usually on a symptom-by-symptom basis.

Although the **parkinsonism** of MSA is typically non- or poorly-levodopa responsive, even a poor response is better than none. Moreover, a significant minority (up to 30%) show at some stage a good, and a few an excellent, motor response to L-dopa, but this usually wanes as the disease progresses. Dosage may be limited by unmasking or worsening of OH, or alternatively by unpleasant dystonic spasms of the face or neck. Some of these patients may better tolerate a dopamine agonist (with domperidone). A minority, perhaps 1 in 5, will also derive useful benefit from amantadine; I usually give a six-week trial up to 100 mg tds, continuing it only in responders.

The few patients treated with pallidotomy have not shown significant benefit. STN DBS can worsen some features,⁵⁷ but may have a useful effect if the patient has a good response to L-dopa,⁵⁸ although it will not improve on the patient’s best L-dopa response. Foetal nigral grafting in one patient misdiagnosed as IPD was, not surprisingly, unhelpful.⁵⁹ Apparent benefit has been reported after injection of autologous mesenchymal stem cells into carotid and vertebral arteries followed by

repeated intravenous infusions of further cells,^{59a} but whether the apparent benefit resulted from the injected cells themselves is open to question.^{59b}

No drugs help the **cerebellar syndrome**.

Urinary urgency and nocturia can be helped by peripherally acting anticholinergics such as oxybutynin, but these can precipitate retention of urine, especially in patients with incomplete bladder emptying. Desmopressin at bedtime can reduce nocturia. A post-micturition residual volume of ≥ 100 ml is usually an indication for intermittent self- or carer-catheterisation, but some patients may require pads, a convener, or indwelling urethral or retropubic catheterisation. Male erectile dysfunction responds to sildenafil in both IPD and (less effectively) MSA, but in the latter the risk of symptomatic OH is greater.⁶⁰ Intra-cavernosal alprostadil (prostaglandin E1) injections are an alternative.

Orthostatic hypotension only needs treatment if it is symptomatic. Simple measures should be used first – high-salt diet, elastic support stockings, head-up tilt of the bed at night, and simple advice about standing up gradually, and getting the head down level with the heart if the patient feels faint, will suffice in many patients. A minority may need the addition of fludrocortisone, midodrine,⁶¹ or L-threo-DOPS.⁶²

Depression or emotional incontinence can often be helped by either a tricyclic or a selective serotonin reuptake inhibitor (SSRI).

RBD may respond to a small dose of clonazepam. Significant sleep apnoea and respiratory stridor should be managed in the first instance with continuous positive airway pressure (CPAP),⁶³ reserving cord lateralisation or tracheostomy for patients who do not respond.

Disease-related **dystonia** or contractures may be helped, or prevented from worsening, by local injections of botulinum toxin. Unfortunately, this usually does not help disproportionate antecollis, in which it may also worsen already impaired speech and swallowing function.

Spasticity rarely needs treatment in its own right, but if marked it is sometimes helped by baclofen. Similarly, **myoclonus** is seldom severe enough to merit treatment, but is sometimes helped by clonazepam or valproate.

Experimental controlled trials of riluzole,^{15a} synthetic human growth hormone, and minocycline have not shown significant benefits.

Allied health professionals have a critical role in relieving symptoms and improving patient quality of life in MSA. Physiotherapists aid mobility and can educate the patient in safe turning and transfers, reducing the risk of falls. Occupational therapists can modify the home environment, and an expert wheelchair assessment and provision of a suitable model should be considered before there is significant danger of falling and fracturing long bones. Speech and swallowing therapists can give advice on speech, swallowing and diet, and breathing. A video fluoroscopic swallow may reveal silent aspiration. Communication aids or a gastrostomy may be required. Finally, the palliative care movement has now extended its remit beyond cancer and ALS to patients with other progressive neurological disorders, and can offer valuable domiciliary, respite and terminal care for patients with MSA.

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