Radiology Case Reports 18 (2023) 1121–1126

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Multiple system atrophy-cerebellar: A case report and literature review ☆,☆☆

Thi Thuong Doan, MD[a], *Thuy Dung Pham, MD*[a], *Duy Duan Nguyen, MD*[b], *Dac Hong An Ngo, MD*[a,*], *Trong Binh Le, MD, PhD*[a], *Thanh Thao Nguyen, MD, PhD*[a]

[a] *Department of Radiology, University of Medicine and Pharmacy, Hue University, 06 Ngo Quyen str., 530000 Hue city, Vietnam*

[b] *Department of Internal Medicine, University of Medicine and Pharmacy, Hue University, Hue, Vietnam*

ARTICLE INFO

Article history:
Received 17 November 2022
Accepted 21 December 2022

Keywords:
Multiple system atrophy
Neuroradiology
MRI

ABSTRACT

We reported a case of a 48-year-old female patient admitted to the hospital due to balance disorder which progressed rapidly within 1 week. Cerebral magnetic resonance imaging showed significant atrophy and hyperintensities at the middle cerebellar peduncles and the "hot cross bun" sign of the pons. The final diagnosis was probable multiple system atrophy, cerebellar subtype. The clinical and imaging findings will be discussed as well as a brief literature review.

Introduction

Multiple system atrophy (MSA) is an uncommon progressive neurodegenerative disorder that usually affects adults and is more predominance in men with male-to-female ratio of 1.3:1 [1,2]. Due to its rareness with an annual incidence of 0.1-3.0 per 100,000, depending on age and geographic region [3,4], MSA is usually missed on clinical examination. The exact cause of MSA is still unclear. Many recent studies suggested relations to the pathogenesis of MSA, including the abnormal deposition of protein α-synuclein (αSyn) in the glial cytoplasmic [5–7].

The onset of MSA usually occurs in older adults in their 50s and 60s [8]. MSA is described as progressive decay of nervous systems including cerebellar, autonomic systems, pyramidal, and extrapyramidal tracts [9]. MSA is defined by specific clinical findings such as a Babinski sign with hyperreflexia, resting and postural tremors, speech disorder, poor response to levodopa, rapid progression rate, and ataxia or characteristic neuroimaging abnormalities based on magnetic resonance imaging (MRI) [10].

Based on the consensus of diagnosis criteria, patients with MSA are clinically classified into 2 main variations: cerebellar (MSA-C) with olivopontocerebellar atrophy and predominant cerebellar features; parkinsonian (MSA-P) with striatonigral degeneration features [11]. MSA-P is more common and characterized by the following features: rigidity, bradykinesia, tremors, posture, and balance disorders [12]. MSA-C patients usually show impaired movement and coordination, slurred

☆ Funding: This work was supported by Hue University under the Core Research Program, grant no. NCM.DHH.2020.09.
☆☆ Competing Interests: The authors report no conflicts of interest in this work.
* Corresponding author.
E-mail address: ngodachongan@hueuni.edu.vn (D.H.A. Ngo).
https://doi.org/10.1016/j.radcr.2022.12.046

language, impaired vision, and swallowing or chewing difficulty [12]. Regardless of their differences, MSA-P and MSA-C have overlapped signs such as urinary incompetence, erectile dysfunction, orthostatic hypotension, and mental disorders [12].

Abnormalities on conventional 1.5 T MRI in patients with MSA may include atrophy of the lower brainstem, middle cerebellar peduncles (MCPs), cerebellum, and pons [13]. Hyperintensities may be seen in the above-implicated areas, commonly referred to as the "hot cross bun sign" when visualized in the pons [13]. Putaminal atrophy findings in MSA-P, T2 putaminal hyperintensity, and abnormally high T2 linear rim surrounding the putamen (putaminal rim sign) are other MRI findings [13].

The disease progresses quickly and deteriorates first. Patients with MSA usually become unable to walk within 5 years and die within 10 years of disease onset [14]. At present, no successful treatment was yet reported for MSA, but various evidence-based therapies can help improve quality of life while reducing the impact of the severe symptoms [15–17].

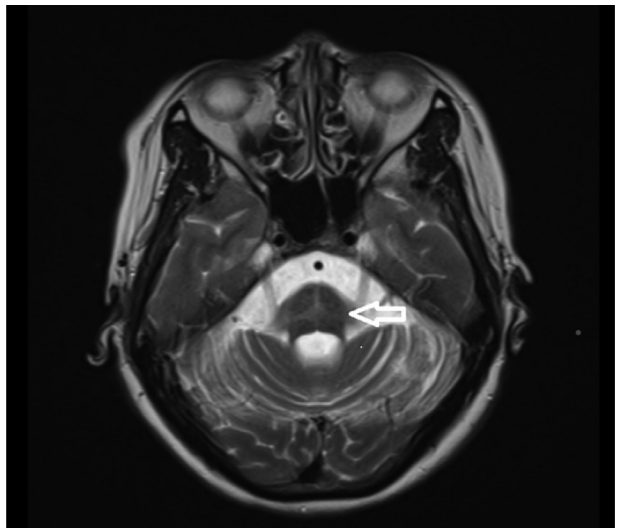

Fig. 1 – Axial T2-weighted images showed "hot cross bun" sign of the pon (arrows).

Case report

A 48-year-old female admitted to our hospital because of balance disorder and walking difficulty due to dizziness. Starting one year previously, she experienced gait ataxia with cerebellar dysarthria and orthostatic dizziness. Later, she developed dyskinesia, walked unsteadily, and might also have difficulty with coordination. Besides, she spoke with a lisp. The patient complained about sloppy handwriting. She didn't have urinary disturbances and residual urine sense. Those mentioned symptoms recurred and became worse 1 week ago. She didn't recall any difficulty in swallowing, no visual disturbances, and no constipation. There was no history of sleep disturbances, dementia, or cognitive impairment.

At the time of admission, her vital signs were within normal limits. Routine workups including chest X-ray, and cardiac and abdominal sonography were normal. Romberg sign was positive and fell in various directions. The finger-to-nose test was positive. There was no sign of resting or postural tremors, rigidity, or bradykinesia. All the modalities of sensation were normal. Deep tendon reflexes were normal in all extremities. Muscle strength was at grade V. Hoffman and Babinski signs were negative. Tests for nystagmus revealed no limitation of ocular movements or abnormalities.

The tilt table test revealed orthostatic hypotension 3 minutes after standing (dropped from 145/80 mmHg in recumbent position to 115/70 mmHg in standing position). The standing and lying blood pressures differed by 30/10 mmHg. Cerebrospinal fluid biomarkers were normal.

She had a healthy living style without use of tobacco or alcohol, and denied any history of genetic diseases or progressive neurological disorders, or similar diseases in her family or relatives.

The follow-up brain MRI showed several abnormalities including the "hot cross bun" sign, a cruciform hypointensity in the pons that resembles the Easter pastry (Fig. 1); symmetric atrophy, and hyperintensities of MCPs (Fig. 2). There were no relevant abnormalities in the basal ganglia (Fig. 3); no abnormalities on brain magnetic resonance angiography by time-of-flight sequence (Fig. 4) and no abnormal diffusion restriction.

Discussion

Multiple system atrophy is a progressive neurodegenerative disease, which typically occurs in male adults at their 30s [11]. Clinical appearance of MSA comprised of various neurological signs and symptoms of cerebellar impairment, autonomic nervous system dysfunction, and dopa-low-reaction Parkinson-like symptoms [18].

Although MSA is reportedly a sporadic disease, Tsuji et al. suggested an association of the COQ2 gene impaired variants with an increased risk of MSA [19]. A meta-analysis reported that the COQ2 V393A gene variant was associated with an increased risk of MSA in East Asian patients [20]. Thus, the hypothesis of a genetic contribution to MSA has been put forward.

Regarding the neuropathological aspect, MSA is defined by the existence of α-synuclein-containing inclusions, especially in the cytoplasm of oligodendrocytes (glial cytoplasmic inclusions), which are observed in motor systems, the supraspinal autonomic sections, the pallidum, the putamen, and the lateral part of caudate nucleus. Therefore, MSA is classified as one of 3 main types of α-synucleinopathy. Oligodendrocytic α-synuclein inclusions are associated with neuronal death in MSA; however, these mechanisms are not fully known. The neurodegeneration in MSA presumably contains the cell-to-cell transmission of α-synuclein in a prion-like manner, α-synuclein accumulation, decreased expression of neurotrophic factors, excitotoxicity, and microglial activation, increased oxidative stress, neuroinflammation, and abnormal expression of tubulin proteins [21,22].

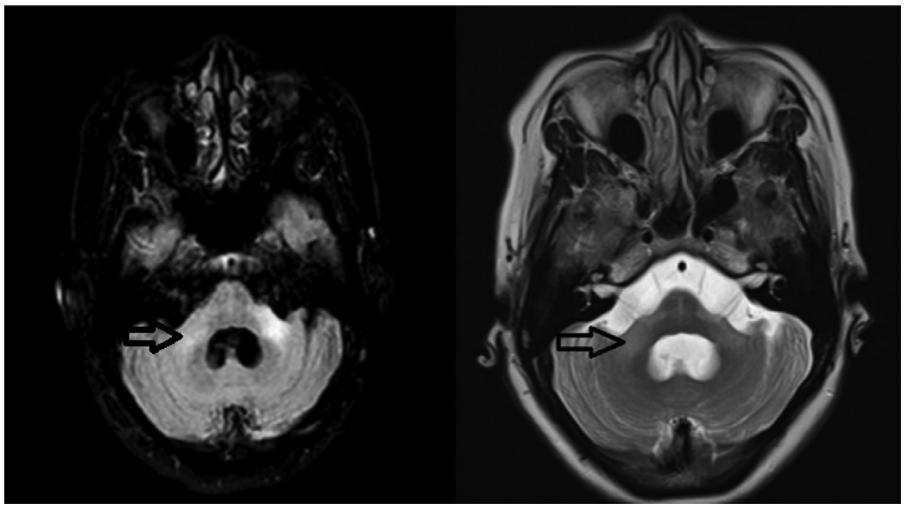

Fig. 2 – Axial FLAIR (left) and T2-weighted images (right) showed symmetric atrophy of middle cerebellar peduncles with hyperintensities (arrows).

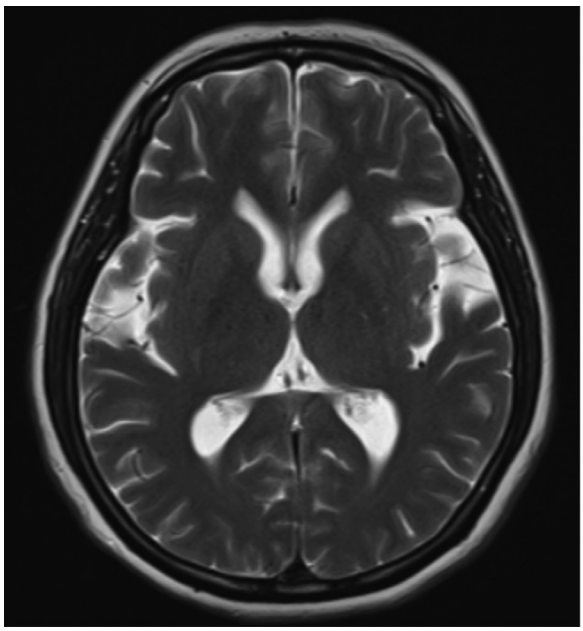

Fig. 3 – Axial T2-weighted image showed no abnormalities in the basal ganglia.

MSA is divided into 2 subtypes based on the main symptom: MSA-C with predominant cerebellar dysfunction and MSA-P with predominant parkinsonism [23]. According to the second consensus criteria for the diagnosis of MSA in 2008, MSA had 3 clinical diagnoses: "definite MSA," "probable MSA," and "possible MSA." A definite MSA diagnosis can only be reached with autopsy confirmation by widespread and abundant cerebral α - synuclein- positive glial cytoplasmic inclusions and neurodegenerative changes in the olivopontocerebellar or striatonigral region. A probable MSA diagnosis is considered when autonomic nervous system dysfunction is combined with a poor levodopa-responsive parkinsonian syndrome (MSA-P) and/or cerebellar ataxia (MSA-C). A possible MSA diagnosis is defined when autonomic dysfunction is accompanied by sporadic adult-onset parkinsonism (MSA-P), or cerebellar ataxia (MSA-C) and at least one of the features on the red flag list [11,24].

In this case, the patient started the disease with symptoms of cerebellar disorders such as loss of balance, titubation, orthostatic dizziness, gait ataxia, coordination disturbance, sloppy handwriting, and Romberg (+), finger-to-nose test (+). Symptoms showed gradual increase. The difference between her standing and prone blood pressure is 30/10 mmHg, showing orthostatic hypotension. It suggested autonomic nervous system dysfunction. She had no symptoms of Parkinsonism. MRI showed atrophy of MCPs, abnormal signal intensities within the pons, and cerebellar peduncles with classic "hot-cross-bun" sign in the pons. Patient's onset is predominant cerebellar dysfunction and autonomic dysfunction. In addition, the patient's MRI images are typical for MSA-C. According to the second consensus statement on the diagnosis of MSA, a probable diagnosis of MSA-C was reached.

The progression of MSA-C patients is usually rapid. Patients are often confined to a wheelchair after 5 years, with an average survival of 6-9 years [11,24].

In MSA-C, there is cerebellar and brainstem atrophy (particularly the MCP and pons) (sensitivity 100%, specificity 82% for brainstem atrophy) [25]. The "hot cross-bun" sign appears as a hyperintense cross in the pons on axial T2-weighted and FLAIR imaging, representing selective degeneration of median pontine raphe nuclei and pontocerebellar fibers. Although the specificity of this sign in MSA-C is high (97%), the sensitivity is only 50% [26]. In addition, MCP degeneration is demonstrated by atrophy and hyperintensity MCP on T2W and FLAIR, which contains the frontocerebellar tracts (connecting to orbitofrontal and dorsolateral prefrontal cortex [27]. This sign is, however, not specific for MSA.

Idiopathic Late-Onset Cerebellar Ataxia (ILOCA) is a slowly progressive, adult-onset ataxia and includes ataxia and urinary dysfunction, abnormal reflexes, and dementia. Currently,

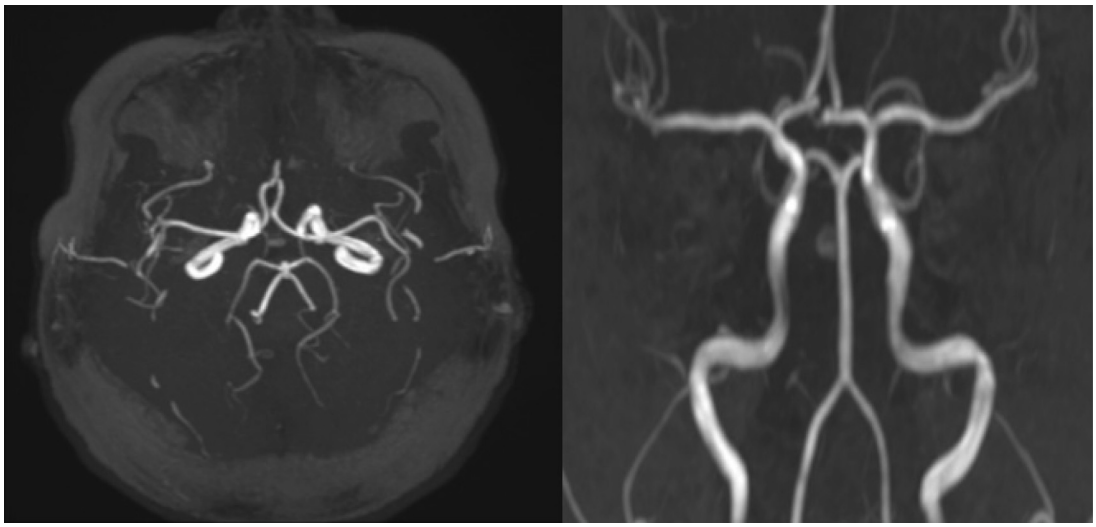

Fig. 4 – Maximum intensity projection (MIP) reconstruction in axial (left) and coronal (right) planes of time-of-flight (TOF) sequence of cerebral arteries showed no abnormalities.

ILOCA is considered to include spinocerebellar ataxias (SCAs), MSA-C, fragile X-associated tremor ataxia syndrome, and autosomal recessive cerebellar ataxia type 1, Friedreich's ataxia, and other genetic disorders. Therefore, it is important to differentiate between MSA-C patients presenting with isolated cerebellar disorders and those with other causes of ILOCA [28]. SCAs are a group of autosomal dominant genetic disorders that are often described by progressive neurodegeneration of the cerebellum and its efferent and afferent connections. A family history of cerebellar ataxia often supports the diagnosis of SCA [29,30]. The "hot cross bun" sign can be seen in MSA-C, SCA 2, SCA 3, SCA 7, and SCA 8 [28,31]. But the diagnosis of MSA may be strongly supported by an early "hot cross-bun" sign [10]. In general, the MSA's progression rate is significantly more rapid than SCAs [32]. Proton Magnetic Resonance Spectroscopy also contributes to the differential diagnosis of MSA-C and SCAs. Jiing et al. demonstrated that subtle differences between MSA-C and subtypes of SCAs could be observed by using Cho/Cr, NAA/Cr and NAA/Cho attained from a 1.5 T MRI [33].

The autonomic disorder is commonly observed in all α-synucleinopathies. MSA should be differentiated from other neurodegenerative diseases that are also classified as α-synucleinopathies such as Parkinson's disease (PD), dementia with Lewy bodies (DLB), and pure autonomic failure (PAF) [10]. Some other diseases with similar clinical symptoms of MSA should also be differentiated such as corticobasal degeneration (CBD), and progressive supranuclear palsy (PSP). Putaminal atrophy is the most characteristic sign of MSA-P [34]. Atrophy and abnormal signals of putaminal, pontine atrophy, cerebellar vermian atrophy, and fourth ventricle dilatation in MSA were more pronounced than in other parkinsonian syndromes and PD. In both CBD and PSP, there might be prominent putaminal atrophy, third ventricle dilatation, and midbrain atrophy [35]. Yekhlef et al. demonstrated that cortical atrophy was significantly more serious in CBD than in MSA [35]. The existence of MCP hyperintensity has a sensitivity of 85% and specificity of 100% when compared with PD, and PSP [36]. The "hummingbird" sign helps to distinguish MSA from PSP [37]. This sign is not present in our patient.

The presence of hyperintense rim to the putamen sign on T2-weighted imaging has the highest specificity (90%) for MSA-P, but the sensitivity is only 72% [38]. Hyperintense putaminal rim sign is only seen at 1.5 T (this is normal at 3 T) [39]. It has been associated with the augmentation of the intertissued space between the putamen and the external capsule. This sign is related to tissue rarefaction with neuronal loss and gliosis [40,41]. A study by Nicoletti showed that MCP width <8 mm on sagittal section had 100% sensitivity and specificity in differentiating MSA from PD patients [42]. One study showed that the parkinsonism index MR [= pontine region/midbrain region) * (MCP / SCP)] distinguishes MSA-P from PSP and PD with high sensitivity and specificity [43].

On DWI, the putaminal diffusivity is raised in MSA-P compared to PD, even in the early stages of the disease. It is one of the most hopeful DWI markers for MSA [44]. DWI also contributes to the differential diagnosis of MSA-P and PSP. In MSA-P, the presence of increased ADC values of MCP and pons had a sensitivity of 91% and specificity of 84% compared with PSP [45]. SWI studies have demonstrated iron deposition in the pallidum and putamen of MSA-P is much higher compared to PD and PSP [46,47]. Meijer et al. performed a study that divided the putamen into 4 regions and suggested that the lower inner part is the best marker to differentiate between MSA-P and PD [48]. In addition, 123I-meta-iodobenzylguanidine cardiac scintigraphy may assist in differentiating MSA from PD, DLB, and PAF [49,50].

The therapeutic option is mostly symptomatic treatment. L-dopa is effective in treating parkinsonism symptoms in nearly one-third of MSA patients, whereas physical therapy is the best treatment option for MSA-C. Symptom management in MSA should target factors that impair the patient's quality of life, such as impaired self-control, motor impairment, and depression [51]. The treatment of urinary disorders and OH

has reached consensus, while strategies for dysarthria, dystonia, or depression have not yet been standardized. Treatment of MSA with recombinant human growth hormone, autologous mesenchymal stem cells, and intravenous immunoglobulins should be further investigated in the future [17].

Conclusion

We reported an uncommon case of MSA-C of a 48-year-old female patient with typical clinical and MRI findings. The case was classified as probable MSA according to the second consensus on the diagnosis of MSA. MRI is an important tool for diagnosing MSA with "hot cross bun" sign and hyperintense lateral putamen ring which are considered typical for MSA.

The diagnosis is often confused with many diseases, so it is necessary to closely coordinate clinical, MRI as well as patient follow-up to achieve an accurate diagnosis. The clinical difference between MSA-C, especially in the early stages, from other sporadic ataxia, is still poorly understood. Further studies in metabolic and morphological biomarkers in MSA can potentially aid differentiation.

Patient consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

REFERENCES

[1] Graham JG, Oppenheimer DR. Orthostatic hypotension and nicotine sensitivity in a case of multiple system atrophy. J Neurol Neurosurg Psychiatr 1969;32(1):28–34. doi:10.1136/jnnp.32.1.28.

[2] Wenning GK, Colosimo C, Geser F, Poewe W. Multiple system atrophy. Lancet Neurol 2004;3(2):93–103. doi:10.1016/s1474-4422(03)00662-8.

[3] Bower JH, Maraganore DM, McDonnell SK, Rocca WA. Incidence of progressive supranuclear palsy and multiple system atrophy in Olmsted County, Minnesota, 1976 to 1990. Neurology 1997;49:1284–8. doi:10.1212/wnl.49.5.1284.

[4] Walsh RR, Krismer F, Galpern WR, Wenning GK, Low PA, Halliday G, et al. Recommendations of the global multiple. System atrophy research roadmap meeting. Neurology 2018;90:74–82. doi:10.1212/WNL.0000000000004798.

[5] Balas M, Balash Y, Giladi N, Gurevich T. Cognition in multiple system atrophy: neuropsychological profile and interaction with mood. J Neural Transm 2010;117:369–75. doi:10.1007/s00702-009-0365-z.

[6] Roncevic D, Palma JA, Martinez J, Goulding N, Norcliffe-Kaufmann L, Kaufmann H. Cerebellar and parkinsonian phenotypes in multiple system atrophy: similarities, differences and survival. J Neural Transm (Vienna) 2014;121:507–12. doi:10.1007/s00702-013-1133-7.

[7] Wenning GK, Geser F, Krismer F, Seppi K, Duerr S, Boesch S, et al. The natural history of multiple system atrophy: a prospective European cohort study. Lancet Neurol 2013;12:264–74. doi:10.1016/S1474-4422(12)70327-7.

[8] Köllensperger M, Geser F, Ndayisaba JP, Boesch S, Seppi K, Ostergaard K, et al. Presentation, diagnosis, and management of multiple system atrophy in Europe: final analysis of the European multiple system atrophy registry. Mov Disord 2010;25(15):2604–12. doi:10.1002/mds.23192.

[9] Quinn N. Multiple system atrophy—the nature of the beast. J Neurol Neurosurg Psychiatry 1989:78–89. doi:10.1136/jnnp.52.suppl.78.

[10] Watanabe H, Riku Y, Hara K, Kawabata K, Nakamura T. Ito M,et al. Clinical and imaging features of multiple system atrophy: challenges for an early and clinically definitive diagnosis. Mov Disord 2018;11(3):107–20. doi:10.14802/jmd.18020.

[11] Gilman S, Wenning GK, Low PA, Brooks DJ, Mathias CJ, Trojanowski JQ, et al. Second consensus statement on the diagnosis of multiple system atrophy. Neurology 2008;71(9):670–6. doi:10.1212/01.wnl.0000324625.00404.15.

[12] Kawai Y, Suenaga M, Takeda A, Ito M, Watanabe H, Tanaka F, et al. Cognitive impairments in multiple system atrophy: MSA-C vs MSA-P. Neurology 2008;70(16 part 2):1390–6. doi:10.1212/01.wnl.0000310413.04462.6a.

[13] Brooks DJ. Proposed neuroimaging criteria for the diagnosis of multiple system atrophy. Mov Disord 2009;24(7):949–64. doi:10.1002/mds.22413.

[14] Matsushima M, Yabe I, Sakushima K, Kanatani Y, Nishimoto N, Matsuoka T, et al. Multiple system atrophy in Hokkaido, Japan: a prospective registry study of natural history and symptom assessment scales followed for 5 years. BMJ Open 2021;11(2):e045100. doi:10.1136/bmjopen-2020-045100.

[15] Colosimo C, Pezzella FR. The symptomatic treatment of multiple system atrophy. Eur J Neurol 2002;9(3):195–9. doi:10.1046/j.1468-1331.2002.00348.x.

[16] Giladi N, Manor Y, Hilel A, Gurevich T. Interdisciplinary teamwork for the treatment of people with Parkinson's disease and their families. Curr Neurol Neurosci Rep 2014;14(11):1–7. doi:10.1007/s11910-014-0493-1.

[17] Perez-Lloret S, Flabeau O, Fernagut P, Pavy-Le Traon A, et al. Current concepts in the treatment of multiple system atrophy. Mov Disord Clin Pract 2015(1):6–16. doi:10.1002/mdc3.12145.

[18] Laurens B, Vergnet S, Lopez MC, Foubert-Samier A, Tison F, Fernagut P-O, et al. Multiple system atrophy—state of the art. Curr Neurol Neurosci Rep 2017;17:41. doi:10.1007/s11910-017-0751-0.

[19] Tsuji S. Susceptibility gene in multiple system atrophy (MSA). Rinsho Shinkeigaku 2014;54(12):969–71. doi:10.5692/clinicalneurol.54.969.

[20] Yang X, Xi J, Zhao Q, Jia H, An R, Liu Z, et al. Association of the COQ2 V393A variant with Parkinson's disease: a case-control study and meta-analysis. PLoS One 2015;10(6):e0130970. doi:10.1371/journal.pone.0130970.

[21] Papp MI, Kahn JE, Lantos PL. Glial cytoplasmic inclusions in the CNS of patients with multiple system atrophy (striatonigral degeneration, olivopontocerebellar atrophy and Shy-Drager syndrome). J Neurol Sci 1989;94(1-3):79–100. doi:10.1016/0022-510x(89)90219-0.

[22] Ikeda T, Mashimoto H, Iwasaki K, Shimokawa I, Matsuo T. A sequential ultrastructural and histoautoradiographic study of early neoplastic lesions in ethylnitrosourea-induced rat glioma. Acta Pathol Jpn 1989;39(8):487–95. doi:10.1111/j.1440-1827.1989.tb01514.x.

[23] Gilman S, Low PA, Quinn N, Albanese A, Ben-Shlomo Y, Fowler CJ, et al. Consensus statement on the diagnosis of multiple system atrophy. J Neurol Sci 1999;163(1):94–8. doi:10.1016/s0022-510x(98)00304-9.

[24] Köllensperger M, Geser F, Seppi K, Stampfer-Kountchev M, Sawires M. Scherfler C,et al. Red flags for multiple system atrophy. Mov Disord 2008;23(8):1093–9. doi:10.1002/mds.21992.
[25] Burk K, Buhring U, Schulz JB, Zuhlke C, Hellenbroich Y, Dichgans J. Clinical and magnetic resonance imaging characteristics of sporadic cerebellar ataxia. Arch Neurol 2005;62(6):981–5. doi:10.1001/archneur.62.6.981.
[26] Schrag A, Good C D, Miszkiel K, Morris H R, Mathias C J, Lees A J, et al. Differentiation of atypical parkinsonian syndromes with routine MRI. Neurology 2000;54(3):697–702. doi:10.1212/wnl.54.3.697.
[27] Kalus S, King J, Lui E, Gaillard F. Fragile X-associated tremor/ataxia syndrome: an under-recognised cause of tremor and ataxia. J Clin Neurosci 2016;23:162–4. doi:10.1016/j.jocn.2015.08.010.
[28] Lin DJ, Hermann KL, Schmahmann JD. Multiple system atrophy of the cerebellar type: clinical state of the art. Mov Disord 2014;29(3):294–304. doi:10.1002/mds.25847.
[29] Abele M, Burk K, Schols L, Schwartz S, Besenthal I, Dichgans J, et al. The aetiology of sporadic adult-onset ataxia. Brain 2002;125(5):961–8. doi:10.1093/brain/awf107.
[30] Schols L, Szymanski S, Peters S, Przuntek H, Epplen JT, Hardt C, et al. Genetic background of apparently idiopathic sporadic cerebellar ataxia. Hum Genet 2000;107:132–7. doi:10.1007/s004390000346.
[31] Soares-Fernandes JP, Ribeiro M, Machado A. "Hot cross bun" sign in variant Creutzfeldt-Jakob disease. Am J Neuroradiol 2009;30(3):e37. doi:10.3174/ajnr.A1335.
[32] Klockgether T, Lüdtke R, Kramer B, Abele M, Bürk K, Schöls L, et al. The natural history of degenerative ataxia: a retrospective study in 466 patients. Brain 1998;121(Pt 4):589–600. doi:10.1093/brain/121.4.589.
[33] Lirng J-F, Wang P-S, Chen H-C, Soong B-W, Guo WY, Wu H-M, et al. Differences between spinocerebellar ataxias and multiple system atrophy-cerebellar type on proton magnetic resonance spectroscopy. PLoS One 2012;7(10):e47925. doi:10.1371/journal.pone.0047925.
[34] Seppi K, Schocke MF, Wenning GK, Poewe W. How to diagnose MSA early: the role of magnetic resonance imaging. J Neural Transm 2005;112:1625–34. doi:10.1007/s00702-005-0332-2.
[35] Yekhlef F, Ballan G, Macia F, Delmer O, Sourgen C, Tison F. Routine MRI for the differential diagnosis of Parkinson's disease, MSA, PSP, and CBD. J Neural Transm 2003;110(2):151–69. doi:10.1007/s00702-002-0785-5.
[36] Rizzo G, Martinelli P, Manners D, Scaglione C, Tonon C. Cortelli P,et al. Diffusion-weighted brain imaging study of patients with clinical diagnosis of corticobasal degeneration, progressive supranuclear palsy and Parkinson's disease. Brain 2008;131(Pt 10):2690–700. doi:10.1093/brain/awn195.
[37] Péran P, Barbagallo G, Nemmi F, Sierra M, Galitzky M, Traon AP-L, et al. MRI supervised and unsupervised classification of Parkinson's disease and multiple system atrophy. Mov Disord 2018;33:600–8. doi:10.1002/mds.27307.
[38] Lee EA, Cho HI, Kim SS, Lee WY. Comparison of magnetic resonance imaging in subtypes of multiple system atrophy. Parkinsonism Relat Disord 2004;10(6):363–8. doi:10.1016/j.parkreldis.2004.04.008.
[39] Lee W-H, Lee C-C, Shyu W-C, Chong P-N, Lin S-Z. Hyperintense putaminal rim sign is not a hallmark of multiple system atrophy at 3T. AJNR Am J Neuroradiol 2005;26(9):2238–42. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7976126/.
[40] Konagaya M, Matsuoka Y, Goto Y, Yoshida M, Hashizume Y. Pathological correlate of the slitlike changes on MRI at the putaminal margin in multiple system atrophy. J Neurol 1999;246:142–3. doi:10.1007/s004150050323.
[41] Matsusue E, Fujii S, Kanasaki Y, Sugihara S, Miyata H, Ohama E, et al. Putaminal lesion in multiple system atrophy: postmortem MR-pathological correlations. Neuroradiology 2008;50:559–67. doi:10.1007/s00234-008-0381-y.
[42] Nicoletti G, Fera F, Condino F, Auteri W, Gallo O. Pugliese P,et al. MR imaging of middle cerebellar peduncle width: differentiation of multiple system atrophy from Parkinson disease. Radiology 2006;239(3):825–30. doi:10.1148/radiol.2393050459.
[43] Quattrone A, Nicoletti G, Messina D, Fera F, Condino F. Pugliese P,et al. MR imaging index for differentiation of progressive supranuclear palsy from Parkinson disease and the Parkinson variant of multiple system atrophy. Radiology 2008;246(1):214–21. doi:10.1148/radiol.2453061703.
[44] Schocke MFH, Seppi K, Esterhammer R, Kremser C, Jaschke W, Poewe W, et al. Diffusion-weighted MRI differentiates the Parkinson variant of multiple system atrophy from PD. Neurology 2002;58(4):575–80. doi:10.1212/wnl.58.4.575.
[45] Paviour DC, Thornton JS, Lees AJ, Jager HR. Diffusion-weighted magnetic resonance imaging differentiates Parkinsonian variant of multiple-system atrophy from progressive supranuclear palsy. Mov Disord 2007;22(1):68–74. doi:10.1002/mds.21204.
[46] Gupta D, Saini J, Kesavadas C, Sankara Sarma P, Kishore A. Utility of susceptibility-weighted MRI in differentiating Parkinson's disease and atypical parkinsonism. Neuroradiology 2010;52(12):1087–94. doi:10.1007/s00234-010-0677-6.
[47] The utility of susceptibility-weighted imaging for differentiating Parkinsonism-predominant multiple system atrophy from Parkinson's disease: correlation with 18F-flurodeoxyglucose positron-emission tomography. Neurosci Lett 2015;584:296–301. doi:10.1016/j.neulet.2014.10.046.
[48] Meijer FJA, van Rumund A, Fasen BACM, Titulaer I, Aerts M, Esselink R, et al. Susceptibility-weighted imaging improves the diagnostic accuracy of 3T brain MRI in the work-up of parkinsonism. AJNR Am J Neuroradiol 2015;36(3):454–60. doi:10.3174/ajnr.A4140.
[49] Mabuchi N, Hirayama M, Koike Y, Watanabe H, Ito H, Kobayashi R, et al. Progression and prognosis in pure autonomic failure (PAF): comparison with multiple system atrophy. J Neurol Neurosurg Psychiatry 2005;76(7):947–52. doi:10.1136/jnnp.2004.049023.
[50] Orimo S, Yogo M, Nakamura T, Suzuki M, Watanabe H. (123)I-meta-iodobenzylguanidine (MIBG) cardiac scintigraphy in α-synucleinopathies. Ageing Res Rev 2016;30:122–33. doi:10.1016/j.arr.2016.01.001.
[51] Schrag A, Geser F, Stampfer-Kountchev M, Seppi K, Sawires M. Köllensperger M,et al. Health-related quality of life in multiple system atrophy. Mov Disord 2006;21:809–15. doi:10.1002/mds.20808.