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Case study

Ocular features of multiple system atrophy

Maria D. Garcia [a], Jose S. Pulido [a,b], Elizabeth A. Coon [c], John J. Chen [a,c,*]

[a] Department of Ophthalmology, Mayo Clinic, 200 First Street, SW, Rochester, MN 55905, USA
[b] Department of Ophthalmology, Ocular Oncology, and Vitreoretinal Diseases, Mayo Clinic, 200 First Street, SW, Rochester, MN 55905, USA
[c] Department of Neurology, Mayo Clinic, 200 First Street, SW, Rochester, MN 55905, USA

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ABSTRACT

The aim of this paper is to gain better understanding of the ocular manifestations of multiple system atrophy (MSA), a neurodegenerative disorder rarely studied in terms of its ophthalmologic features. We performed a retrospective case series (1/1/05–12/31/14) to search for patients seen at Mayo Clinic, Rochester, MN, who had mention of MSA in the medical record and an eye examination, which yielded 285 cases. Of the 285, we identified 39 cases of true MSA. Each of these 39 patients was further reviewed for ocular abnormalities potentially related to MSA. Ocular findings potentially attributable to MSA were found in 64% of patients. Most common were dry eye (N = 14), conjugate eye movement abnormalities (N = 13), and ocular misalignment (N = 7). One patient had dry eye and monocular diplopia from trichiasis due to cicatricial pemphigoid, one had bilateral optic atrophy, and one had Adie's tonic pupil. Conjugate eye movement abnormalities (33%) and ocular misalignment (18%) were more common in patients with MSA-C. Patients with ocular findings, excluding dry eye, had a significantly shorter lifespan from time of initial neurologic symptoms to death. Our study confirms conjugate eye movement abnormalities and misalignment are common ocular findings in patients with MSA. Bilateral optic atrophy and cicatricial pemphigoid are possibly attributable to the disease. Ocular manifestations in MSA predict a poor prognosis as these patients have a significantly shorter lifespan. Therefore, we recommend patients with MSA have a comprehensive neuro-ophthalmologic exam at time of diagnosis, and thereafter, to screen for eye findings that may indicate a shorter lifespan.

1. Introduction

Multiple system atrophy (MSA) is an often fatal neurodegenerative disease characterized by three major features: autonomic failure with predominant cerebellar dysfunction (MSA-C) or parkinsonism (MSA-P) [1]. MSA is characterized by rapid progression with patients having an average survival of six to ten years after symptoms have developed [1]. The average age of onset is in the mid-fifties to sixties, and it is seen equally in both sexes [1].

Ocular symptoms have been reported in MSA with studies focusing on abnormalities in eye movements and reactivity of the pupil [2–5]. Despite the description of these specific ocular findings, there is no systematic analysis of the eye diseases that are present in patients with MSA [6]. The goal of our study was to determine the ocular manifestations of MSA by examining cases of MSA with concurrent ocular disease.

2. Materials and methods

After obtaining approval from the Mayo Clinic Institutional Review Board, we conducted a retrospective, single-center case series. We began by identifying a cohort of patients that had a mention of MSA in the medical record; 4135 cases were identified, but 108 were excluded because they did not have research authorization (Fig. 1). We then identified 285 patients who had eye exams, either in the setting of an identified refractive error or due to ocular symptoms, at Mayo Clinic Rochester in the period between January 1, 2005, and December 31, 2014 (Fig. 1).

We then used the Mayo Clinic electronic medical record to review each of these 285 cases and verify if the diagnosis of MSA was valid (Fig. 1). We identified 39 cases that met probable or possible criteria for MSA and excluded cases due to other neurodegenerative diseases, such as progressive supranuclear palsy, Parkinson disease, Lewy body dementia, and corticobasal syndrome (Fig. 1) [7]. None of the patients in our cohort had a "definite" diagnosis of MSA, as none had an autopsy with pathologic analysis of the brain tissue. Diagnostic criteria was based on the second consensus statement of the diagnosis of multiple system atrophy by Gilman

* Corresponding author.
E-mail addresses: pulido.jose@mayo.edu (J.S. Pulido), Coon.Elizabeth@mayo.edu (E.A. Coon), Chen.John@mayo.edu (J.J. Chen).

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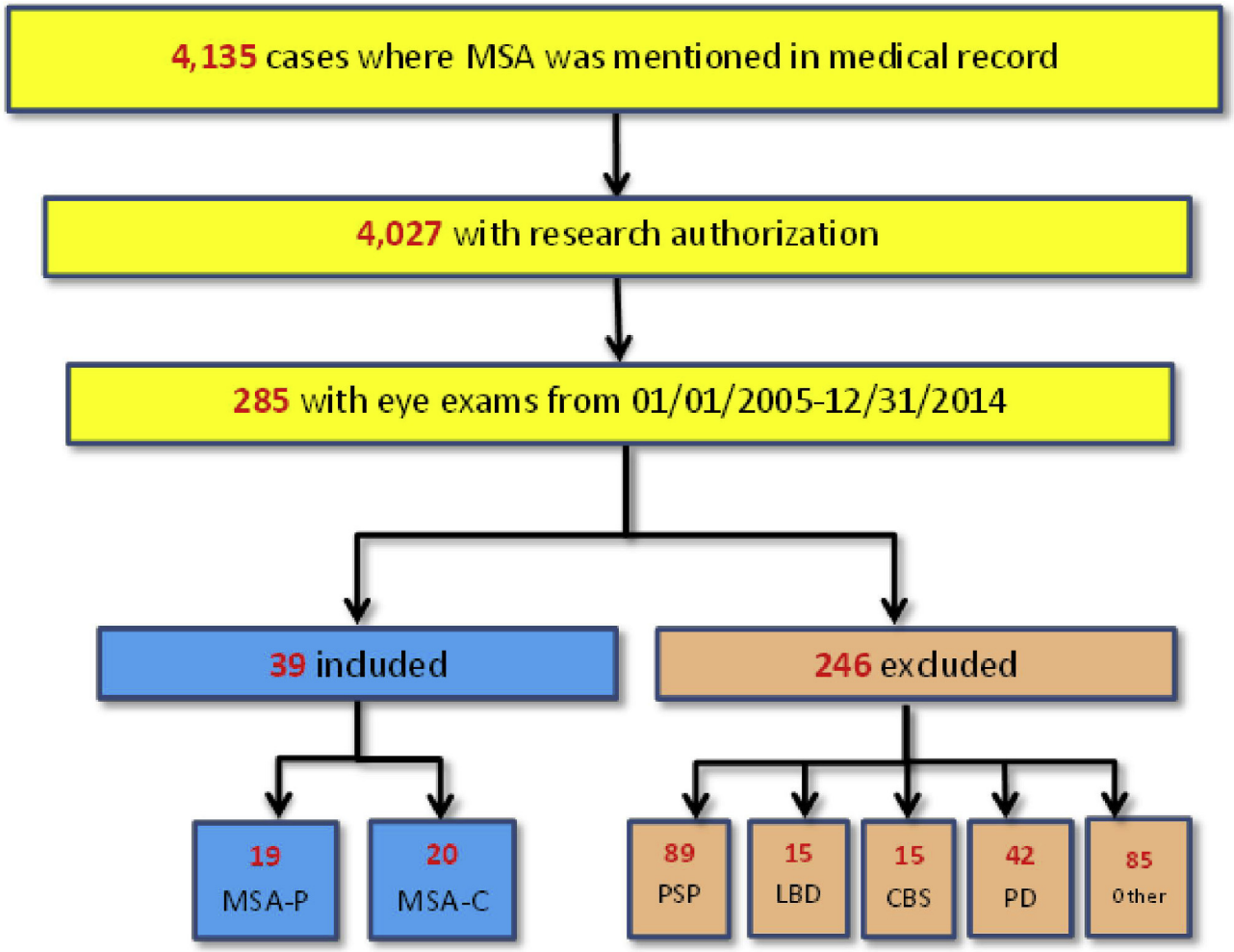

Fig. 1. Flow chart of methods. PSP = Progressive supranuclear palsy; LBD = Lewy body dementia; CBS = corticobasal syndrome; PD = Parkinson disease and nonspecific parkinsonism.

et al. and confirmed by one of the authors (EAC) [7]. There were 19 cases of MSA-P and 20 of MSA-C (Fig. 1). Each of these 39 patients was further analyzed for ocular abnormalities (Fig. 1). The ocular findings were reviewed and determined to be either independent or potentially attributable to MSA based on prior literature and the known pathophysiology of the disease.

Statistical analyses included t-test and chi-square, which were performed using SigmaPlot. Paired t-test was used to compare the average age of symptom onset, average age of death, and average time from symptom onset to death between patients with and without ocular findings attributable to MSA. Chi-square was used to compare sex among the MSA subtypes as well as the number of MSA-C and MSA-P patients with and without ocular findings attributable to MSA. SigmaPlot was utilized to create Kaplan-Meier curves. Statistical significance was defined as $p \leq .05$.

Although there is a plausible link between dry eye and MSA, especially MSA-P, dry eye is also common in the general aging population; therefore, it is not possible to prove that the dry eye was attributable to MSA. For this reason, the comparative analyses were done including and excluding the dry eye patients.

3. Results

3.1. Demographics

The MSA cohort consisted of 19 cases of MSA-P and 20 MSA-C (Table 1). Forty-one percent (N = 16) were females, and the average age of symptom onset was 63.7 years (Table 1). There were no significant differences between the different subtypes of MSA in terms of sex (p = .65) or average age of symptom onset (p = .18).

3.2. Findings potentially attributable to MSA

Of 39 patients in the cohort, 14 (36%) did not have ocular findings associated with MSA. However, the remaining 64% had ocular findings that could potentially be attributed to MSA. When dry eye, a common finding in the general population, was excluded, 28% of cases still had ocular abnormalities likely attributable to the disease.

Dry eye was the most common finding possibly associated with MSA, which was seen in 14 patients (36%) and caused symptomatic monocular diplopia in 5 patients (Fig. 2). One patient had monocular diplopia from trichiasis due to ocular cicatricial pemphigoid (Fig. 2). Dry eye was most prevalent in patients with MSA-P compared to MSA-C (Fig. 2).

Conjugate eye movement abnormalities and misalignment were the most common findings in patients with MSA-C when compared to MSA-P (p = .002). Misalignment causing diplopia from MSA was observed in 7 out of 39 patients (18%) (Fig. 2). Six out of the seven (86%) cases of misalignment were seen in patients with MSA-C, with the remaining case seen in a patient with MSA-P (Fig. 2). There were four cases due to skew deviation and three of divergence insufficiency (Fig. 2). Of 39 patients, 13 (33%) had

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