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Parkinson's Plus Syndromes - Clinical Dilemmas Regarding Parkinson's Disease: A Case Report

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Abstract

BACKGROUND: Parkinson-plus syndrome is a clinical entity characterized by symptoms and signs of damage to the extrapyramidal system (bradykinesia, tremor, rigidity, and postural instability), pyramidal tracts (spasticity, hyperreflexia), the cerebellum, and the autonomic nervous system. This group includes Corticobasal Degeneration, Progressive Supranuclear Palsy, and Multiple System Atrophy. Parkinson-plus syndromes have different clinical presentations, courses, and prognoses compared to Parkinson's disease, emphasizing the importance of precise diagnosis.

CASE PRESENTATION: A 46-year-old female patient presented acutely with symptoms including speech and swallowing difficulties, general weakness, malaise, left-sided hemiparesis, and gait instability with a tendency to fall backward. Neurological examination revealed dysarthric and soft speech, hypomimia, left-sided spastic hemiparesis, bradykinesia, rigidity, postural instability, and dysautonomic symptoms like hyperhidrosis, gastroparesis, and arterial hypotension. Routine blood analyses, thyroid hormones, immunological analyses, paraneoplastic antibodies, and virological serology were normal. MRI of the brain showed an arachnoid cyst in the right temporal region without parenchymal changes; echocardiography, carotid artery Doppler ultrasound, cytochemical analysis, and electrophoresis were normal.

CONCLUSION: The presence of dominant extrapyramidal symptomatology, postural instability, and backward falls suggests Progressive Supranuclear Palsy (PSP) as the most likely diagnosis.

Introduction

The term "Parkinson-plus syndromes" refers to a group of diseases where parkinsonism is present along with additional ("plus") symptoms and signs not expected in Parkinson's disease [1]. A thorough and comprehensive examination of these patients is fundamental for the differential diagnosis of parkinsonism, involving the analysis of at least three entities for each patient [2]:

1. Analysis of extrapyramidal symptoms.
2. Identification of "plus" symptoms and signs.
3. Monitoring response to dopaminergic therapy.

The cardinal symptoms of atypical parkinsonism include bradykinesia, tremor, rigidity, and postural instability. Some authors consider motor blocks or the "freezing of gait" phenomenon (FOG) as the fifth cardinal symptom [3], [4].

We aimed to present a case of patient with acute symptomatology in Parkinson-plus syndrome with clinical dilemmas regarding Parkinson's disease.

Case presentation

In this report, we present the case of a 46-year-old female patient with acute symptomatology, starting three months prior with slowed and less intelligible speech. Over the following days, she had trouble swallowing, general weakness, malaise, and slowness, with weakness in the left extremities. No fever or infection symptoms were noted, though a few days before symptom onset, she had numbness in her arms (up to the elbows) and legs (up to the calves).

Her condition worsened, with persistent walking difficulties and a tendency to fall backward

(though she hadn't fallen). No weight loss was observed, but chewing became slow with early satiety. For the past two to three years, she noticed increased sweating.

Somatic Status: Afebrile, with vitiligo on the face and extremities, rhythmic heart action with clear tones, BP=95/65 mmHg. Extremities without edema or deformities.

Neurological Status: Conjugate eye movements in all directions without strabismus, nystagmus, or diplopia. Normal sensory innervation in all three branches of the trigeminal nerve. Reduced facial expression. Dysarthric and dysphonic speech. Dysphagia for both liquid and solid foods. The right palatal arch appeared lower than the left, but both elevated normally during phonation, with central uvula position and enhanced palatine and pharyngeal reflexes. No atrophy or fasciculations of the tongue (appears grooved). General muscle strength preserved; moderate left-sided hemiparesis with mild asymmetry of reflexes on the left, no pathological reflexes. Coordination tests were performed slowly but accurately. No rigidity or tremor noted during passive movements. Gait characterized by small steps with slight circumduction of the left leg, absent arm swing. Postural reflexes impaired. No sensory deficits. Sphincters controlled. Autonomic symptoms included hyperhidrosis, gastroparesis, and arterial hypotension.

Psychiatric Status: Conscious, contactable, properly oriented, unobtrusive.

Paraclinical Investigations

- CSF cytochemistry and electrophoresis were normal.

- Brain MRI (post-contrast): No focal lesions or expansive changes in the cerebellum and brainstem. Right temporal arachnoid cyst (3x2 cm) noted; otherwise, normal brain parenchyma, normal ventricular system, and retrobulbar changes.

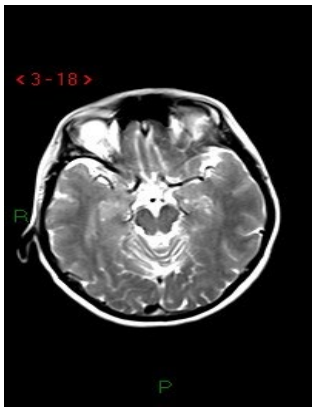

Figure1: A) Sagittal weighted post contrast images showing initial midbrain atrophy; B) Axial weighted post contrast showing a reduced anteroposterior midline-midbrain diameter

- Electromyoneurography (EMNG) of upper and lower extremities, including the styloglossus muscle. Spontaneous denervation activity in the form of fasciculations was recorded in the right quadriceps femoris muscle (m. quadriceps femoris dex), and fibrillation activity in the form of fasciculations was noted in the right extensor digitorum brevis muscle (m. extensor digitorum brevis dex). Other examined muscles showed electrical silence at rest.

- During moderate and maximal voluntary activity in the extensor digitorum brevis muscle (m. ext dig brevis) bilaterally, more pronounced on the right, there was a reduction in the innervation pattern from moderate to moderately severe, with polyphasic and prolonged duration action motor potentials (AMP). A moderate reduction was also observed in the quadriceps femoris muscle bilaterally (m. quadriceps femoris bil), tibialis anterior muscle bilaterally (m. tibialis ant bil), deltoid muscle on the left (m. deltoideus sin), and biceps brachii muscle on the left (m. biceps brachii sin) with high voltage, polyphasic, and prolonged AMPs. A mild to moderate reduction was also noted in the genioglossus muscle (m. genioglossus). The ENG (electroneurography) examination of the motor and sensory nerves was normal.

- EMNG Findings: Indicate a chronic lesion of the proximal part of the peripheral motor neuron, characterized by axonal degeneration of moderate to moderately severe degree for L5-S1 roots bilaterally and moderate degree for L3-L4 and C5-C7 roots. No tremor or other electrophysiological indicators of extrapyramidal disease were noted, nor active denervation of tongue muscles.

Discussion

Our patient was hospitalized due to acute/subacute onset symptomatology, clinically presenting with dysphonia, dysarthria, dysphagia, left extremity weakness, postural reflex disturbances, and gait difficulties, under suspicion of atypical parkinsonism or subacute pyramidal-cerebellar syndrome of possible paraneoplastic etiology. Neurologically, pyramidal-extrapyramidal and pseudobulbar symptomatology dominated, prompting multiple investigations towards extrapyramidal diseases. Routine biochemical analyses, tumor markers, and immunological blood tests were within reference ranges. Contrast brain MRI showed a right temporal arachnoid cyst with no other abnormalities. To rule out paraneoplastic etiology, chest X-ray, abdominal ultrasound, and CT of the abdomen and pelvis with IV contrast were performed, all with normal findings; small reactive lymph nodes were noted on chest CT. Pneumoslide testing revealed a Mycoplasma pneumoniae infection, treated with Azithromycin.

Electrophysiological studies indicated chronic

lesions of the proximal peripheral motor neuron without signs of extrapyramidal disease or active denervation of tongue muscles. CSF cytochemical analysis and electrophoresis were normal, as were antinuclear antibody tests and a paraneoplastic syndrome panel. A therapeutic trial with Amantadine and Levodopa/Carbidopa showed slight improvement in speech, swallowing, and motor functions. The overall clinical presentation suggests Parkinson-plus syndrome, likely Progressive Supranuclear Palsy (PSP). The patient remains under continuous neurological monitoring.

Atypical parkinsonian syndromes, also known as Parkinson-plus syndromes, encompass a diverse group of movement disorders, including dementia with Lewy bodies (DLB), progressive supranuclear palsy (PSP), multisystem atrophy (MSA), and corticobasal degeneration (CBD) [5]. In DLB, FDG-PET typically reveals parieto-occipital hypometabolism with involvement of the cuneus, while dopaminergic imaging techniques like [123I]-FP-CIT SPECT (DaTscan) or fluorodopa (FDOPA)-PET can serve as diagnostic aids [6]. PSP often presents midbrain atrophy on structural imaging, with FDG-PET useful for detecting frontal lobe hypometabolism, and tau-PET confirming the presence of underlying tauopathy [7]. In MSA, putaminal or cerebellar atrophy is commonly observed, with FDG-PET highlighting characteristic nigrostriatal or olivopontocerebellar hypometabolism, respectively [8]. CBD typically shows asymmetric atrophy in the superior parietal lobules and corpus callosum, with FDG and tau-PET revealing asymmetric hemispheric and subcortical involvement opposite to the side of clinical symptoms [9]. Additional advanced neuroimaging techniques discussed may aid in diagnosis or represent promising areas for future research.

Parkinson's plus syndromes, such as PSP, MSA, CBD, and VaP, present unique clinical features, imaging findings, and varied responses to levodopa, making it challenging to distinguish them from Parkinson's disease (PD). Lewy body dementia (LBD) is marked by the presence of Lewy bodies containing α-synuclein, leading to both motor and cognitive impairments. PD and Alzheimer's disease (AD) share a complex interplay, including overlapping pathogenic processes, genetic predispositions, and dementia-related clinical features. The interconnectedness of PD, Parkinson's plus syndromes, LBD, and AD underscores the importance of understanding their shared disease mechanisms. Common factors like abnormal protein aggregation, mitochondrial dysfunction, increased oxidative stress, and brain inflammation offer potential targets for specific treatments. Further research is crucial to unravel these complex relationships and develop effective therapies for these intricate neurological disorders [10].

Conclusion

The presence of dominant extrapyramidal symptomatology, postural instability, and backward falls suggests Progressive Supranuclear Palsy (PSP) as the most likely diagnosis.

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