NÖRO PSİKİYATRİ ARŞİVİ
ARCHIVES OF NEUROPSYCHIATRY

CASE REPORT

Arch Neuropsychiatry 2025;62:94–96
https://doi.org/10.29399/npa.28517

Anti-Ri Associated Paraneoplastic Cervical Dystonia and Laryngospasm in a Patient with Nasopharyngeal Carcinoma

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ABSTRACT

Oromandibular dystonia and laryngospasm are defined as paraneoplastic syndromes of anti-Ri antibody. Herein, we report a 50-year-old woman admitted to the outpatient clinic with cervical contraction, speech and gait disturbance, and mental deterioration persisting for one year. She was diagnosed with undifferentiated nasopharyngeal carcinoma during further examination for two years of tinnitus and underwent radiotherapy. Her neurological symptoms started six months after radiotherapy. During this period, she underwent a tracheostomy due to a sudden laryngospasm. Anti-Ri antibody was positive in the paraneoplastic antibody screening. Her cervical dystonia and mental deterioration partially improved with intravenous pulse steroid and immunoglobulin therapies. However, the patient deceased due to aspiration pneumonia after six months. This rare clinical presentation, characterized by cervical dystonia, laryngospasm, spastic quadriparesis, and mental deterioration, should be considered anti-Ri antibody-associated paraneoplastic syndrome for patients with nasopharyngeal carcinoma.

Keywords: Anti-Ri antibody, cervical dystonia, laryngospasm, nasopharyngeal carcinoma

Cite this article as: Hanağası H, Çakar A, Hanağası F, Samancı B, Tüfekçioğlu Z, Bilgiç B et al. Anti-Ri Associated Paraneoplastic Cervical Dystonia and Laryngospasm in a Patient with Nasopharyngeal Carcinoma. Arch Neuropsychiatry 2025;62:94–96.

INTRODUCTION

Anti-Ri, also known as anti-neuronal antibody type 2 (ANNA-2), has been reported in serum and cerebrospinal fluid (CSF) of patients who typically present with subacute onset neurological syndrome involving the brainstem, cerebellum, and spinal cord, usually in association with breast or lung carcinoma (1). Neurological disorders such as brainstem syndrome (including opsoclonus, myoclonus, or both), cerebellar syndrome, myelopathy, peripheral or cranial neuropathy, movement disorders, encephalopathy, Lambert–Eaton syndrome, and seizures have been reported (1,2). Oromandibular or cervical dystonia and laryngospasm have also been described as paraneoplastic syndrome (PNS) related to anti-Ri antibody (3).

Paraneoplastic syndrome in nasopharyngeal carcinoma (NPC) is rare (4). There are few reports about NPC-related PNS, and both the central and peripheral nervous systems can be affected (4–6).

Here, we present a patient with anti-Ri antibody-positive paraneoplastic syndrome associated with NPC who presented with cervical dystonia, laryngospasm, spastic quadriparesis, and mental deterioration.

Highlights

- **Dystonia and laryngospasm are defined as paraneoplastic syndromes of anti-Ri antibody.**
- **Anti-Ri antibody might be associated with nasopharyngeal carcinoma.**
- **Laryngospasm may cause the death of patients with anti-Ri antibodies.**

CASE REPORT

A 50-year-old woman was admitted with complaints of tinnitus persisting for two years and cervical contraction, speech and gait disturbances, and mental deterioration for one year. She was diagnosed with undifferentiated NPC while being investigated for tinnitus persisting for two years. She underwent radiotherapy (44 Gy, 22 fractions). The maximum cervical and brainstem doses were 20 Gy each. There was no local invasion or metastatic lesion during this period. Her tinnitus improved after radiotherapy. She then underwent a tracheostomy six months later due to a sudden laryngospasm. After hospitalization, she had gait difficulty and cervical dystonia, and she was unable to walk after a few months. She had difficulties with speech and swallowing and has suffered from forgetfulness for the last six months.

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Received: 19.06.2023, **Accepted:** 04.09.2023, **Available Online Date:** 15.02.2025

She had hypertension and diabetes mellitus in her medical history. There was no consanguineous marriage history. Her father had died from complications of NPC. Her physical examination was insignificant. She was under treatment with oral antidiabetics and antihypertension drugs.

On neurological examination, she was alert and disoriented of time and localization. She also had dysarthria and left torticollis. Sensory and cerebellar examinations were within normal limits. She had quadriparesis, spasticity, and brisk reflexes in all four extremities with bilateral Babinski sign. Mental examination revealed global cognitive deterioration. She had a spastic and unsteady gait. She had urinary incontinence. Her Mini-Mental State Examination Score (MMSE) was 19/30 (7).

Hematological and biochemical screening, protein electrophoresis, urine analysis, thyroid and parathyroid function tests, serum vitamin B12 and vitamin E levels, serum copper and ceruloplasmin, total copper in 24-hour-urine, immune electrophoresis, and serologic tests in serum were all normal. The oligoclonal band pattern was 3. Other serological tests in CSF were unremarkable. Electroencephalography, brainstem-evoked potentials, and tibial somatosensory-evoked potentials were normal. Nerve conduction studies revealed mild sensory and motor neuropathy prominent in the lower extremities. There were no significant findings on brain and spinal (cervical, thoracic, lumbar) magnetic resonance imaging scans (Figure 1).

Her paraneoplastic antibody screening in serum and cerebrospinal fluid (CSF) resulted in a high titer of anti-Ri antibodies. Other paraneoplastic markers were negative. The patient was re-evaluated for breast and gynecological cancers. Malignancy screenings were within normal limits, including mammography, breast ultrasound, pelvic MRI, gastroscopy, and colonoscopy. Her whole body FDG-PET scan was negative.

Her cervical dystonia partially improved with botulinum toxin injection. Mental deterioration partially improved with intravenous pulse steroid (1 g per day, five days) and immunoglobulin therapies (5 days), and cervical dystonia improved after these treatments. The patient deceased due to aspiration pneumonia six months after treatment.

DISCUSSION

We reported a case of anti-Ri antibody-associated PNS consisting of dystonia and laryngospasm with spasticity. Initial reports of anti-Ri-positive patients emphasized breast and lung cancer (2). Other cancer associations that have been reported with anti-Ri include carcinomas of the gynecological system, bladder, and neuroendocrine system (1).

Ri is an antibody directed against ribonucleic acid (RNA) binding protein, and the spectrum of associated neurological dysfunction is broad (8). The most common clinical features are opsoclonus-myoclonus and

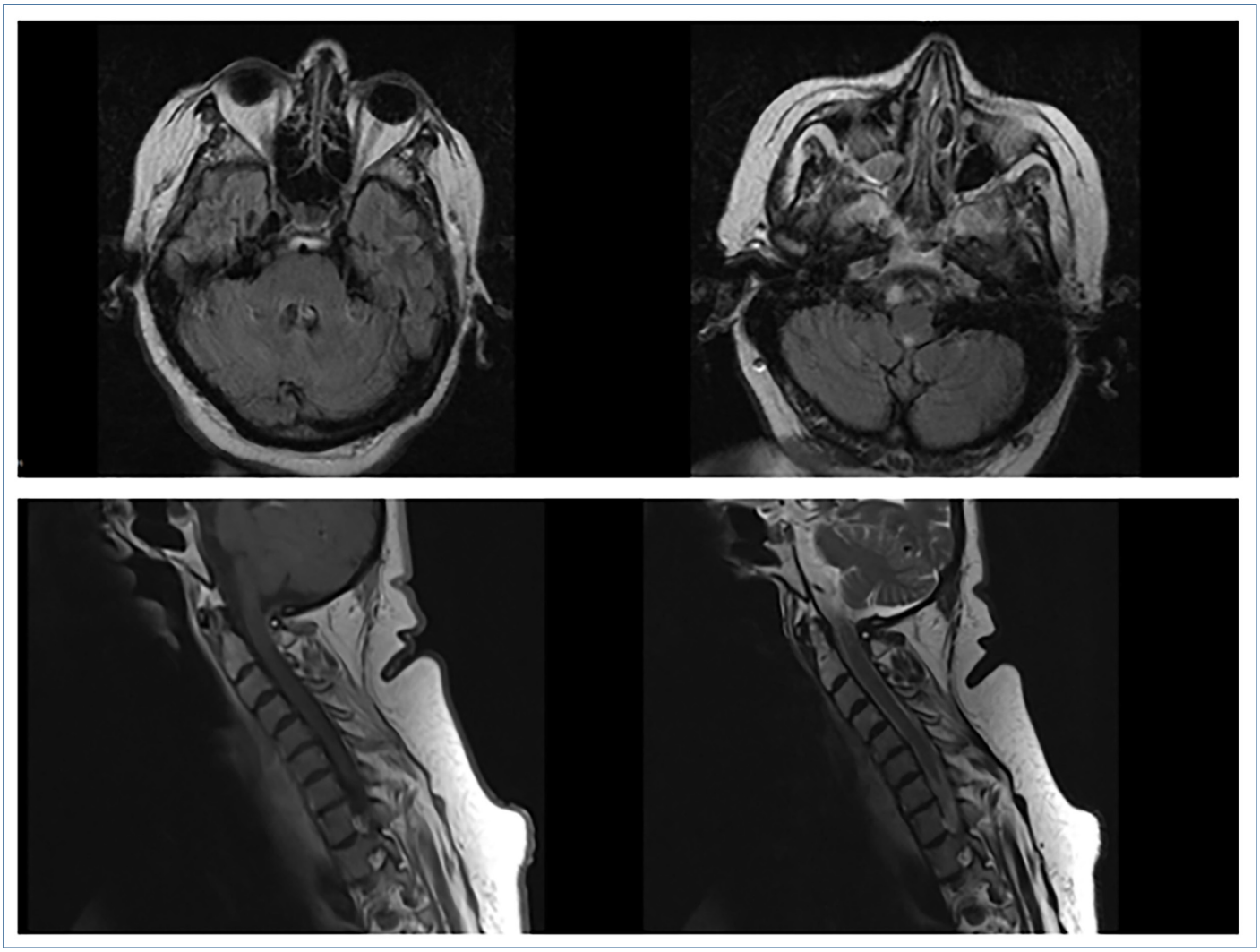

Figure 1. Brain and cervical magnetic resonance imaging scans of the patient after radiotherapy. Brainstem can be seen on the first line, and cervical medulla spinalis on the second line. There are no significant findings on the scans.

cerebellar ataxia (1). The presence of jaw-opening dystonia is reported as frequent as 25% (3). As our patient, the predominance of women with dystonia and other clinical features has been reported. Laryngospasm with respiratory failure necessitated tracheostomy in our patient. Laryngospasm may cause the death of patients with anti-Ri antibodies (1). In the autopsy series of patients with dystonia and laryngospasm, diffuse perivascular and interstitial lymphoplasmacellular infiltration and gliosis were detected in basal ganglia, amygdala, frontal cortex, and white matter and neuronal loss in the spinal gray matter was noted (3). Simard et al. (1) reported that patients with Ri-PNS could not walk unassisted at one year and that half of the patients died within three years of disease onset.

The incidence of NPC-associated PNS is unknown. Early treatment of the underlying malignancy and PNS immunotherapy may improve morbidity and mortality rates (1,9). Our patient partially benefited from the corticosteroid and IVIG treatment. In addition, improvement after botulinum toxin injection into cervical muscles was partial and short-acting in our patient.

As a result, to the best of our knowledge, this is the first report of a patient with cervical dystonia, laryngospasm, and spastic quadriparesis related to NPC with anti-Ri antibodies. Similar rare clinical presentations should be considered with the anti-Ri antibodies-associated PNS spectrum for patients with NPC.

Acknowledgments: We thank the patient and family members for participating in this study.

Informed Consent: The caregiver of the study participant gave written informed consent before inclusion in this work.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept- HH, FH; Design- HH, AÇ, FH, BS, ZT, BB, ME; Supervision- HH, AÇ, FH, BS, ZT; Resource- HH, AÇ, BS, ZT; Materials- AÇ, BS, ZT; Data Collection and/or Processing- HH, AÇ, FH, BS, ZT, BB, ME; Analysis and/or Interpretation- HH, FH, BB, ME; Literature Search- HH, AÇ, FH, BS, ZT, BB, ME; Writing- AÇ, FH, BS, ZT; Critical Reviews- HH, BB, ME.

Conflict of Interest: The authors declared that there is no conflict of interest.

Financial Disclosure: None

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