Paraneoplastic Cochleovestibulopathy in Adolescence
Illustrative Case, Large Series, and Clues Toward Earlier Diagnosis

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INTRO & OBJECTIVES

- Paraneoplastic rhombencephalitis is a potentially devastating neurologic autoimmune syndrome that can begin with cochlear or vestibular dysfunction
- Describe an adolescent male presenting with hearing loss as the initial symptom of KLHL11-IgG-associated cochleovestibulopathy and rhombencephalitis
- Provide comprehensive description of the features associated with paraneoplastic cochleovestibulopathy
- Evaluate long term clinical outcomes

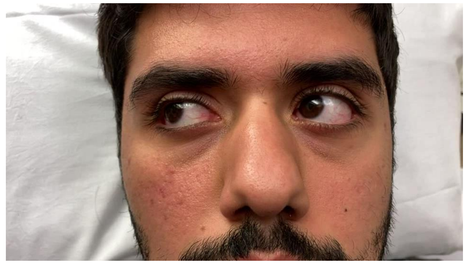
METHODS

- Retrospectively identified medical records of 144 Mayo Clinic patients with hearing impairment and/or vestibulopathy evaluated for paraneoplastic neural-specific antibodies from 2007 to 2021
- Included: a) Patients with sensorineural hearing loss, tinnitus, vestibular dysfunction, who b) Underwent full paraneoplastic neural-specific antibodies and cancer screening, and c) Onset of cochleovestibulopathy within 3 years before or after tumor/antibody detection
- Excluded: a) Alternative etiologies of hearing loss (chemotherapy, presbycusis), or b) Unknown onset of cochleovestibulopathy

CASE REPORT

- A 17-year-old male developed progressive right-sided hearing loss over 3 years and underwent cochlear implant but then developed profound left hearing loss followed by progressive gait and limb ataxia, head motion-induced oscillopsia, and intermittent binocular diplopia and became wheelchair bound
- Examination and vestibular evaluation showed combined effects from cerebellar dysfunction and bilateral vestibulopathy, including head motion-induced oscillopsia aggravated by head titubation, gaze evoked nystagmus, impaired pursuit, saccadic dysmetria, and impaired visually-enhanced vestibulo-ocular reflex and head impulse test (video 1)
- Serum and CSF revealed KLHL11-IgG antibodies, and PET-CT demonstrated a mediastinal mass that proved to be a seminoma (figure 1)

VIDEO 1



Ocular motor and vestibular exam findings characteristic of combined cerebellar and bilateral vestibular dysfunction

RESULTS

DEMOGRAPHICS

- 26 patients had findings consistent with paraneoplastic cochleovestibulopathy
- Majority were males (n=23, 88%), median age of 45 years (range 28-70 years)
- Median follow up period of 20 months (range 1-133 months)

PRESENTING SYMPTOMS & HEARING LOSS

- 15 of 26 patients (58%) had cochleovestibulopathy as their initial presenting symptoms (8 vertigo only, 4 hearing loss only, 3 both together)
- 10 of 26 (38%) developed cochleovestibulopathy with or after rhombencephalitis or encephalomyelitis
- 24/26 (92%) developed hearing loss: Usually with tinnitus, bilateral (symmetric=asymmetric), severe-profound, worsened despite treatment

VESTIBULAR & OCULAR MOTOR FEATURES

- Vertigo in 16 of 26 patients (62%): acute/subacute constant > episodic positional
- Nystagmus in most: gaze-evoked or spontaneous vertical > horizontal
- Ocular motor findings in most: impaired pursuit > abnormal saccades and ocular misalignment
- Overall type of vestibulopathy: central > combined > peripheral

FIGURE 1

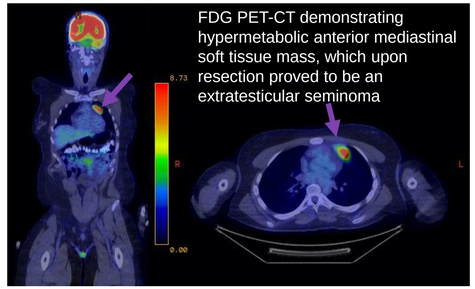
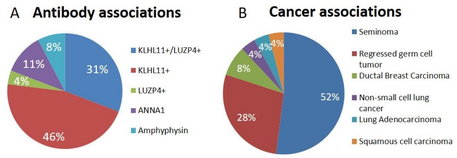
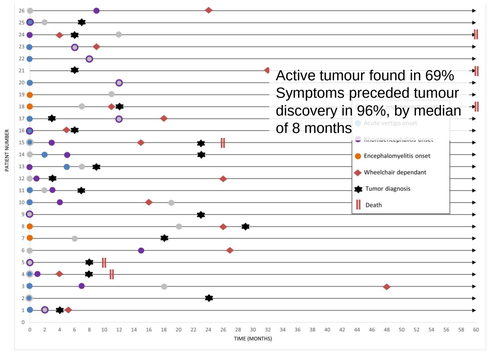


FIGURE 2



Antibody and cancer associations in 26 patients with paraneoplastic cochleovestibulopathy. None had Ma2 antibodies.

FIGURE 3



Timeline of symptom onset, wheelchair dependence, and tumour diagnosis

TREATMENT & OUTCOMES

- All patients (26) received immunotherapy: first steroids, IVIg, PLEX; then cyclophosphamide, rituximab, mycophenolate mofetil
- Most patients (17) received cancer treatment: surgery, chemotherapy, radiotherapy
- Hearing loss worsened among 16/22 (73%)
- Most patients' neurological function worsened over time (16/26, 62%); 6 patients died

CONCLUSIONS

- Paraneoplastic cochleovestibulopathy is a distinguishable phenotype, most often affecting young males with occult seminoma
- KLHL11-IgG is the most commonly associated neural-specific antibody
- Most patients present with acute/subacute vestibular syndrome with or followed by sensorineural hearing loss
- Hearing loss has asymmetric onset, usually with rapid progression and refractory course
- Nearly all patients soon develop brainstem and/or cerebellar features
- Earlier recognition may lead to early tumor detection and treatment and improved outcomes

REFERENCES

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