

Teaching Course
Current Topics in Neuro-Oncology

**Paraneoplastic and Other Encephalitides
in Cancer Patients**

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Disclosure



I have NO financial disclosure or conflicts of interest with the presented material in this presentation.

Learning Objectives



After completing this activity, participants will be able to:

- Describe definition, complex heterogeneities and clinical manifestations of paraneoplastic and other encephalitides (e.g. from immunotherapy) in cancer patients;
- Investigate and diagnose paraneoplastic and other encephalitides in cancer patients;
- Summarize the principles of treatment of paraneoplastic and other encephalitides in cancer patients.

Key Messages

- Paraneoplastic encephalitis: immune-mediated CNS dysfunction induced by systemic cancer.
 - Encephalitis in otherwise healthy (no known cancer) individuals.
 - High-risk phenotypes: encephalomyelitis, limbic encephalitis, rapidly progressive cerebellar syndrome, opsoclonus-myoclonus.
 - Clinical diagnosis with supporting investigations such as brain MRI, EEG, blood & CSF neuronal autoantibody panel testing.
 - Exclude other causes such as infection.
- Neuronal autoantibodies associated with encephalitis:
 - High-risk (>70% with cancer): Hu (ANNA-1), CV2/CRMP5, Yo (PCA-1), Ri (PCA-2), SOX1, amphiphysin, Ma, Ma2, Tr (DNER), KLHL11.
 - Intermediate-risk (30%-70% with cancer): AMPAR, GABA_BR, mGluR5, P/Q VGCC, NMDAR.
 - Low-risk (<30% with cancer): mGluR1, GABA_AR, CASPR2, GFAP, GAD65, LGI1, DPPX, GlyR, AQP4, MOG.

Key Messages

- Cancer screening: Chest/abdomen/pelvis CT, mammography/breast MRI, pelvic/testicular ultrasonography, PET-CT.
- Treatments of most paraneoplastic encephalitis consist of tumor-directed therapy and early immunosuppression:
 - First-line treatment: Corticosteroids +/- IVIg or plasma exchange.
 - Second-line treatment: Rituximab, cyclophosphamide.
- Neurologists should be aware of encephalitis as an immune-related adverse event caused by cancer immunotherapy such as immune checkpoint inhibitor (ICI) and CAR-T cell therapy.
- Paraneoplastic encephalitis with high-risk antibodies may be precipitated or worsened by ICI treatment.
 - Treatment: withhold ICI, corticosteroids.

References

1. Graus F, Vogrig A, Muniz-Castillo S, et al. Updated diagnostic criteria for paraneoplastic neurologic syndromes. *Neurol Neuroimmunol Neuroinflamm* 2021;8:e1014.
2. Abboud H, Probasco JC, Irani S, et al. Autoimmune encephalitis: proposed best practice recommendations for diagnosis and acute management. *J Neurol Neurosurg Psychiatry* 2021;0:1-12.
3. Flanagan EP. Paraneoplastic disorders of the nervous system. *J Neurol* 2021 April 27. doi: 10.1007/s00415-021-10570-1.
4. Nersesjan V, McWilliam O, Krarup LH, et al. Autoimmune encephalitis related to cancer treatment with immune checkpoint inhibitors: Systematic review. *Neurology* 2021. doi: 10.1212/WNL.0000000000012122.
5. Graus F, Dalmau J. Paraneoplastic neurological syndromes in the era of immune-checkpoint inhibitors. *Nat Rev Clin Oncol* 2019;16:535-548.
6. Dalmau J, Armangue T, Planaguma J, et al. An update on anti-NMDA receptor encephalitis from neurologists and psychiatrists: mechanisms and models. *Lancet Neurol* 2019;18:1045-1057.
7. Uy CE, Binks S, Irani SR. Autoimmune encephalitis: clinical spectrum and management. *Pract Neurol* 2021;0:1-14.