Anti-AK5 limbic encephalitis in a patient with pleural mesothelioma

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BACKGROUND

Limbic encephalitis with antibodies against adenylate kinase 5 (AK5) is rare, typically presenting with severe episodic amnesia. Although it shares features with paraneoplastic encephalitis, including the intracellular antigen localization, no association with malignancy has been reported so far.[1-3]

OBJECTIVE

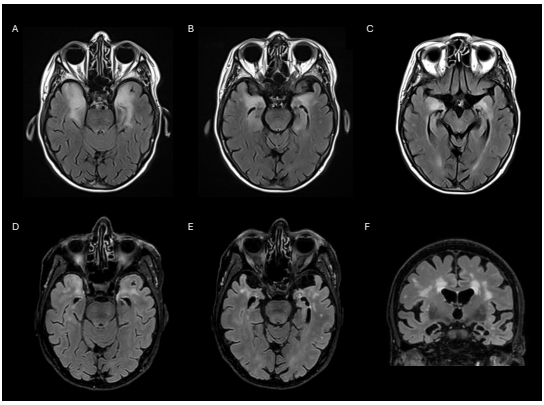
To describe a case of anti-AK5 limbic encephalitis in association with pleural mesothelioma, and to investigate AK5 antigen expression in cancer cells.

METHODS

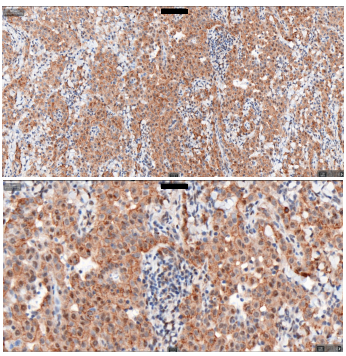
Immunohistochemistry (IHC) for AK5 was performed with commercially available anti-AK5 antibodies[4] on the patients' tumor tissue sample, on one age- and sex-matched control mesothelioma sample, on one lung adenocarcinoma sample.

RESULTS

- 82-year-old woman with subacute-onset memory deficits, asthenia and weight loss. Prior history of pleural mesothelioma diagnosed 2 years before, stable and in surveillance after 4 months of chemotherapy (CT)
- Brain MRI → bilateral T2/FLAIR hyperintense signal alterations in the temporal lobes (Figure A-B-C) evolving toward severe atrophy within 3 months (Figure D-E-F)
- Neuropsychological testing → severe anterograde episodic amnesia, spatiotemporal disorientation, reduced cognitive flexibility
- CSF → normal cells, glucose and protein levels
  CSF-restricted oligoclonal bands
  Tau 427 ng/L, normal p-tau and β-amyloid 1-42
  Ab anti-AK5 +
- Full-body CT scan → mesothelioma progression
- Treatment → 2nd line CT (carboplatin and pemetrexed)
  IV methylprednisolone, IVIg, Rituximab
- No significant therapeutic response was observed; cancer progressed
- Last follow-up (2 years from onset) → neurologically stable (severe memory deficits, full independence in basic daily activities)

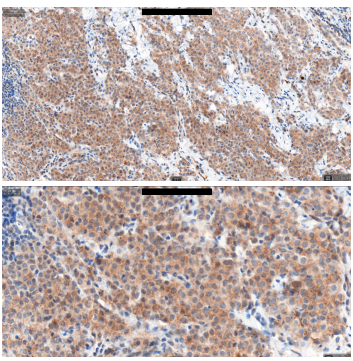


Patients' mesothelioma



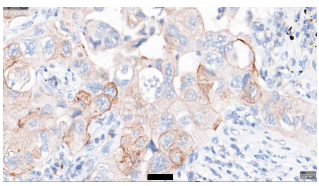
IHC staining revealed AK5 membranous and cytoplasmic expression in 100% tumor cells

Control mesothelioma



No differences observed

Control lung adenocarcinoma



AK5 expression in 10% of tumor cells

CONCLUSIONS

- We described a patient with anti-AK5 limbic encephalitis and pleural mesothelioma, demonstrating AK5 antigen expression in all cancer cells
- We can hypothesize a paraneoplastic autoimmunity, but we cannot draw any definitive conclusions
- Caution in using tumor expression of the cognate antigen as evidence of a pathogenic link with PNS in cases of unexpected tumor and antibody occurrence

References

1. Mullia-Castrillo S, Hedou JJ, Ambati A, Jones D, Vogrig A, Pinto AL, et al. Distinctive clinical presentation and pathogenic specificities of anti-AK5 encephalitis. Brain J Neurol. 2021 Oct 22;144(9):2709–21.
2. McKeon-Makki I, McKeon A, Yang B, Pittock SJ, Lopez-Chiriboga S, Komorowski L, et al. Adenylate kinase 5 (AK5) autoimmune encephalitis: Clinical presentations and outcomes in three new patients. J Neuroimmunol. 2022 Jun 15;367:577861.
3. Do LD, Chanson E, Desestret V, Joubert B, Ducray F, Brugière S, et al. Characteristics in limbic encephalitis with anti-adenylate kinase 5 autoantibodies. Neurology. 2017 Feb 7;88(6):514–24.
4. Sigma-Aldrich.https://www.sigmaaldrich.com/IT/it/specificationsheet/SIGMA/HPA057255.