NEUROPSYCHIATRIC SYMPTOMS OF PARANEOPLASTIC DISORDERS: AN UPDATE

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INTRODUCTION

- **Paraneoplastic disorders (PD)** result from indirect, nonmetastatic effects of cancer. These may affect the **central nervous system (CNS)**
- PD are a consequence of substances produced by the tumour (hormones or cytokines), or by an **immune response** against the tumour.
  - ✓ **Antineuronal antibodies** that recognize various antigens throughout the nervous system
  - ✓ Antibodies are characterized by the cellular location of the antigens they recognize: **intracellular antigens or cell-surface antigens**
- Most commonly associated malignancies: small cell lung cancer (SCLC) (3-5%), thymoma (20%), breast and gynecologic tumors (<1%)
- In many cases, the first symptoms are **psychiatric manifestations** affecting cognition, consciousness, behavior, mood and perception
- The majority of PD manifest themselves in the form of **limbic encephalitis (LE)**:
  - ✓ Inflammation and degeneration of the temporal gray matter in the limbic area
  - ✓ Subacute onset of short-term memory loss, seizures, irritability, depression and cognitive decline.

OBJECTIVES AND METHODS

This research aims to describe the types of paraneoplastic disorders associated with neuropsychiatric symptoms. For this purpose, a literature review of scientific articles was conducted about this issue through the Pubmed database.

RESULTS

Syndromes associated with cell-surface antigens

- Antibodies against voltage-gated potassium channels (VGKC)
  - ✓ SCLC and thymoma
  - ✓ Midlife or elderly
  - ✓ Manifestations: LE, confusion, acute and severe memory impairment, behaviour changes, apathy, visual hallucinations
- Anti-NMDA receptor Antibodies
  - ✓ Many are firstly diagnosed as psychiatric disorders
  - ✓ Women (75%) (ovarian teratoma) or children
  - ✓ Viral prodrome (1 week) followed by neuropsychiatric symptoms: delusions, hallucinations, mania, agitation (1-3 weeks); then, neurologic complications: movement abnormalities, dysautonomia, seizures (weeks-months)
  - ✓ 85% maintain prolonged deficits (attention deficit, impulsivity, behavioural disinhibition, sleep disorder) despite treatment
- Anti-AMPA receptor Antibodies
  - ✓ SCLC, breast cancer, thymoma
  - ✓ Midlife, women
  - ✓ Manifestations: LE with prominent psychiatric features
- Anti-GABA_B receptor Antibodies
  - ✓ SCLC
  - ✓ Manifestations: seizures, confusion, psychosis, hallucinations
- Others: LGI1, Caspr2, Anti-GluR1, Anti-GluR5, anti-AChR

Syndromes associated with intracellular antigens

- Anti-Hu Antibodies
  - ✓ SCLC
  - ✓ Midlife, smokers
  - ✓ Manifestations: LE, sensory neuropathy, confusion, short-term memory loss, sleep disturbance, agitation, hallucinations
- Anti-Ma Antibodies
  - ✓ Testicular tumours
  - ✓ Manifestations: LE, short-term memory loss, mood disturbance, panic reactions, obsessive-compulsive disorders (OCD)
- Anti-CRMP5 and Anti-CV2 Antibodies
  - ✓ SCLC and thymoma
  - ✓ Manifestations: LE, chorea, acute memory deficits, psychosis, mood disturbance, personality changes, OCD
- Others: Anti-Yo, Anti-Ri, Anti-Tr/DNER, Anti-GAD, Anti-recoverin, Anti-bipolar cells, Anti-amphiphysin

When to suspect?	
Yellow Flags ↓ level of consciousness Abnormal postures or movements Autonomic instability Focal neurological deficits Aphasia or dysarthria Rapid progression of psychosis Hyponatremia Catatonia Other autoimmune diseases	Red Flags Cerebrospinal fluid lymphocytic pleocytosis Epileptic seizures Faciobrachial dystonic seizures Suspected malignant neuroleptic syndrome MRI abnormalities Electroencephalogram abnormalities

Treatment: Early recognition and diagnosis; Immunotherapy (steroids, immunosuppression, immunomodulation); Tumour treatment

CONCLUSIONS

PD are difficult to diagnose mainly because of the wide variety of presentation symptoms. Early recognition is of extreme importance for the most successful treatment possible. There aren't many studies on the impact of treating psychiatric symptoms in PD, or on the drugs to be used. Clinicians should be alert for the possible psychiatric presentation of these disorders, which may be misdiagnosed as psychiatric conditions.

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