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**Paraneoplastic Cerebellar Degeneration in Patients With Gastrointestinal Malignancies**

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**Background:** Paraneoplastic cerebellar degeneration (PCD) is a rare neurodegenerative disease of unclear etiology that may point to the presence of an occult malignancy. It is usually associated with ovarian, uterine, and breast carcinoma in females and rarely with gastrointestinal malignancies. While diagnostic criteria are generally accepted, therapy is largely debatable with only few anecdotal reports of success. Management of the syndrome is often unsatisfying, with severe neurologic sequelae. We present the first review of epidemiology, clinical findings, and outcomes of patients with PCD associated with gastrointestinal malignancies.

**Methods:** A PubMed and OVID database search of the literature between January 1981 and July 2009 was performed using the keyword PCD in combination with gastrointestinal malignancy, etiology, and management. All relevant articles were reviewed and references screened for additional articles. Data regarding patient age and gender, pathology, treatment, and outcome were recorded. Our search yielded 15 reported cases of PCD in patients with GI cancers.

**Results:** The mean age at the time of diagnosis was 61.6 years with M:F ratio of 2:1. The onset of neurologic symptoms preceded the diagnosis of malignancy in 72% of cases. Ataxia, dysarthria, diplopia and weakness were the most common presenting symptoms. Adenocarcinoma was present in 73% of cases, with stomach (63%), esophagus (27%), and colon (9%) being the three sites of disease. Three patients had small cell carcinomas (esophagus n=2, duodenum n=1) and one patient had anaplastic carcinoma of jejunum. All tumors with associated PCD had evidence of regional lymph node involvement

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at the time of diagnosis. Stabilization of PCD with partial improvement of the neurologic symptoms was seen in two cases after tumor removal, but the majority of patients remained severely disabled. No clinical response was reported with prednisone, plasmapheresis, or intravenous immunoglobulins (IVIG) in any reported case. However, all of the patients were treated after progressive and possibly irreversible neurologic deterioration. PCD followed a progressive clinical course in >80% of patients; 60% died within 2 years of cancer diagnosis with neurologic deterioration being the primary cause of death in >33%.

**Conclusions:** a) Early recognition of PCD and a search for occult malignancy can help diagnose gastrointestinal cancer at an early stage in more than two-thirds of patients, before widespread metastases, hence increasing the window of opportunity for curative surgical resection.

b) The invasion of regional lymph-nodes implies that tumor must reach nodes to trigger an immune response, suggesting a role of T- and B- lymphocytes in mediating this disorder.

c) Therapy, including surgical resection of cancer, may be most beneficial if given early, suggesting that PCD should always be included in the differential diagnosis of patients with unforeseen neurologic symptoms, and empiric immunomodulatory therapy should be well thought-out.