Paraneoplastic syndrome

A paraneoplastic syndrome is a syndrome that is the consequence of cancer in the body, but unlike mass effect, is not due to the local presence of cancer cells.

In contrast, these phenomena are mediated by humoral factors (such as hormones or cytokines) secreted by tumor cells or by an immune response against the tumor.

Paraneoplastic syndromes are typical among middle-aged to older patients, and they most commonly present with cancers of the lung, breast, ovaries, or lymphatic system (lymphoma).

Sometimes, the symptoms of paraneoplastic syndromes show before the diagnosis of a malignancy, which has been hypothesized to relate to the disease pathogenesis. In this paradigm, tumor cells express tissue-restricted antigens (e.g., neuronal proteins), triggering an anti-tumor immune response that may be partially or, rarely, completely effective in suppressing tumor growth and symptoms.

Patients then come to clinical attention when this tumor immune response breaks immune tolerance and begins to attack the normal tissue expressing that (e.g., neuronal) protein.

The abbreviation PNS is sometimes used for paraneoplastic syndrome, although it is used more often to refer to the peripheral nervous system.

Paraneoplastic syndromes affecting the nervous system

Occurs in < 1% of cancer patients. Peripheral sensory neuropathy of unknown etiology has been associated with cancer since its earliest description. Therefore, in patients with sensory neuropathy of unknown etiology, occult neoplasms should be ruled out. If the work-up is negative, the patient should be followed since up to 35% of patients will be found to have cancer after a mean interval of 28 months after the onset of neuropathy (range: 3–72 months) (no one particular cancer type predominated, in spite of the fact that historically lung cancer is the most frequent neoplasm associated with sensory neuropathy).

Paraneoplastic syndromes (PNS), AKA “remote effects of cancer.” Develop acutely or subacutely. May mimic or be mimicked by metastatic disease. The neurologic disability is usually severe and may precede other manifestations of cancer by 6–12 mos. Often one particular neural cell type is predominantly affected. The presence of a PNS may portend a more benign course of cancer. 16% of patients with lung Ca, and 4% with breast cancer develop a paraneoplastic syndrome. Pathogenesis is unknown. Theories:? toxin;? competition for the essential substrate;? opportunistic infection;? auto-immune process.

Kerezoudis et al. from the Mayo Clinic Rochester published a case of a middle-aged woman with a diffuse, nonenhancing, progressively atrophic T2-hyperintense lesion involving the left frontotemporal lobes and insula found to be synchronous high-grade sinonasal neuroendocrine carcinoma (SNEC) after initial endonasal resection. In 2014, a 47-year old woman underwent resection of a left-sided high-grade ethmoidal neuroendocrine carcinoma after presentation with weight gain and increased

levels of serum and urine cortisol. Concurrent with the initial presentation, she was noted to have a nonenhancing, hyperintense signal change on T2-weighted images on the left frontotemporal lobes and insula thought to be paraneoplastic. Moreover, low titer antibodies to voltage-gated potassium channels were present, raising concern for limbic encephalitis. However, the patient was asymptomatic. A little more than a year after initial presentation, she noted excessive fatigue, daytime somnolence, and cognitive decline. Imaging revealed a gradually progressive, nonenhancing, T2-hyperintense signal abnormality with progressive atrophy in the left anteroinferior frontal lobe, anteromedial temporal lobe, insula bilateral cingulate gyri, and bilateral thalami. Given the progressive nature of the abnormality, stereotactic biopsy was performed, which confirmed the lesion to be metastatic, infiltrative SNEC. In summary, this is a rare case of a synchronous presentation of a high-grade SNEC with an unusual appearance that diffusely infiltrated the brain, likely directly involving the left olfactory nerve and spreading along olfactory projections. This case draws physicians' attention to the possibility that although paraneoplastic syndromes are most likely benign, dissemination of the primary cancer is a diagnostic possibility [1)].

1)

Kerezoudis P, Maloney PR, McCutcheon B, Janus J, Jentoft M, Kaufmann T, Lachance DH, Van Gompel JJ, Bydon M. Paraneoplastic syndrome or metastatic sinonasal neuroendocrine carcinoma? Clinical conundrum. Ear Nose Throat J. 2018 Oct-Nov;97(10-11):E15-E18. PubMed PMID: 30481850.