

Intracranial germ cell tumor diagnosis

Neuropathology

Intracranial **germinomas** are characterized by a massive **immune cell** infiltrate.

Histologically equal to gonadal seminoma, apart from granulomatous reaction which is relatively frequent in extracranial lesions, but quite unusual in the intracranial ones ^{1) 2)}.

Zapka et al. systematically characterized these immune cells in 28 germinomas by immunophenotyping and image analysis. mRNA expression was analyzed by Nanostring technology and in situ RNA hybridization. Tumor infiltrating lymphocytes (TILs) were composed of $61.8\% \pm 3.1\%$ (mean \pm SE) CD3-positive T cells, including $45.2\% \pm 3.5\%$ of CD4-positive T-helper cells, $23.4\% \pm 1.5\%$ of CD8-positive cytotoxic T cells, $5.5\% \pm 0.9\%$ of FoxP3-positive regulatory T cells, and $11.9\% \pm 1.3\%$ PD-1-positive TILs. B cells accounted for $35.8\% \pm 2.9\%$ of TILs and plasma cells for $9.3\% \pm 1.6\%$. Tumor-associated macrophages consisted of clusters of activated PD-L1-positive macrophages and interspersed anti-inflammatory macrophages expressing CD163. Germinoma cells did not express PD-L1. Expression of genes encoding immune cell markers and cytokines was high and comparable to mRNA levels in lymph node tissue. IFNG and IL10 mRNA was detected in subfractions of TILs and in PD-L1-positive macrophages. Taken together, the strong immune reaction observed in germinomas involves inflammatory as well as various suppressive mechanisms. Expression of PD-1 and PD-L1 and infiltration of cytotoxic T cells are biomarkers predictive of response to anti-PD-1/PD-L1 therapies, constituting a rationale for possible novel treatment approaches ³⁾.

MRI

Intracranial germ cell tumor magnetic resonance imaging

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Schmalisch K, Pantazis G, Ebner FH, et al. Pineal germinoma with granulomatous reaction, often a pitfall in endoscopic biopsy. Report of two cases and review of the literature. Clin Neurol Neurosurg 2012;2013:741-5

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Mueller W, Schneider GH, Hoffmann KT, et al. Granulomatous tissue response in germinoma, a diagnostic pitfall in endoscopic biopsy. Neuropathology 2007;2013:127-32

³⁾

Zapka P, Dörner E, Dreschmann V, Sakamoto N, Kristiansen G, Calaminus G, Vokuhl C, Leuschner I, Pietsch T. Type, Frequency, and Spatial Distribution of Immune Cell Infiltrates in CNS Germinomas: Evidence for Inflammatory and Immunosuppressive Mechanisms. J Neuropathol Exp Neurol. 2017 Dec 11. doi: 10.1093/jnen/nlx106. [Epub ahead of print] PubMed PMID: 29237087.

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