Tumour necrosis factor-α in malignant melanomatous meningitis

Meningeal infiltration by neoplastic cells is an ominous prognostic sign in patients suffering from systemic cancer. After carcinoma of the breast and bronchus, malignant melanoma is the third most common primary tumour in patients with diffuse leptomeningeal metastasis.1

Intrathelial synthesis of IgG and detection of oligoclonal immunoglobulin bands on isoelectric focussing gels of CSF in meningeal carcinomatosis, suggest immune recognition of tumour cells within the CNS.2 We determined the levels of two cytokines, tumour necrosis factor-α (TNFα) and interferon gamma (IFNγ), in paired serum and CSF samples obtained from 45 patients with meningeal malignancies. Cytokines, for example, interleukins, interferons, and TNFα, are multifunctional messenger molecules currently evaluated for new approaches of immunotherapy in disseminated malignancies. Our study included CSF and serum samples, stored at −70°C after lumbar puncture and centrifugation without further processing, from patients with diffuse leptomeningeal metastasis from cancer of the breast (14), bronchus (7), ovary, cervix, prostate, kidney, stomach (1 each), and unknown origin (4), malignant melanoma (4), non-Hodgkin lymphoma (9), multiple myeloma (1), and Hodgkin’s disease (1). Commercial ELISA kits were purchased from British Biotechnology, Oxford, UK, (TNFα), and Endogen, Boston, USA (IFNγ). Sensitivity was 50 ng/l for IFNγ and 40 ng/l for TNFα. IFNγ was found in the CSF in carcinomatosis from two cases of breast cancer (322 and 899 ng/l), one case of cancer of unknown origin (639 ng/l), and one case of non-Hodgkin lymphoma (66 ng/l). IFNγ in serum was positive in two cases of cancer of the breast (56 and 901 ng/l) neither of which had detectable IFNγ in the CSF, and one case of cancer of the bronchus (526 ng/l). IFNγ was also present in the serum of the patient with non-Hodgkin lymphoma (48 ng/l) who had IFNγ in the CSF.

TNFα was detected in three of four CSF samples but not in the serum of patients with meningeal infiltration from melanoma (61, 78, and 166 ng/l) or in CSF in other neoplastic diseases. TNFα was, however, detected in sera from three patients with meningeal carcinomatosis (breast, 534 ng/l; bronchus, 46 ng/l; unknown origin, 118 ng/l) and one patient with non-Hodgkin lymphoma (48 ng/l). None of the CSF or serum samples contained both IFNγ and TNFα. TNFα may mediate inflammatory tissue destruction in bacterial meningitis, particularly severe meningococcal disease,3 inflammatory demyelination,4 and tumour cell cytotoxicity5 in vitro.

To our knowledge, this is the first report on TNFα in meningeal malignancies. New approaches to an immunotherapy of malignant melanoma are evolving rapidly, and are based on specific immunogenic features of this malignancy, for example, inhibition of tumour cell proliferation in vitro by IFNγ and TNFα.6 Although elevated levels of TNFα in the CSF of patients with malignant melanomatous meningitis are still a preliminary finding, the lack of similar results in a large control group of other meningeal malignancies confirms the existence of specific interactions between melanoma cells and the host’s immune system. This warrants further investigation.

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