Re: Personality and the Risk of Cancer

Nakaya et al. (1) presented a large prospective study demonstrating that personality does not play a substantial role in the causation of cancer. As the authors concluded, the association between neuroticism and prevalent cancer may be a consequence, rather than a cause, of cancer diagnosis or symptoms. This result obviously contrasts with those of other studies [e.g., (2)] showing that chronically depressed individuals, especially among the elderly, are at increased risk of developing cancer.

We have obtained laboratory results from immunologic evaluation of cancer patients that are consistent with the findings of Nakaya et al. Among other markers of immune activation and inflammation, concentrations of neopterin are increased in serum and urine of patients with various types of cancer, with higher concentrations predicting worse prognosis. Increased amounts of neopterin are released by monocyte-derived macrophages on induction with interferon-γ and indicate Th1-type immune activation (3). In parallel to promoting the formation of neopterin, interferon-γ induces the enzyme indoleamine–2,3-dioxygenase (IDO) in a variety of cells (4). IDO converts the essential amino acid tryptophan to kynurenine within the nicotinamide–adenine dinucleotide biosynthetic pathway. When endogenous interferon-γ is formed in humans, not only neopterin concentrations but also tryptophan conversion is increased, diminishing blood tryptophan concentrations.

Accordingly, enhanced degradation of tryptophan and thus diminished tryptophan concentrations are detectable in the blood of patients with malignancy and are associated with poor prognosis (5,6).

Because tryptophan is a precursor for the biosynthesis of the neurotransmitter 5-hydroxytryptamine (5HT; serotonin), diminished tryptophan is associated with decreased serotonin production. In patients with colorectal cancer, lowered tryptophan concentrations have been found to be associated with reduced quality of life (6). And, interestingly, an association between decreased tryptophan concentrations and depressive symptoms has been observed in patients with cancer who are undergoing cytokine therapy (7).

We conclude that a tumor with a more drastic challenge of the immune system, as indicated by increased neopterin production, will be responsible for increased mortality. Depletion of tryptophan and the resulting neurotransmitter disturbances may underlie a higher susceptibility for depression in patients with more severe forms of cancer.

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REFERENCES


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