Paraneoplastic Disorder Study: A Look at the Effects of Cancer on Certain Cells in the Brain

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Paraneoplastic neurological disorders are syndromes found in cancer patients, not directly due to spread of cancer and involving destruction of specific populations of neurons. Characteristic antibodies against target neurons are found in serum and cerebrospinal fluid (CSF) of some patients with these disorders. In other patients, however, antibodies cannot be detected despite severe neuronal loss and clinical illness. Confocal microscopy, which allows 3-dimensional imaging of microscopic sections, provides a powerful tool to detect antibodies not visible with conventional microscopy. We studied serum and CSF from nine antibody-negative patients with unequivocal paraneoplastic syndromes. All patients had paraneoplastic syndromes but had not been found to have serum antineuronal antibodies by conventional light microscopy. These samples were compared with five antibody-positive patients with similar paraneoplastic syndromes. Serum from a normal individual without cancer was used as the negative control. Sections of human cerebellum were reacted with patient serum or CSF, stained with a fluorescent tag, fluorescein (FITC)-conjugated rabbit anti-human IgG, antibodies to neurons show green fluorescence staining Purkinje or other nerve cells. Samples from cancer patients known to have antibody produced bright staining of cerebellar neurons, specific for the type of tumor involved. In contrast, none of the samples from our nine patients produced specific staining. These studies indicate that some patients with paraneoplastic syndromes may not exhibit a detectable antibody response to neurons, making it less likely that destruction of nerve cells in these patients is caused by antibody. Destruction of nerve cells in these patients might thus be caused by T lymphocytes rather than antibody. It is also possible, however, that antibodies to nerve transmitter receptors or other cell surface structures might be present but bind to an area too small to be seen using light microscopy.