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Circulating endothelial progenitor cells in malignant gliomas.

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Object Recent experimental work suggests that circulating endothelial progenitor cells (cEPCs) are recruited to the angiogenic vascular system of malignant gliomas. Consequently, the level of cEPCs has been proposed as a novel biomarker for the diagnosis and monitoring of these lesions. The aim of the present study was to examine the level of cEPCs and the level of EPC mobilizing mediators in the blood of patients with malignant gliomas. The authors were also interested in whether a correlation could be observed between the level of cEPCs and the extent of glioma angiogenesis determined by conventional methods. **Methods** Peripheral blood mononuclear cells from the whole blood of 12 patients with malignant gliomas (all glioblastomas multiforme [GBMs]), 10 with metastases to the brain, and 10 healthy volunteers were isolated using Ficoll density gradient centrifugation. The number of cEPCs was quantified by fluorescence-activated cell sorting analysis using antibodies against CD34, CD133, and VEGFR-2. Serum concentrations of VEGF and granulocytemacrophage colony-stimulating factor (GM-CSF) were determined using the enzyme-linked immunosorbent assay. **Histological analysis** of tumor blood vessel density was performed by CD34 immunohistochemical staining. **Results** The number of cEPCs was significantly higher in patients with GBMs than in those with metastases ($p < 0.04$) or in the healthy volunteers ($p < 0.004$). The serum VEGF concentrations in patients with GBMs and metastases were significantly higher than in the healthy volunteers ($p < 0.0001$). Similar findings were observed for concentrations of GM-CSF. In addition, the patients in the GBM group with higher levels of cEPCs had significantly higher tumor blood vessel densities (1.71 +/- 1.17% of total area) compared with patients who had low levels of cEPCs (0.62 +/- 0.28% of total area; $p < 0.02$). **Conclusions** Endothelial progenitor cells are increasingly mobilized in patients with malignant gliomas, and their levels correlate with tumor angiogenic activity. Therefore, the authors' results suggest that cEPCs may have the potential to serve as a novel biomarker for the identification of patients who would benefit from antiangiogenic therapy for GBM.

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