CORRESPONDENCE

Glioproliferative Lesion of the Spinal Cord as a Complication of "Stem-Cell Tourism"

TO THE EDITOR: Commercial stem-cell clinics have been highly publicized in the lay press and operate worldwide with limited or no regulation.[1] We report the case of a 66-year-old man who underwent intrathecal infusions for the treatment of residual deficits from an ischemic stroke at commercial stem-cell clinics in China, Argentina, and Mexico. He was not taking any immunosuppressive medications. In reports provided to him by the clinics, the infusions were described as consisting of mesenchymal, embryonic, and fetal neural stem cells. Progressive lower back pain, paraplegia, and urinary incontinence subsequently developed. Magnetic resonance imaging (MRI) revealed a lesion of the thoracic spinal cord and thecal sac; a biopsy specimen was obtained (Fig. 1).

Neuropathological analysis revealed a densely cellular, highly proliferative, primitive neoplasm with glial differentiation. Short tandem repeat DNA fingerprinting analysis indicated that the mass was predominantly composed of nonhost cells (see the Supplementary Appendix, available with the full text of this letter at NEJM.org). On the basis of histopathological and molecular studies, this glioproliferative lesion appeared to have originated from the intrathecally introduced exogenous stem cells. The lesion had some features that overlapped with malignant gliomas (nuclear atypia, a high proliferation index, glial differentiation, and vascular proliferation) but did not show other features typical of cancer (no cancer-associated genetic aberrations were detected on next-generation sequencing of 309 cancer-associated genes [see the Supplementary Appendix]). Thus, although the lesion may be a considered a neoplasm (i.e., a "new growth"), it could not be assigned to any category of previously described human neoplasm on the basis of the data we gathered. Radiation therapy led to decreased back pain, improved mobility of the right leg, and decreased the bulk of the lesion on MRI.

Embryonic and other stem cells have tumorigenic potential and have been proposed as a source of common origin for cancer. Embryonic stem cells form teratomas when injected into mice, and murine neural stem cells can transform into malignant gliomas with minimal genetic changes.[2] Furthermore, rapidly dividing cells in culture can acquire mutations that may predispose the cells to malignant transformation.

This case and others in which tumors have developed in the context of stem-cell tourism[3,4] (a trend in which patients travel for the purpose of obtaining therapy) illustrate an extremely serious complication of introducing proliferating stem cells into patients. Investigators have attempted to reduce the risk of stem-cell–related tumors in clinical trials by means of the measured administration of pluripotent stem cells or by differentiating stem cells in vitro into postmitotic phenotypes before administration.[5,6]

The unregulated commercial stem-cell industry is not only potentially harmful to individual patients but also undermines attempts to study stem-cell therapies in clinical trials. This case provides further support for the conclusions of an article advocating increased investigation of commercial stem-cell clinics and increased patient education regarding the risks of stem-cell

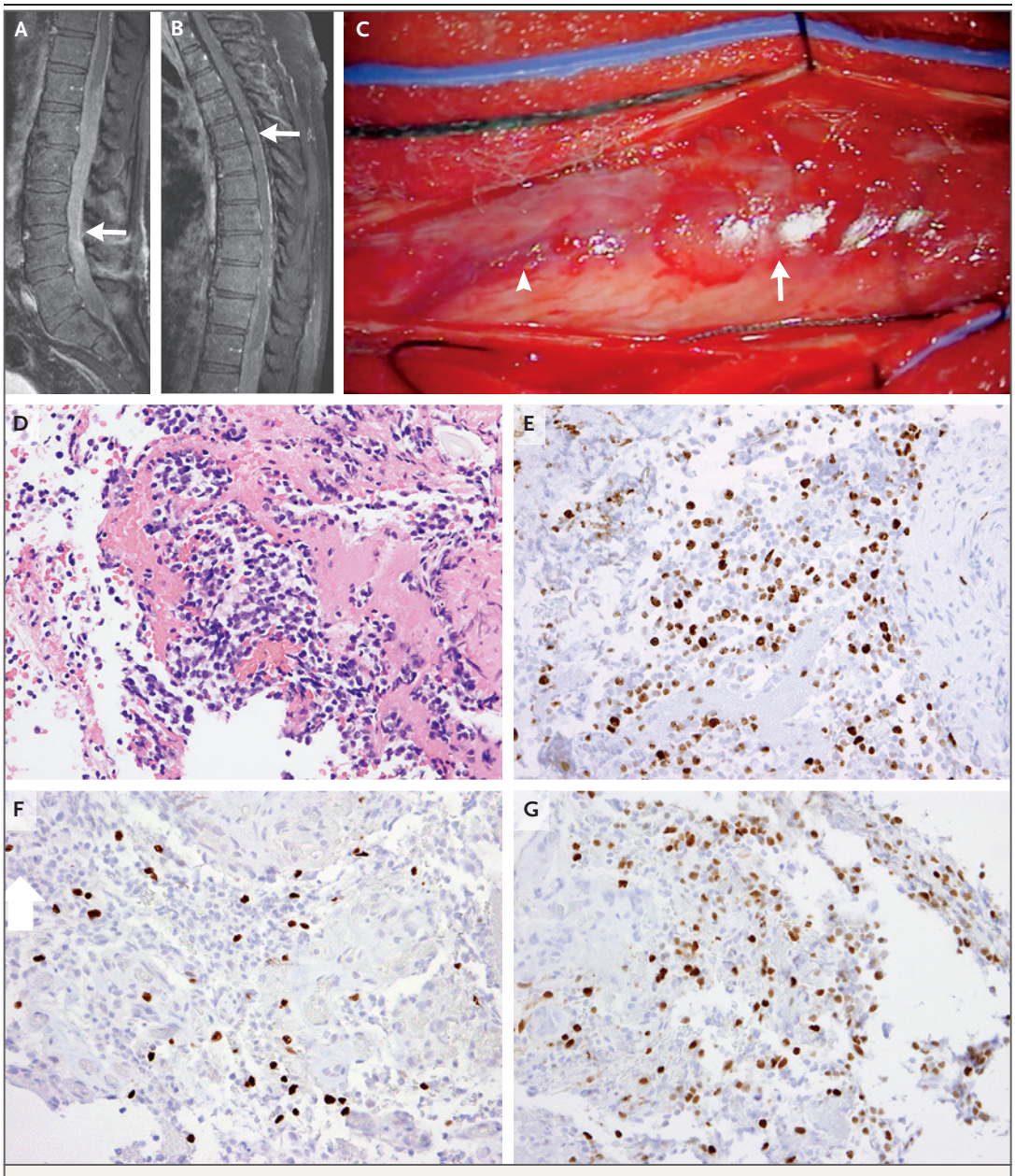

Figure 1. Findings Obtained on MRI, during Surgery, and after Biopsy.

Panels A and B show sagittal, T_1-weighted magnetic resonance imaging (MRI) scans of the spine obtained after the administration of contrast material. Panel A shows areas of enhancement in an intradural mass that extends throughout the lumbar spine (arrow), and Panel B shows the rostral extent of enhancement in the thoracic spine (arrow). Panel C shows abnormal arachnoid mater (arrow) and an engorged vein (arrowhead) during surgery after a dural incision was made. Panels D through G show histopathological specimens of lesional cells. Panel D shows intradural primitive atypical cells after staining with hematoxylin and eosin. Panels E, F, and G show the results of immunohistochemical testing for MIB-1 (MKI67), a marker of cellular proliferation, for OLIG2, a glial marker, and for SOX2, a glial stem-cell marker, respectively.

tourism.[1] Such experimental treatments must be studied in a safe, regulated environment.

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