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Putting a Stop to Cancer Pain

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Although analgesics as well as adjuvant medications can effectively control pain in most patients with cancer, side effects such as fatigue, anorexia, loss of short-term memory, sedation, delirium, constipation, itching and nausea can adversely affect performance status and diminish function and quality of life to the extent that anticancer therapies may not be tolerated.

Intrathecal Drug Delivery Offers an Alternative

Intrathecal drug delivery (ITD) offers an effective pain-control approach for cancer patients whose pain is not otherwise controlled or who develop analgesic-related side effects. Studies have established that patients receiving ITD had reduced pain, fewer drug toxicities and improved survival. Administration of intrathecal opioids and adjuvant medications also allows reductions of up to 200 percent in the amount of administered oral or parenteral medication with minimal side effects. Rapid pain relief also results in fewer hospitalizations for pain control and thus saves healthcare dollars.

Patient Selection and Drug Regimen

Patients who are intolerant to oral opioids or with pain refractory to high-dose opioids benefit from intraspinal opioids. Further, the addition of gamma-amino-butyric acid agonists and alpha-2 agonists to an opioid/local anesthetic regimen allows for control of severe neuropathic pain. In patients with visceral tumors or autonomic dysfunction that results in

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Endoscopic Endonasal Pituitary Surgery: Favorable Outcomes, Shorter Recovery Time

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Neurosurgeons have now developed a procedure in which an endoscope is inserted directly into the nostril and used to guide a direct endonasal sphenoidotomy to remove tumors of the pituitary gland. Pituitary tumors are relatively common, accounting for about seven percent of all primary brain tumors, and the majority of these tumors are pituitary adenomas. This new endoscopic-endonasal method represents the most novel trend in pituitary surgery in the past 30 years.

At the Maxine Dunitz Neurosurgical Institute, a fully endoscopic-endonasal method using image-guided surgical navigation and/or intra-operative MRI is routinely employed to remove pituitary gland tumors and to treat CNS leaks. Nasal packing is only rarely used, which improves patient comfort significantly. Most patients are discharged within one to two days after surgery and can return to normal work and other activities within two weeks. The fully endoscopic-endonasal procedure takes advantage of the dramatic mobility of the endoscope within the sphenoid sinus, coupled with the wide visual angle subtended to provide extensive exposure, good surgical mobility and a minimum of tissue destruction for improved patient outcome.

Endoscopic endonasal pituitary and skull base surgery is a rapidly advancing field that is leading to shorter hospitals stays, greater patient comfort, less tissue destruction and equivalent tumor removals when compared to the standard transphenoidal operation. The procedure is technically challenging and requires some specialized equipment, but because it represents a true advance in patient care will continue to become more common and is likely to largely replace the microscopic procedure over the next decade. The Maxine Dunitz Neurosurgical Institute is in the forefront of leading this trend toward the use of this innovative and effective procedure.

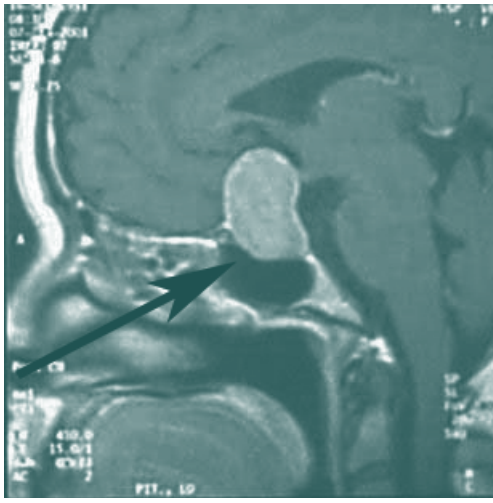

Figure 1: Schematic of direct endonasal endoscopic approach to a pituitary tumor. Since no incisions are visible, this is occasionally referred to as a "natural incision" surgery.

Targeting Brain Tumor "Stem" Cells

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The brain tumor research team at the Maxine Dunitz Neurosurgical Institute has observed and documented similarities between the self-renewal mechanisms of stem cells and cancer cells, lending validation to the new concept of the cancer stem cell. In a pending peer-reviewed article, *Brain Tumor Stem Cells: New Targets For Clinical Treatments*, the team explains how cells with a high self-renewal potential were identified in cases of leukemia, multiple myeloma and breast cancer. Furthermore, the team found that these cells were able to drive the formation and growth of malignant tumors. Brain tumors also were found to possess a sub-population of stem-like cancer cells with multipotent capacity and the ability to proliferate and self-renew. When grafted into mice, cancer stem cells are able to generate a tumor that recapitulates those of the patient from which they were derived.

The identification and characterization of this new category of cells calls for new tools that are able to selectively target and kill these multi-faceted cells. While more studies are necessary to better understand the biology and behavior of cancer stem cells, it is evident that these cells represent a prime target for future tumor therapies.

Participants in this research effort include Patrizia Tunici, PhD; Morris-Irvin, PhD; Gentao Liu, PhD; Xiangpeng Yuan, PhD; Zeng Zhaohui, PhD; Hiushan Ng, MS; Keith L. Black, MD and the author, John S. Yu, MD, all of the Maxine Dunitz Neurosurgical Institute at Cedars-Sinai Medical Center.

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gut dysmotility, anorexia, early satiety and nausea, ITD improves gut function through chemical sympatholysis. Chemical sympatholysis is achieved by administration of local anesthetics and clonidine to the upper thoracic nerve roots, which blocks pain generating from visceral afferent fibers and reduces efferent fiber signals that influence visceral dysmotility.

Following ITD, most patients have increased appetite, less constipation, fewer pseudo-obstructions and augmented weight gain. ITD therapy is also beneficial in patients with severe neuropathic pain from tumor invasion of neural plexuses or with painful impending spinal cord paralysis. Finally, in cancer survivors who develop complex regional pain syndrome secondary to cancer treatment, intraspinal therapy may offer an effective long-term treatment option.

Drug Delivery Systems

Implantable devices used to deliver intrathecal therapy include a disposable short-term intrathecal catheter, a long-term tunneled intrathecal catheter, and an implantable infusion pump and catheter system, both with programmable options. For the terminal patient, a short-term intrathecal catheter can be implanted at the patient's home, hospice or palliative-care unit at minimal cost. The procedure takes approximately 10 minutes and causes minimal discomfort. The other systems are usually placed in sterile conditions under fluoroscopic guidance. The long-term systems can generally be implanted in less than one hour.

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