Surgical Management of Parkinson’s Disease

Medical Section

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Surgery was the main stream of treatment of Parkinson’s disease before the usage of L-dopa in late sixties. Afterwards surgery became nearly obsolete. In the early eighties, surgery was resurrected because of the decrease efficacy and increase side effect after long term therapy with L-dopa and its derivatives. The improvement in imaging, stereotactic technique and hardware also contribute to the rebirth of surgery in management of Parkinson’s disease.

There are three main modalities of surgical treatment, namely lesioning, stimulation (neuro-modulation) and neural transplantation.

Lesioning
Radiofrequency ablation of the lateral part of the thalamus (thalamotomy) was widely used in the late fifties and early sixties in managing tremor of Parkinson’s disease. Lesioning of the globus pallidus interna (palidotomy) was found to be effective against dykinesia due to L-dopa and akinesia. Lesioning has the disadvantage of irreversibility and further lesioning may be required as the disease progress. The effect of bilateral lesioning will lead to speech and mental complication also make the procedure less optimal.

Stimulation (Neuromodulation)
It was found that high frequency stimulation of the thalamus could abolish tremor in Parkinson’s disease patients. Not until early eighties, hardware like pacemaker and electrodes can be developed and implanted into the human brain. The underlying mechanism is still unknown. It is thought that the high frequency signal ‘confuses’ the output of the cells being stimulated, as a result the final output is decrease and has a similar effect as lesioning. The beauty of stimulation is that it can be reversible without any structural changes. Furthermore, it also allows reprogramming according to the progress of the disease. However replacement of battery and fine tuning of the system require recurrent cost and expertise in maintenance. Currently the nucleus ventral intermedius (Vim) is the target for tremor. Globus pallidus internus (GPI) is the target for dyskinesia and rigidity. Subthalamic nucleus (STN) is a newly developed target in the early eighties. It has the advantage of reducing both tremor and rigidity, it also allow reduction of drug which contributes to the cost reduction and indirectly decreases dyskinesia by medication reduction. Currently in Hong Kong, about 30 patients had undergone implantation of deep brain electrodes for Parkinson’s disease with considerable improvement in their symptoms.

Neural transplantation
Previously autologous adrenal medulla cells had been used to transplant into the caudate nucleus in Parkinson’s disease patients. The result was disappointing. Mesencephalic cells from human embryo was used to transplant to the caudate nucleus since early seventies. Recently a randomized controlled trial was published and suggested that only young Parkinson’s disease patient (age < 60) had significant improve in Unified Parkinson’s Disease Rating Score (UPDRS). After the improvement in the first year, fifteen percent of them have recurrence of dyskinesia and dystonia.

Radioisotopes imaging and postmortum studies in some of these patients confirmed the survival and activities of the transplanted cells. The availability of human embryo and its ethical implication still makes neural transplantation experimental.

Future directions
Deep brain stimulation seems to be an acceptable option in managing Parkinson’s disease patients who are refractory to medical treatment. Its high cost and recurrent expenses still limits its availability. Genetic engineering may help to develop cells that are suitable for transplantation. Researches also concentrate on various growth factors and drug delivery system may help to control the disease.
Medical Section

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**Introduction**

Surgery for pituitary adenoma is an important entity in neurosurgical practice. With the exception of prolactinoma, surgical removal is the treatment of choice in most cases. Over the years, the transsphenoidal approach has become the ‘gold-standard’ while the transcranial approach is largely reserved for large tumours. Although the overall treatment outcome has been satisfactory, there remain cases in which tumour resection is incomplete and associated hormonal and surgical morbidities continue to call for improvement. This article addresses some recent developments in this field which have important impact on current neurosurgical practice and patient outcome.

**Endonasal endoscopic transsphenoidal surgery**

Conventional microsurgical transseptal approach, through either a sublabial or transnasal incision, requires extensive dissection within the nose. Patients often suffer from dental numbness, sinusitis, septal perforation and nasal congestion afterwards. The nasal passage, on the other hand, provides a natural anatomical route to the sphenoidal sinus. An endonasal approach using conventional operating microscope had previously been developed for patients with large nostrils such as white or acromegalic patients. For patients with small nostrils such as oriental people, the use of endoscopic techniques is an alternative. In many neurosurgical centres nowadays, it has already replaced the conventional microsurgical transseptal technique as the method of choice.

Technically, the endonasal endoscopic technique does not require any sublabial incision, submucosal dissection or fracturing of the nasal septum, and post-operative morbidities are greatly reduced. The surgical endoscopes also provide close-up and angled views within the pituitary fossa. This facilitates maximal tumour clearance and the preservation of normal pituitary tissue and other vital structures.

The clinical outcome is encouraging. Complete resection of both functional and non-functional pituitary adenomas is achieved in over 70% of cases which is comparable with traditional microsurgical technique. The incidence of post-operative complications such as cerebrospinal fluid (CSF) leakage, meningitis, hormonal dysfunction and sinusitis is similar to the conventional technique. A series from the Mayo Clinic has demonstrated a reduction in operating time and hospital stay. A prospective randomized study comparing the endoscopic and endonasal and microsurgical transseptal approaches has been conducted by our center. During the initial phase, 20 patients (10 in each arm) were randomized. Gross total tumour removal was achieved in all but one endoscopic case and recurrence occurred in one endoscopic case. Forty percent of patients from each groups suffered from post-operative sinusitis or other nasal symptoms but the duration of symptoms was significantly shorter with the endoscopic group. There is as yet no large study documenting the long-term oncological and endocrinological outcomes such as tumour recurrence and pituitary function.

**Combined transcranial and transsphenoidal approach**

For certain macroadenomas which extend well superiorly into the hypothalamus or the third ventricle, the transsphenoidal approach may be ineffective. The superior portion of the tumour may fall to descend towards the operating field. Aggressive and essentially ‘blind’ resection in the suprasellar space may result in optic nerve or carotid artery injuries. The residual tumour may be also complicated by post-operative haemorrhage and obstructive hydrocephalus. Transcranial resection of these tumours is frequently associated with severe intra-operative haemorrhage within the subarachnoid space which renders surgery difficult and hazardous.

Several institutions including our own center have recently advocated the combined transcranial and transsphenoidal approach for these difficult tumors. Using this technique, the transcranial surgeon approaches the suprasellar portion of the tumour through a conventional craniotomy and dissects the tumour free from adjacent vital structures. No tumour resection is attempted in the cranial compartment; instead, the tumour capsule is deliberately kept intact and the tumour is then delivered inferiorly towards the sphenoidal sinus. The transsphenoidal surgeon operates simultaneously to remove the tumour so delivered from the sellar opening. The main advantages are that bleeding is limited in the sphenoidal compartment, major intracranial structures are protected under direct vision and complete tumour removal is more assured. The disadvantages are the increased surgical trauma but with modern microneurosurgical techniques, the associated mortality and morbidity of the additional craniotomy should be minimal.

**Stereotactic image-guided neurosurgery**

The development of stereotactic technology has revolutionized modern neurosurgery. Using image-guided localized based on pre-operative imaging studies, the surgeon may navigate accurately both within the brain and amongst complex skull base structures. In pituitary surgery, stereotaxy enables the accurate localization of the internal carotid arteries, optic nerves as well as the sella turcica, so to minimize trauma. This is particularly important in patients with abnormal anatomy and those with previous transsphenoidal surgery whose normal anatomical landmarks are grossly distorted. For small functioning microadenomas, for example, in Cushing’s disease, stereotaxy may facilitate accurate tumour localization and complete removal with minimal damage to the normal pituitary gland.
Intra-operative magnetic resonance imaging (MRI) study
The transphenoidal approach only provides a limited view of the suprasellar space. Small portions of tumour may remain out of the surgeon's view and failure to recognize this frequently results in incomplete tumour removal. Over-aggressive exploration, on the other hand, can be dangerous. The use of intra-operative MRI therefore not only reveal any residual tumour but also its exact location and enables its safe removal. Unfortunately, this facility is not widely available at present and the cost of MRI-compatible surgical instruments is high.

Radiosurgery
Stereotactic radiotherapy, using either gamma-knife or linear-accelerator (LINAC or X-knife), enables the delivery of high-dose and focused irradiation to the tumour. Unlike conventional wide-field irradiation, the exposure of surrounding brain to irradiation is much reduced and treatment is usually conducted in a single session. Its accuracy is a major advantage for pituitary adenoma which is situated close to the optic nerves. Radiosurgery has been widely employed for the treatment of residual non-functioning tumours, especially those within the cavernous sinus which are not amenable to further resection. Long-term endocrinological control for functioning adenomas, as in Cushing's disease and acromegaly, are also promising. The major side-effect is panhypopituitarism.

Conclusion
Recent advances in pituitary surgery have been tremendous and have significantly improved patient outcome. It must be mentioned that developments in molecular neuro-oncology must not be over-looked and will continue to open up new directions for the future of neurosurgery. New pharmacological agents, such as growth hormone antagonist, are also important for the treatment of functioning adenomas.