Lactotroph Adenoma Surgery

Surgery is typically necessary in patients refractory to DA or other medical therapies, or in emergency situations in patients presenting with pituitary apoplexy and rapidly progressing neurological symptoms due to mass effect.

Surgery provides the additional benefit of sampling the tumor pathology and a means to gauge the aggressiveness of the tumor, which may be evident on histopathology. It also allows for an immediate decrease in the mass effect and tumor burden. Increasingly, these tumors are being treated using the endoscopic endonasal technique. In the large cohort of 200 patients, Dehdashti et al. treated 25 prolactinomas with endoscopic endonasal surgery with a 92 % gross total resection rate and 88 % remission rate [1].

Indications

Lactotroph Adenoma Surgery is safe and efficient. It is particularly suitable for enclosed prolactinomas. The patient should be well informed of the pros and cons of the treatment options, which include dopamine agonist (DA) and transsphenoidal microsurgery, and the patient's preference should be taken into account during decision-making [2].

In the majority of prolactinoma patients, disease remission can be achieved through surgery, with low risks of long-term surgical complications, and disease remission is less often achieved with dopamine agonists [3].

Prolactin level < 500 ng/ml in prolactinomas that are not extensively invasive: PRL may be normalized with surgery.

PRL > 500 ng/ml: the chances of normalizing PRL surgically are very low [4].

If no acute progression, an initial attempt of medical therapy should be made as the chances of normalizing PRL surgically with preop levels > 500 ng/ml are very low [5] (these tumors may shrink dramatically with bromocriptine).

If tumor not controlled medically (≈ 18 % will not respond to bromocriptine: surgery followed by restitution of medical therapy may normalize PRL).

Barrow et al. reviewed the results of transsphenoidal microsurgical management in 69 patients with prolactin-secreting pituitary neuroendocrine tumors who had preoperative serum prolactin levels over 200 ng/ml. The patients were divided into three groups based on their preoperative serum prolactin levels: over 200 to 500 ng/ml (Group A); over 500 to 1000 ng/ml (Group B); and over 1000 ng/ml (Group C). The percentage of successful treatment (“control rate”) was 68%, 30%, and 14%, respectively, in these three groups of patients. Based on these results, the authors offer guidelines for the management of patients with prolactin-secreting pituitary neuroendocrine tumors associated with exceptionally high serum prolactin levels. The surgical control rate of 68% in Group A seems to justify

surgery for these patients, while primary medical care with bromocriptine is recommended for most patients with serum prolactin levels over 500 ng/ml [6].

Dopamine agonist therapy is the first line of treatment for prolactinomas because of its effectiveness in normalizing serum prolactin levels and shrinking tumor size. Though withdrawal of dopamine agonist treatment is safe and may be implemented following certain recommendations, recurrence of disease after cessation of the drug occurs in a substantial proportion of patients. Concerns regarding the safety of dopamine agonists have been raised, but its safety profile remains high, allowing its use during pregnancy. Surgery is typically indicated for patients who are resistant to medical therapy or intolerant of its adverse side effects, or are experiencing progressive tumor growth. Surgical resection can also be considered as a primary treatment for those with smaller focal tumors where a biochemical cure can be expected as an alternative to lifelong dopamine agonist treatment. Stereotactic radiosurgery also serves as an option for those refractory to medical and surgical therapy [7].

Many guidelines and reports that caution against surgical treatment are based on data over a decade or more old using different techniques such as microsurgical transsphenoidal surgery or from the nascent era of endoscopic transphenoidal surgery [8].

Endoscopic techniques have continued to evolve and provide for excellent visualization, low Cerebrospinal fluid fistula rates, and high rates of gross total resection. In a study of DA-resistant prolactinomas, Vroonen et al. showed that surgical debulking led to a significant de- crease in prolactin levels at a significantly lower DA dose [9].

Kreutzer et al. report a remission rate of 91 % in patients who had elective surgery of microprolactinomas, and Babey et al. also had a high long-term remission rate, without morbidity or mortality for patients with microprolactinomas [10] [11].

Cost considerations are also a concern, especially in countries such as the USA, which is undergoing rapid changes in its healthcare system. A study by Jethwa and Patel et al. found surgical resection of microprolactinomas to be more cost effective long term than medical therapy [12].

Tumor size and invasion of extrasellar and/or cavernous sinuses have typically been seen as limitations of surgery, and some patients with refractory very large or giant tumors may necessitate multistage surgical procedures with a combi- nation of endonasal and transcranial approaches.

see Lactotroph adenoma radiosurgery.

Expanded endoscopic endonasal techniques have been developed that allow for safe treatment of larger adenomas that have extra-/parasellar extension as long as the extension is in the cranio-caudal direction and not lateral to the carotids. However, the issue of partial resection and the risk of apoplexy in the residual irritated tumor is of some concern. As in many other areas of neuro-oncology, a combination approach may be optimal. Surgical resection may allow for definitive removal of the

tumor and relief of the mass effect and provide tissue for precisely targeted therapies to prevent recurrence. Sophisticated immunohistochemistry and genetic testing are rapidly being applied to many other tumors and may in the future allow for superior targeted adjuvant therapies in prolactinomas and help reduce recurrences. Finally, surgery might be an answer to the long-term cost of medical therapy specifically in younger patients. However, this issue should be carefully assessed on an individual basis to not jeopardize the standard of care in prolactinoma management by unnecessary surgical treatment. Medical treatment remains the first and the treatment of choice in the general population with recently diagnosed prolactinoma in the absence of rapidly progressive neurological symptoms [13].

Costs

Few studies address the cost of treating prolactinomas.

The Department of Neurological Surgery, University of California at San Francisco, performed a cost-utility analysis of surgical versus medical treatment for prolactinomas. Materials and Methods We determined total hospital costs for surgically and medically treated prolactinoma patients. Decision-tree analysis was performed to determine which treatment produced the highest quality-adjusted life years (QALYs). Outcome data were derived from published studies. Results Average total costs for surgical patients were $19,224 (± 18,920). Average cost for the first year of bromocriptine or cabergoline treatment was $3,935 and $6,042, with $2,622 and $4,729 for each additional treatment year. For a patient diagnosed with prolactinoma at 40 years of age, surgery has the lowest lifetime cost ($40,473), followed by bromocriptine ($41,601) and cabergoline ($70,696). Surgery also appears to generate high health state utility and thus more QALYs. In sensitivity analyses, surgery appears to be a cost-effective treatment option for prolactinomas across a range of ages, medical/surgical costs, and medical/surgical response rates, except when surgical cure rates are ≤ 30%. Conclusion Our single institution analysis suggests that surgery may be a more cost-effective treatment for prolactinomas than medical management for a range of patient ages, costs, and response rates. Direct empirical comparison of QALYs for different treatment strategies is needed to confirm these findings [14].

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