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EDITORIAL (BY INVITATION)

Does the medical treatment for prolactinoma remain the standard of care?

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With the increasing use of endoscopic transsphenoidal surgery for the treatment of pituitary tumors, it is important to examine its role in the management of prolactinomas. We therefore reviewed with interest the article by Akin et al. about the "Reasons and Results of Endoscopic Surgery for Prolactinomas." In this retrospective review of 142 consecutive patients, the authors found that endoscopic transsphenoidal resection of pituitary prolactinomas can be a safe and effective treatment. They achieved a nearly 75 % remission rate at a median follow-up of 36 months, with a complication rate of less than 3 %. In this study, surgical treatment was indicated when patients had dopamine agonist (DA) intolerance or resistance, visual field deficit, pituitary hemorrhage, giant adenoma, and/or patient preference. Older age, large tumor volumes, and cavernous sinus invasion were found to have no effect on outcomes.

This study nicely summarizes many of the surgical indications for the treatment of prolactinomas in the era of endoscopic transsphenoidal surgery. Patients who are deemed DA resistant or cannot tolerate DA treatment can be referred for surgery and less ideally radiosurgery. There is controversy over the length of DA treatment before declaring a patient resistant to therapy and exploring other options. While some patients do experience regression of their tumors only after a few months on DA therapy, longer duration of DA has been associated with increased fibrosis in the tumor, potentially making surgical treatment more difficult and risky [1].

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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 [2]. In this much larger series, Akin et al. achieved relatively good outcomes with endoscopic resection of pituitary prolactinomas—approximately 50 % immediate remission rate and overall 75 % in remission with adjuvant DA. However, it seems that the crossover from medical to surgical management occurred sooner than expected. Although patient preference might have played a role, it is not possible to set the criteria on this article as the standard surgical criteria for prolactinoma surgical resection.

Meanwhile, we do support surgical treatment of prolactinoma when deemed indicated. 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 [3]. Endoscopic techniques have continued to evolve and provide for excellent visualization, low CSF leak 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 decrease in prolactin levels at a significantly lower DA dose [4]. Numerous other centers and surgical teams report strong efficacy and low morbidity with endoscopic endonasal treatment. Of interest are recent reports of elective surgery for

prolactinomas. 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 [5, 6]. 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 [7]. The latter however remains a matter of controversy as to suggesting an invasive, higher risk approach only for the sake of cost-effectiveness.

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 combination of endonasal and transcranial approaches. Radiosurgery could be considered as an adjunct treatment for residual disease although there is a risk of hypopituitarism and potential damage to the optic apparatus. Refinements in radiosurgery technology including more precise imaging, planning software, and delivery devices have improved the efficacy and reduced morbidity.

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.

Compliance with ethical standards

Conflict of interest None.

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