Research Progress in the Treatment of Pituitary Tumors

Wengan Ji[1], Ruixue Xie[1], Shaoze Qin[1], Long Wang[2*], Wenlong Tang[2*]

1. Department of Changzhi Medical College, Changzhi 046000, China.

2. Department of Neurosurgery, Heping Hospital Affiliated to Changzhi Medical College, Changzhi 046000, China.

Abstract: Pituitary tumor is a common intracranial neuroendocrine tumor, generally belonging to benign tumors. It mainly originates from pituitary cells in the sella region. There is no significant difference in the ratio of men to women. The tumor grows to the lower part of the parasellar thalamus, and may even reach the third ventricle to involve the cavernous sinus, extend into the middle cranial fossa, grow into the interpeduncular cistern, and enter the nasopharynx in the sphenoid sinus. A few tumors are rich in blood supply and easy to bleed, leading to pituitary tumor stroke. The incidence of pituitary tumor ranks the third among intracranial tumors. In recent years, with the development of endocrine examination and imaging technology, the detection rate is increasing year by year. The hormone disorder and the pressure on the surrounding important tissues will have a great impact on the quality of life of patients, and have a great impact on the growth and development of patients, labor ability, growth and development and social psychology. In this paper, the research progress of three methods for the treatment of pituitary tumor (surgical therapy, drug therapy, radiation therapy) is reviewed, aiming to provide reference for the clinical treatment of this disease.

Keywords: Pituitary Tumor; Treatment; Research Progress

Introduction

Adenohypophysial, neurohypophysial and residual squamous epithelial cells of embryonic craniopharyngeal tube sac are the main sources of pituitary tumors, among which the pituitary adenoma originating from adenohypophysial gland is the most common, with the incidence of pituitary tumors up to 16.7%. Most pituitary tumors in intracranial tumors are benign, accounting for about 15% [1], after glioma and meningioma, and malignant pituitary tumors are less than 1%. Among pituitary tumors, prolactinomas accounted for 32% ~ 66%, growth hormone tumors accounted for 8% ~ 16%, adrenocorticotropin tumors accounted for 2% ~ 6%, thyrotropin stimulating tumors accounted for 1%, and nonfunctional tumors accounted for 15% ~ 54% [2]. The common clinical symptoms of pituitary tumor include the expression of hormone enhancement and decrease, mass effect, pituitary tumor stroke. Pituitary tumor generally grows slowly. If it is not interfered for a long time, it may cause headache, blindness, heart failure and other symptoms, and is easy to be complicated by cerebrovascular accident, diabetes, infection, and even loss of labor force or death in severe cases. This article reviews the research progress of three methods for the treatment of pituitary tumor (surgical therapy, drug therapy and radiotherapy), aiming to provide reference for the clinical treatment of this disease.

1. Surgical treatment of pituitary tumor

Surgical treatment is the preferred initial treatment for patients with pituitary tumor [3]. In 1889, the first pituitary tumor resection through frontal approach was successfully performed in the world. In 1907, Jing Dijie Road was established; In

1912, it improved and created a new surgical method of resection of vertical tumor through the sublip, nasal septum and sphenoid sinus. In 1960, the Hopkins cylindrical endoscope and instrument system appeared, and the hardware technology of neuroendoscopy made a leap forward. In 1967, with the aid of Hardy microscope and X-ray, the transsphenoidal approach was revived, and then craniotomy gradually decreased. In 1992, the first endoscopic transnasal sphenoidal resection of pituitary adenoma was performed. With the development of imaging and medical instruments, surgical strategies for pituitary tumors have been changing. The development of modern surgical microscopes has allowed for better illumination and resolution of the deep structures through the nasal tunnel, thus providing a closer view, better illumination, and thus a more complete understanding of the environment at the base of the skull. Endoscopy can not only be used for simple intraoperative observation, but also as an auxiliary tool for transsphenoidal surgery under the microscope. A large number of data show that endoscopy can improve the resection rate of tumors with fewer complications. Single-nostril resection of tumors through neuroendoscope or microscopy-assisted sphenoidal approach is currently a clinically recognized classic surgical approach around the world. The extended transsphenoidal approach can be designed as a wide opening at the base of the skull, so endoscopy can provide almost unrestricted observation of intracranial anatomy. However, some technical problems still limit the wide application of these approaches, such as the difficulty of skull base reconstruction, the high incidence of cerebrospinal fluid leakage, and the unskilled endoscopic technique.

2. Radiotherapy of pituitary tumor

Due to the pituitary internal and external irradiation due to more side effects, has been less used. Radiotherapy is a second-line treatment in the treatment of pituitary tumor, mainly applicable to tumor patients with postoperative residual tumor, tumor recurrence, no surgical indications, intolerance to surgical treatment or refusal to surgical treatment. Conventional 2-D radiotherapy has a high complication rate and takes a long time to effectively control abnormal hormone levels. Therefore, conventional radiotherapy is gradually replaced by stereotactic radiotherapy (SRT)/stereotactic radiosurgery (SRS) in recent years [4]. SRS is as effective as craniotomy, but it does not have the morbidity and mortality associated with craniotomy. SRS is less invasive, bloodless, and infection-free, and has no damage to important tissue structures around the lesion target area. Traditional radiotherapy is mainly used in cases where the tumor is difficult to achieve volume reduction and the hormone level is not up to standard after surgery, but the pituitary dysfunction and nervous system damage that may be caused by radiotherapy greatly limit its use [5]. The development of CT and MRI, as well as its integration with the gamma knife radiation platform, has been critical to the advancement of radiation therapy for pituitary tumors. Similarly, advances in the computerised SRS programme have led to safer and more precise doses per unit of time. In patients with residual, recurrent and recalcitrant pituitary tumors, endocrine or surgical decompression is usually used. However, clinical data over the past 10 years support the use of SRT because of its good local tumor control, endocrine remission, and low toxicity. The basic principle of radiotherapy for all pituitary tumors is to deliver a high dose of radiation to the tumor tissue while minimizing the dose to key structures such as the optic structure,hypothalamus, internal temporal lobe, and brain stem.

3. Drug therapy of pituitary tumor

There are mainly two kinds of pituitary tumor treatment drugs: the first kind acts directly on tumor cells to inhibit proliferation and hormone secretion, which is the most ideal treatment method; Studies have shown that the specific expression of genes or proteins in pituitary tumors provide a good target for diagnosis and treatment of pituitary tumors. The most widely used drugs of this kind are bromohentine and carbergoline. In addition, potential targets under investigation are estrogen receptors, retinoic acid receptors and peroxisome proliferator-activated receptor-γ, folate receptor-alpha. The

second is to indirectly control the symptoms and complications caused by excessive hormones, which are widely used in acromegaly and Cushing's disease, mostly hormone release inhibitors and hormone receptor antagonists.

3.1 Bromocriptine

Bromocriptine is an ergot derivative that binds D_1 and D_2 dopamine receptors. Most prolactinomas atrophy within 6 weeks of taking bromocriptine. Side effects such as indigestion, nausea and vomiting, dizziness and headache, movement disorders, hypotension, and syncope can limit tolerance. However, it is still an effective drug for those who can tolerate it. After treatment, 80% ~ 90% of microprolactinomas and 70% of large prolactinomas return to normal prolactin, tumor regression, and gonadal function recovery [6]. The results of bromocriptine administration were similar to those of surgical intervention, with a meta-analysis showing that 74% of microadenomas and 32% of macroadenomas returned to normal prolactin within 12 weeks after surgery [7].

3.2 Carbergoline

Carbergoline is a D_2 receptor agonist. Compared with bromocriptine, carbergoline is better tolerated and has fewer side effects. It can normalize prolactin levels and is currently the preferred initial treatment for prolactinoma. According to the results of Webster et al. [8], 7% of the patients taking cabegoline had abnormal menstruation, while 16% of the patients taking bromoannetin had abnormal menstruation. Only 3% of patients stopped carbergoline because of side effects, compared with 12% of those taking bromocriptine. Another multicentre randomized study of 120 female patients with prolactinoma showed that 93% of the patients taking cabergoline returned to normal prolactin, while only 48% of the patients taking bromohentine returned to normal prolactin, further confirming the superiority of cabergoline monotherapy in the treatment of prolactinoma [9].

3.3 Other drugs

Octreotide has a good effect on acromegaly of auxin adenoma, but a poor effect on the tumor itself. Mifepristone has a long half-life and shows dose-dependent anti-glucocorticoid effect. It is the only glucocorticoid receptor antagonist currently available for clinical use, which can antagonize the effects of cortisol and progesterone [10]. Cyproheptadine has a certain effect on patients with increased cortisol, but the effect is not satisfactory, and can only be used as short-term adjuvant therapy. Temozolomide is used as a first-line chemotherapy agent for refractory pituitary adenoma and pituitary cancer in the clinical guidelines for refractory pituitary adenoma and pituitary cancer released by the European Endocrine Society [11].

4. Summary and Outlook

As a complex neuroendocrine tumor, the treatment of pituitary tumor requires close collaboration and cooperation among various departments, such as neurosurgery, radiology and endocrinology. However, with the development of science and technology, its treatment concepts and methods are constantly updated, and the boundaries of the treatment of pituitary tumors in various departments gradually expand and even overlap with each other. Endoscopic therapy for prolactinoma may bring some risk of trauma and surgical failure to patients, while drug therapy should consider the long-term medication costs and side effects, and it is necessary to weigh the benefits of the two treatments. In addition, more large-scale clinical studies are needed to determine the exact dose of pituitary radiation and the duration of dopamine therapy. At present, frontier researches at home and abroad are trying to understand the pathogenesis of pituitary tumor from the microscopic aspects of genes, proteins, transcription factors, etc. With the deepening of the research, it will bring more good news to patients with pituitary tumor.

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