Efficacy and Complications of Pituitary Irradiation

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KEYWORDS

• Pituitary tumor • Pituitary radiotherapy • Hypopituitarism

KEY POINTS

- Radiation therapy is widely used in the management of intracranial (including sellar and parasellar) and systemic disorders.
- The place radiation therapy has in the management algorithm of pituitary tumors depends on the type of tumor, and it is usually recommended postoperatively to prevent relapse or to control hormonal hypersecretion.
- The efficacy of radiation therapy varies widely mainly depending on the type of tumor, degree of hormonal hypersecretion and radiation technique, and schedule used.
- With the advances in radiation planning and delivery, the long-term complications have improved, although hypopituitarism remains the protagonist in the list of adverse sequelae.

INTRODUCTION

Radiation therapy is widely used in the management of intracranial (including sellar and parasellar) and systemic disorders. These intracranial disorders mainly include pituitary adenomas, other (para)sellar tumors (eg, craniopharyngiomas, meningiomas, germinomas, schwannomas, chordomas/chordosarcomas, hemangiopericytomas, gliomas, pituicytomas, pinealomas, medulloblastomas, brain metastases, and vascular malformations), hematologic malignancies (eg, acute lymphoblastic leukemia, lymphomas), and face, neck, and skull base tumors (eg, nasopharyngeal carcinomas).[1] Although in many cases the irradiation aims to prevent the growth or regrowth and to control the hormonal hypersecretion of a pituitary tumor, in many others, it adversely affects the hypothalamo-pituitary function simply because this area receives significant doses of radiation offered for non–hypothalamo-pituitary disorders.

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This review focuses on the efficacy of various types of radiation techniques in the most common pituitary tumors and on the complications after irradiation, including in the hypothalamo-pituitary area.

EFFICACY OF PITUITARY IRRADIATION

The aim of radiation treatments to the sellar region is to prevent tumor (re)growth and to control the hormonal hypersection while sparing the surrounding normal structures. Conventional fractionated radiotherapy delivers megavoltage doses of irradiation in fractions separated over time. The irradiation is given through multiple beams from a high-energy radiation source focused on the tumor. Radiation treatments are most commonly delivered through photons (high-energy x-rays) generated by a linear accelerator (LINAC). Cobalt 60 as a source of high-energy gamma radiation has been mostly replaced, with the exception of a multiheaded cobalt unit (gamma knife). Charged particle beams in the form of photons and, more recently, helium and carbon ions have been also used as therapeutic radiation sources. Localized irradiation is achieved by offering treatment in 3 to 4 beams each shaped to conform to the shape of the tumor by using a multileaf collimator. Multileaf collimator leaves can also modulate the intensity of radiation (intensity-modulated radiotherapy [IMRT]).[1] In pituitary adenomas, the most commonly used protocol includes a total dose of 45 to 50 Gy offered in fractions of 1.6 to 1.8 Gy, 4 to 5 times per week over 5 to 6 weeks. Stereotactic techniques are related with further improvement in immobilization using relocatable or fixed frames, improved imaging, and more precise treatment delivery. Stereotactic irradiation is offered as single-fraction radiotherapy using either cobalt 60 gamma radiation emitting sources (gamma knife) or a LINAC or as stereotactic conformal radiotherapy delivered as fractionated treatment using a LINAC.

Acromegaly

The aims of the treatment of acromegaly are to inhibit growth hormone (GH) hypersecretion, normalize insulin-like growth factor-1 (IGF-1) levels and reduce or control tumor growth, leading to symptom control and minimizing the associated clinical signs and comorbidities.[2] Biochemical control is generally defined as a normal IGF-I for age and gender and a GH less than 1.0 ng/mL on an oral glucose tolerance test. With sensitive assays, a GH of less than 0.4 ng/mL would be consistent with remission.[2] Radiotherapy is generally reserved as third- or second-line treatment in cases in which surgery or medical therapy have not achieved tumor growth control or normalization of hormone levels. It may also be used for those on medical therapy aiming to stop it after the irradiation has led to hormonal control.[2] Based on series with strict remission criteria, fractionated radiotherapy achieves remission rates in 50% to 60% of the patients within 10 years (**Table 1**). Predictive factors for remission are the initial GH and IGF-I levels.[3,4] Within the first 2 years after irradiation, the GH levels are found to decrease by 50% to 70% followed by a slow gradual reduction over the next 10 to 20 years.[5] Data on the efficacy of fractionated proton beam irradiation in acromegaly are limited with no conclusive evidence on the superiority of this treatment. Stereotactic radiosurgery has been used in patients with small residual tumor, not close to the optic pathways, and biochemical remission has been reported in 35% to 100%; the variable rates reflect the different observation periods and the different criteria used to assess control of the disease.[6]