Disruption of Hypothalamic Regulation of Appetite Associated with Proton Beam Therapy

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Introduction

- Proton beam therapy (PBT) is being used increasingly for the treatment of craniopharyngioma because radiation dose to the temporal lobe, the hypothalamus and the optic apparatus is reduced. This is perceived as a major benefit; however its real therapeutic gain has yet to be established.
- We are report two patients diagnosed with craniopharyngioma, treated with PBT, who and presented with profound anorexia and weight loss following irradiation.

Case 1

- A 12 year old girl presented with history of headache, generalised tonic-clonic seizure
- MRI revealed obstructive hydrocephalus and posterior fossa tumor
- Hydrocephalus was drained and an ommaya reservoir was inserted
- A near total resection of the craniopharyngioma was performed leaving minimal tumor adherent to the posterior cerebral artery and hypothalamus.
- Assessment of pituitary function following surgery demonstrated panhypopituitarism, including diabetes insipidus.
- 4 months following surgery, she received PBT (50.4 CGE in 28 daily fractions)
- She became anorexic with weight loss (BMI SDS decrease by 1.84) (Figure 1)
- After rigorous monitoring and continuous active intervention she gained weight
- Over period of years developed excessive eating and obesity requiring intervention.

Case 2

- A 4 year old boy with short stature was diagnosed with growth hormone deficiency.
- MRI revealed a suprasellar tumour.
- A subtotal resection removed all tumor except small layer at pituitary stalk and base of hypothalamus. Histology confirmed craniopharyngioma
- Assessment of pituitary function following surgery demonstrated panhypopituitarism, including diabetes insipidus.
- Four months following surgery MRI revealed a moderate-size cyst, which was fenestrated and an ommaya reservoir was inserted
- Eleven months later he received PBT (54 CGE in 30 daily fractions)
- Following PBT there was an abrupt onset of anorexia.
- and BMI decreased = 2SD, requiring supported nutrition by gastrostomy.
- One year following PBT, appetite recovered and gastrostomy was removed.

Figure 1: Serial weight and BMI of case 1

Discussion

- The most recent advances in the treatment of craniopharyngioma, including precision radiotherapy, focus on minimizing treatment-related toxicity.
- Cranial irradiation is a leading cause of hypothalamic and pituitary injury. The hypothalamus has a critical role in energy homeostasis, which is regulated by a complex neuroendocrine system. Injury to the hypothalamus can lead to anorexia, weight loss or obesity.
- A proton has a defined maximum penetration depth, called the Bragg peak, at which the majority of its energy is released over a few millimeters beyond which it has no energy and early clinical results report good favorable clinical outcomes.
- A relative low rate of hypothalamic dysfunction has been described associated with PBT as compare to conventional radiotherapy. However, a recent study shows an association of radiation dose with hypothalamic and pituitary damage.

Conclusion

- Although PBT is generally well-tolerated for the treatment of craniopharyngioma, long-term follow up and larger cohort studies are necessary to establish whether dosimetric advantages of PBT translates to clinical benefits in in reducing long-term toxicity.
- Hypothalamic involvement of craniopharyngioma and treatment-related lesions of hypothalamic areas are major risk factors for impaired survival, neuropsychological deficits.
- Any patient receiving PBT/conventional radiotherapy should be followed up for acute and long term sequelae of radiation.
- Until further data regarding the long term outcomes of PBT treated patients are available, we suggest surveillance should be based on radiation dose, rather than the modality of radiation delivery.

References:


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