Traumatic brain injury (TBI) and cancer-induced growth hormone deficiency (GHD)

Cancer-induced GHD

GHD can be induced by a tumor (eg optic pathway glioma or pituitary macroadenoma), neurosurgery or radiotherapy in the hypothalamic-pituitary (HP) area.

GHD can also be induced by immune checkpoint or tyrosine kinase inhibitors.

The level of HP damage by radiotherapy depends on the scatter of the radiotherapy dose, which varies with the type of radiotherapy (Figure 4).

How common is GHD in childhood cancer survivors (CCS)?

GH is usually the first hormone to be affected by radiotherapy, and GHD is the most common anterior pituitary dysfunction in CCS.

50–100% of patients treated for non-pituitary central nervous system (CNS) tumors develops GHD after cranial radiotherapy of 30–50 Gy.

Almost all patients treated with HP irradiation of 30–50 Gy (eg high-risk medulloblastoma, pituitary adenoma, CNS germinoma) develop GHD by 5 years after cranial radiotherapy.

How can cancer or cancer treatment cause GHD?

GH deficiency can also be induced by immune checkpoint or tyrosine kinase inhibitors.

The risk of GHD after radiotherapy increases with:

- Radiation dose
- Time
- Number of radiation fractions

Immune checkpoint inhibitors (eg ipilimumab)

Can be associated with hypopituitarism, more commonly ACTH or TSH deficiencies rather than GHD.

When does GHD manifest after cranial radiotherapy?

After lower doses of cranial radiotherapy (eg 18–24 Gy), pubertal GH insufficiency is more common than prepubertal GHD.

When does GHD manifest after cranial radiotherapy? (Figure 5)

Decreased peak GH level is seen earlier and is more pronounced after higher doses of cranial radiotherapy.

How can cancer or cancer treatment cause GHD?

GHD can also be induced by immune checkpoint or tyrosine kinase inhibitors.

TBI-induced GHD

How can TBI cause GHD?

TBI can result in primary mechanical events and consequent secondary effects that lead to hypopituitarism.

The anatomy of the pituitary gland (Figure 2) places TBI patients at higher risk of GHD than other pituitary deficiencies.

How common is GHD after TBI?

There were >837,000 TBI-related emergency department visits, hospitalizations and deaths in the USA for children in 2014.

Younger children (aged 0–4 years): falls

Older children (aged 5–14 years): being struck, eg sports injuries, violence

Adolescents (aged 15–17 years): motor vehicle accidents

When does GHD manifest after TBI?

The acute stress response confounds evaluation of GHD in the initial phases after TBI.

GH resistance: High rates after initial trauma but diminishes by year.

Hypopituitarism tends to persist even 5 years after severe TBI.

Recovery of some pituitary function may possibly occur years after TBI.

How should TBI-induced GHD be detected and treated?

GH therapy is recommended for patients with TBI-induced GHD, and it:

- Reduces depression
- Reduces fatigue
- May improve cognition

How should cancer-induced GHD be detected and treated?

GH therapy for CCS diagnosed with GHD, based on demonstrated safety and efficacy.

Long-term periodic clinical assessment for CCS improved to HP axis radiotherapy of 21 Gy.

Suggest waiting until patients have been disease-free for 1 year before starting GH therapy.

If patients have chronic stable disease (eg optic pathway tumors), discuss appropriateness and timing of GH therapy with an oncologist.

References

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9. Cherry et al., J Clin Oncol 2015;33:480–500