The role of IGF-1 as a screening tool in radiation-induced growth hormone deficiency in childhood cancer survivors

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Conflicting outcomes have been reported about the role of low IGF-1 levels in predicting radiation-induced growth hormone deficiency (GHD) in childhood cancer survivors (CCS). IGF-1 <-2 SDS was found to have a sensitivity between 28 and 95% in different studies on CCS, but these results were drawn from small samples of irradiated patients or from mixed cohorts including patients with GHD due to different aetiologies. Our aim was to analyse the screening role of low IGF-1 levels in CCS at risk of developing GHD after cranial radiotherapy (RT) involving the hypothalamic-pituitary (HP) area.

Results

Sensitivity of IGF-1 and IGFBP-3 levels <-2 SDS in the RT-NHP cohort:
- IGF-1: 31.86%.
- IGFBP-3: 7.37%

Both results were remarkably lower than the sensitivity reported in non-irradiated GH deficient patients.

IGF-1 <-2 SDS at diagnosis of GHD in childhood showed:
- Statistically significant association with GH peaks < 3 μg/L in childhood (χ²=8.65, p 0.003)
- Statistically significant association (χ²=9.1, p 0.003) and correlation (r:0.47, p 0.004) with GH peaks at final height reassessment

IGF-1 <-2 SDS at final height reassessment:
Sens: 35% Spec: 100% PPV: 100% NPP 58%

IGF-1 <-2 SDS at final height reassessment had a poor sensitivity in predicting radiation-induced GHD. However, a child with IGF-1 < -2 SDS had a higher risk of severe GHD (peak<3 μg/L) both in childhood and at final height retesting.

IGF-1 <-2 SDS at final height reassessment had a PPV of 100% in our study: this result suggests that dynamic retesting in young adults with a previous history of GHD in childhood could be virtually not performed when IGF-1 levels are persistently low at the end of growth. Normal IGF-1 levels despite overt radiation-induced GHD were particularly frequent in leukemic patients treated with only TBI (low pituitary radiation doses). In this cohort, IGF-1 < -2 SDS had a sensitivity of only 7.1%

Conclusion

IGF-1 as a screening tool for radiation-induced GHD in childhood cancer survivors is not reliable. A low sensitivity was found both in childhood and at final height reassessment. However, a child with IGF-1 < -2 SDS had a poor sensitivity and a high predictive value at final height reassessment. Normal IGF-1 levels despite overt radiation-induced GHD were frequently found in leukemic patients treated with only TBI. We found a negative statistical correlation between pituitary radiation dose administered and GH peaks achieved after stimulation test, GH dropped by an average value of 0.1 μg/L for each additional pituitary Gy.

The number of deficient pituitary hormones showed no correlation with IGF-1 SDS:
- at diagnosis of GHD in childhood (r 0.10)
- at final height retesting (r 0.12)

We found a weak negative correlation between IGF-1 SDS levels and Δheight SDS at final height (Pearson’s r: -0.36, p 0.04)

Data Source:
- Patient’s medical records and growth charts for demographic, aetiological or clinical data
- Pituitary radiation doses were estimated from each RT plan.

Patients:
158 CCS:
- 123 brain tumours
- 29 leukemias
- 6 irradiated cranial rhabdomyosarcomas

In order to describe the specific detrimental role of irradiation on GH secretion, we finally selected a cohort of 117 patients with tumours not involving the HP area (RT-NHP cohort).

Diagnosis of GHD
GH peak < 7 μg/L after a single stimulation test

Improvement in height SDS after treatment was statistically lower in patients treated with TBI than with cranial or craniospinal RT at all time-points.

We found a weak negative correlation between IGF-1 SDS levels and Δheight SDS at final height (Pearson’s r: -0.36, p 0.04)

Conclusions

Statistically significant association between GH peaks and IGF-1 in occurring sub-groups

Δ Height SDS 1, 2 years after start of rhGH therapy and at final height

Correlation pituitary dose (Gy, X) - GH peaks (μg/L, Y)

GH peaks and IGF-1 in oncological sub-groups
1 Medulloblastomas (MB)
2 Leukaemias (LK)
3 Cranioparyngiomas (CR)
4 Extra-optic gliomas
5 Optic-pathway gliomas

Protocol presented at: The ROYAL MARSDEN