

## Craniopharyngioma recurrence

Occur even after documented gross total resections necessitating a combination of therapeutic strategies.

Obtaining a cure of this tumor in adults without producing major side effects continues to remain elusive.

Minimally invasive techniques such as [cyst](#) aspiration, insertion of a catheter with [Ommaya reservoir](#), when combined with stereotactic radiosurgery/IMRT is an effective and safe option for management and long-term control of adult CPs.

Ommaya catheter by itself could act as a stent, creating a tract allowing gradual drainage of cyst fluid and stabilization without necessitating any further interventions in selected cases <sup>1)</sup>.

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Thirty-two patients with [craniopharyngioma recurrence](#) underwent [phosphorus 32](#) colloid [interstitial radiotherapy](#). The tumor imaging features were classified into 4 types according to the thickness of the [cyst](#) wall and signals of the cyst contents as shown by [computed tomography](#) (CT) and [magnetic resonance imaging](#) (MRI) images. Protein expressions of [VEGF](#) and [VEGFR-2](#) in [craniopharyngioma](#) tissues were evaluated with [immunohistochemistry](#) before [radiotherapy](#). The tumor [radiosensitivity](#) was determined at 12 months after the interstitial radiotherapy. VEGF mainly expressed in the tumor cytoplasm, and VEGFR-2 expressed either in vascular endothelial cells or in tumor endothelial cells. VEGF/VEGFR-2 expressions varied significantly in cases sensitive or insensitive to the radiotherapy (VEGF:  $P=.028$ ; VEGFR-2:  $P=.017$ ). Tumor imaging features were associated with the therapeutic efficacy of interstitial radiotherapy ( $P=.000$ ). VEGF expression had no association with the imaging features of tumors ( $P=.226$ ), but VEGFR-2 expression was associated with the imaging features of tumors ( $P=.008$ ). Our results confirmed the association among imaging features, VEGFR-2 expressions, and tumor radiosensitivity in craniopharyngiomas. Imaging features and VEGFR-2 expressions may add useful data to the radiosensitive assessment of craniopharyngiomas <sup>2)</sup>.

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All the patients with craniopharyngioma followed-up at the Departments of Endocrinology or Paediatrics in Oxford and treated or not with GH were studied retrospectively. These were recruited from the databases of the departments consisting of subjects diagnosed between January 1964 and July 2005. The impact of GH replacement upon recurrence was evaluated after adjusting for possible confounding factors.

Forty-one subjects received GH replacement. Nine of them did not have follow-up imaging during GH therapy and were not included in the statistical analyses. The remaining 32 (22 males/10 females) received GH for a mean period of  $6.3 \pm 4.6$  years (median 5.1, range 0.8-22); 21 started during childhood (13 of them continued after the achievement of final height with an adult dose) and 11 during adult life. The mean duration of their follow-up (from surgery until last assessment) was  $10.8 \pm 9.2$  years (range 1.9-40). Fifty-three subjects had not received GH therapy (30 men/23 women). The mean duration of their follow-up (from surgery until last assessment) was  $8.3 \pm 8.8$  years (range 0.5-36). During the observation period, 4 patients treated with GH and 22 non-GH treated ones developed tumour recurrence. After adjusting for sex, age at tumour diagnosis and type of tumour therapy (gross total removal, partial removal, surgery + irradiation), GH treatment was not a

significant independent predictor of recurrence ( $P = 0.06$ ; hazard ratio = 0.309). Similar results were obtained when the impact of GH replacement was assessed according to its duration ( $P = 0.18$ ; hazard ratio = 0.991/month of treatment). None of the nine patients with insufficient imaging data for inclusion in the statistical analyses [5 men/4 women, 3 treated with GH during childhood/6 during adult life, mean duration of GH therapy  $2.9 \pm 2.4$  years (median 1.8, range 0.4-7)] showed clinical features suggestive of recurrence during the period of GH replacement.

Based on the data of the craniopharyngiomas database in Oxford, there is no evidence that GH replacement is associated with an increased risk of tumour recurrence <sup>3)</sup>.

The object of a study was to establish recurrence rates in patients with [craniopharyngioma](#) postoperatively treated with [recombinant human growth hormone](#) (rhGH) as a basis for determining the risk of rhGH therapy in the development of recurrent tumor.

The study included 739 pediatric patients with craniopharyngioma who were naïve to GH upon entering the Genentech [National Cooperative Growth Study](#) (NCGS) for treatment. Reoperation for tumor recurrence was documented as an adverse event. Cox proportional-hazards regression models were developed for time to recurrence, using age as the outcome and enrollment date as the predictor. Patients without recurrence were treated as censored. Multivariate logistic regression was used to examine the incidence of recurrence with adjustment for the amount of time at risk.

Fifty recurrences in these 739 surgically treated patients were recorded. The overall craniopharyngioma recurrence rate in the NCGS was 6.8%, with a median follow-up time of 4.3 years (range 0.7-6.4 years.). Age at the time of study enrollment was statistically significant according to both Cox ( $p = 0.0032$ ) and logistic ( $p < 0.001$ ) models, with patients under 9 years of age more likely to suffer recurrence (30 patients [11.8%], 0.025 recurrences/yr of observation,  $p = 0.0097$ ) than those ages 9-13 years (17 patients [6.0%], 0.17 recurrences/yr of observation) and children older than 13 years (3 patients [1.5%], 0.005 recurrences/yr of observation).

Physiological doses of GH do not appear to increase the recurrence rate of craniopharyngioma after surgery in children, but long-term follow-up of GH-treated patients is required to establish a true natural history in the GH treatment era <sup>4)</sup>.

1)

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2)

Hu C, Chen J, Meng Y, Zhang J, Wang Y, Liu R, Yu X. Phosphorus-32 interstitial radiotherapy for recurrent craniopharyngioma: Expressions of vascular endothelial growth factor and its receptor-2 and imaging features of tumors are associated with tumor radiosensitivity. *Medicine (Baltimore).* 2018 Jun;97(26):e11136. doi: 10.1097/MD.00000000000011136. PubMed PMID: 29952957.

3)

Karavitaki N, Warner JT, Marland A, Shine B, Ryan F, Arnold J, Turner HE, Wass JA. GH replacement does not increase the risk of recurrence in patients with craniopharyngioma. *Clin Endocrinol (Oxf).* 2006 May;64(5):556-60. PubMed PMID: 16649976.

4)

Smith TR, Cote DJ, Jane JA, Laws ER. Physiological growth hormone replacement and rate of recurrence of craniopharyngioma: the Genentech National Cooperative Growth Study. *J Neurosurg Pediatr.* 2016 Oct;18(4):408-412. PubMed PMID: 27286443.

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