Peginterferon alfa-2a for cystic craniopharyngioma treatment

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Craniopharyngiomas, especially their cystic forms, pose unique management challenges due to their proximity to critical neurovascular structures. Intracystic therapies offer a minimally invasive alternative to repeated surgical interventions. Over the past decade, **interferon-alfa-2a/2b** emerged as a viable intracystic treatment due to its anti-proliferative and immune-modulating properties, coupled with low toxicity. However, **discontinuation of commercial availability** prompted the search for alternatives.

Commercial Availability of Intracystic Agents

Agent	Commercial Status	Notes
Interferon alfa-2a / alfa-2b	'Withdrawn / Unavailable' in many countries	Discontinued by manufacturers (e.g., Roferon-A, Intron A); previously used off-label intracystically.
Peginterferon alfa-2a	'Available'	Marketed as Pegasys® for hepatitis B/C; used off-label for cystic craniopharyngioma; accessible in many countries.
Bleomycin	'Widely available'	Generic cytotoxic drug; found in most hospital formularies; requires careful intracystic preparation.
Radioisotopes (e.g., P-32, Y-90)	⚠ 'Restricted'	Requires certified radiopharmacy and institutional licensing; typically used in specialized centers only.

'Note:' Drug availability may vary by country or institution. Always confirm with hospital pharmacy and regulatory bodies.

Hedrich et al. describes a retrospective case series, including five patients with intracystic peginterferon alfa-2a for cystic craniopharyngioma treatment according to an innovative care protocol. After initial CP cyst aspiration, peginterferon alfa-2a was injected once per week via an Ommaya reservoir for 6 weeks followed by response assessment with MRI.

Patients' age ranged from 4 to 54 years (four patients <12 years, one adult patient). Intracystic therapy with peginterferon alfa-2a was tolerated well by all five individuals without any major

toxicities and resulted in cyst shrinkage in all of the five patients. The importance of a permeability study prior to commencing intracystic therapy became apparent in one patient who suffered from cyst leakage.

Intracystic treatment with peginterferon alfa-2a was found to be a tolerable and efficacious treatment modality in patients with cystic craniopharyngioma. This experience warrants further research with a larger number of patients with measurement of long-term efficacy and safety outcomes [1)].

The authors propose **peginterferon alfa-2a**, a pegylated form with extended half-life and established safety profile in other indications, as a substitute, presenting a **retrospective case series** evaluating its feasibility and safety.

Study Design and Methodology

- **Design**: Retrospective case series

- **Sample**: 5 patients (age 4–54; 4 children, 1 adult)

- **Protocol**: After initial cyst aspiration, peginterferon alfa-2a was administered weekly for 6 weeks via an Ommaya reservoir.

- **Follow-up**: MRI for response assessment

- **Pre-treatment**: Permeability study was highlighted as essential following one adverse case of leakage.

 Strengths:

- Innovative use of peginterferon alfa-2a to fill a therapeutic gap.

- Uniform protocol across cases.

- Clear documentation of safety and early efficacy.

- Broad age range increases generalizability.

⚠ **Limitations**:

- **Very small sample size** (n=5) limits statistical validity.

- **Retrospective nature** introduces potential bias and lacks standardized outcome metrics.

- **Short-term follow-up**; no data on recurrence, endocrine impact, or long-term survival.

- **No comparator group** (e.g., standard interferon alfa-2a or surgery-only) limits interpretation of relative efficacy.

Results

- **Safety**: No major toxicities reported in any patient.

- **Efficacy**: Cyst shrinkage achieved in all five patients.

- **Complication**: One patient experienced leakage, underscoring the need for a permeability test.

The data supports the hypothesis that peginterferon alfa-2a is a **safe and potentially effective** intracystic agent in this context.

Discussion and Clinical Relevance

This study provides **preliminary real-world evidence** that peginterferon alfa-2a can serve as an effective intracystic treatment option for cystic craniopharyngiomas, particularly important in the wake of discontinued access to interferon alfa-2a. The lack of significant toxicity is encouraging, especially in pediatric patients.

However, due to the small number of cases and lack of long-term outcome data, the findings should be interpreted as **hypothesis-generating** rather than practice-changing. Further research in **prospective, multi-institutional trials** with larger cohorts is warranted.

Conclusion Hedrich et al. offer a promising alternative approach for managing cystic craniopharyngiomas using **peginterferon alfa-2a**. The treatment appears **feasible, safe, and effective in the short term**. Yet, the study's limitations — particularly its size and retrospective design — mean that **broader validation is essential** before widespread clinical adoption.

Comparative Analysis of Intracystic Treatments

Peginterferon alfa-2a vs Bleomycin vs Radioisotopes

Feature/Agent	Peginterferon alfa-2a	Bleomycin	Radioisotopes (e.g., P-32, Y-90)
Mechanism of Action	Immunomodulatory and antiproliferative	Cytotoxic antibiotic causing DNA strand breaks	Beta radiation causing localized cyst wall necrosis
Dosing Protocol	Weekly x6 via Ommaya	Multiple instillations (e.g., 4–6 doses over weeks)	Single or repeated instillation; dosimetry-based
Age Use	Pediatric and adult	Caution in young children due to neurotoxicity	Generally avoided in children <5–6 years old
Safety Profile	Excellent short-term tolerability in small series	Risk of chemical meningitis, neurotoxicity	Risk of CSF leak, radiation necrosis, hypothalamic damage
Key Risks	Cyst leakage (1 case in 5); minimal toxicity	Seizures, necrosis if drug leaks to parenchyma	Radiation exposure to critical adjacent structures
Regulatory Access	Off-label, emerging use	Widely available	Often restricted, requires radiopharmacy services
Onset of Response	Gradual shrinkage over weeks	Moderate to rapid	Rapid but with potential delayed adverse effects
Imaging Follow-up	MRI after 6 weeks	MRI at regular intervals	Imaging + dosimetry (CT/SPECT) required

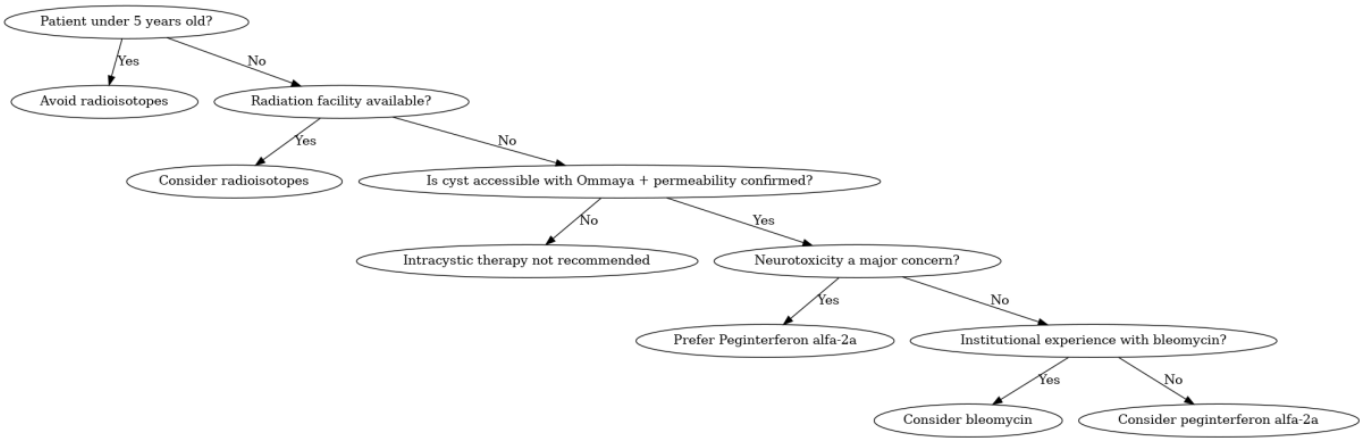
Feature/Agent	Peginterferon alfa-2a	Bleomycin	Radioisotopes (e.g., P-32, Y-90)
Long-Term Data	Limited (new approach, case series only)	Moderate, decades of use	Available, esp. from Europe, but often in outdated protocols
Procedure Requirements	Ommaya reservoir; permeability test recommended	Ommaya reservoir or catheter	Ommaya + radiation safety protocols

Summary Recommendations

Agent	Advantages	Disadvantages
Peginterferon alfa-2a	Favorable safety, non-cytotoxic, off-label alternative to IFN-α2a	Limited experience, unclear long-term outcomes
Bleomycin	Effective and accessible; longer track record	Neurotoxicity risk if leakage occurs; more systemic side effects
Radioisotopes	Potent and often effective with fewer instillations	Technically demanding; radiation risks; contraindicated in very young children

When to Consider Each Treatment?

* **Peginterferon alfa-2a** → Ideal for younger children or when minimal toxicity is essential. Requires close monitoring and permeability testing. * **Bleomycin** → Suitable where experience exists with its use. Effective but requires caution regarding leakage and systemic toxicity. * **Radioisotopes** → Best reserved for specialized centers with radiation safety protocols and older pediatric or adult patients with refractory cysts.



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 Flowchart Logic

Is the patient under 5 years old?

→ Yes → Avoid radioisotopes

→ No → Radioisotopes may be considered

Is radiation facility & radiopharmacy available?

→ Yes → Consider radioisotopes

→ No → Proceed to next

Is cyst accessible with Ommaya and permeability confirmed?

→ No → Intracystic therapy not recommended

→ Yes → Proceed to next

Is neurotoxicity a major concern (e.g., very young child, hypothalamic proximity)?

→ Yes → Prefer Peginterferon alfa-2a

→ No → Proceed to next

Institutional experience with bleomycin?

→ Yes → Consider bleomycin

→ No → Consider peginterferon alfa-2a

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Case Report: Intracystic Sellar/Suprasellar Cystic Mass in a School-aged Child

This case report is an 8-year-old child presenting with a sellar/suprasellar cystic lesion suggestive of craniopharyngioma. Following transfer from a referring hospital, the patient underwent a comprehensive diagnostic and stabilization process including mechanical ventilation, anticonvulsant and steroid therapy, and preparation for potential neurosurgical intervention. This case highlights the early multidisciplinary approach to pediatric intracranial cystic masses, focusing on timely imaging, supportive care, and surgical planning.

Case Presentation

An 8-year-old school-aged child (30 kg) was transferred from a Hospital after brain MRI revealed a sellar/suprasellar cystic lesion suggestive of a craniopharyngioma.

On admission (24/03), the patient was sedated with propofol following discontinuation of midazolam the night before.

He remained under conventional analgesia.

Neurological exam: isochoric, reactive pupils.

Treatment ongoing with **levetiracetam** and **dexamethasone**.

An EEG was scheduled and was pending at the time of assessment.

Clinical Findings

Respiratory:

- Mechanical ventilation (FiO_2 0.4)
- O_2 saturation: 100%
- VBG: pH 7.36, pCO_2 39 mmHg, lactate 0.8 mmol/L, base excess –3, HCO_3^- 21.6 mmol/L

❤ Cardiopulmonary:

- Regular rhythm, no murmurs
- Preserved vesicular breath sounds

Temperature & Infection:

- Afebrile in past 24h
- Receiving cefuroxime

Keywords

1)
Hedrich C, Patel P, Haider L, Taylor T, Lau E, Hook R, Dorfer C, Roessler K, Stepien N, Lippolis MA, Schned H, Koeller C, Mayr L, Azizi AA, Peyrl A, Lopez BR, Lassaletta A, Bennett J, Gojo J, Bartels U. Feasibility, tolerability, and first experience of intracystic treatment with peginterferon alfa-2a in patients with cystic craniopharyngioma. Front Oncol. 2024 Jul 10;14:1401761. doi: 10.3389/fonc.2024.1401761. PMID: 39050573; PMCID: PMC11266088.