



# An 81-year-old man with alteration of consciousness for 5 days

Presenter: Fl Issaree Rattarasarn  
Advisor: Methus Jantarapootirat  
Assoc Prof Wallaya Jongjaroenprasert



# Final Diagnosis: Spontaneous Ruptured of Craniopharyngioma with Chemical Meningitis



# Differential Diagnosis of Cystic Sellar Lesion

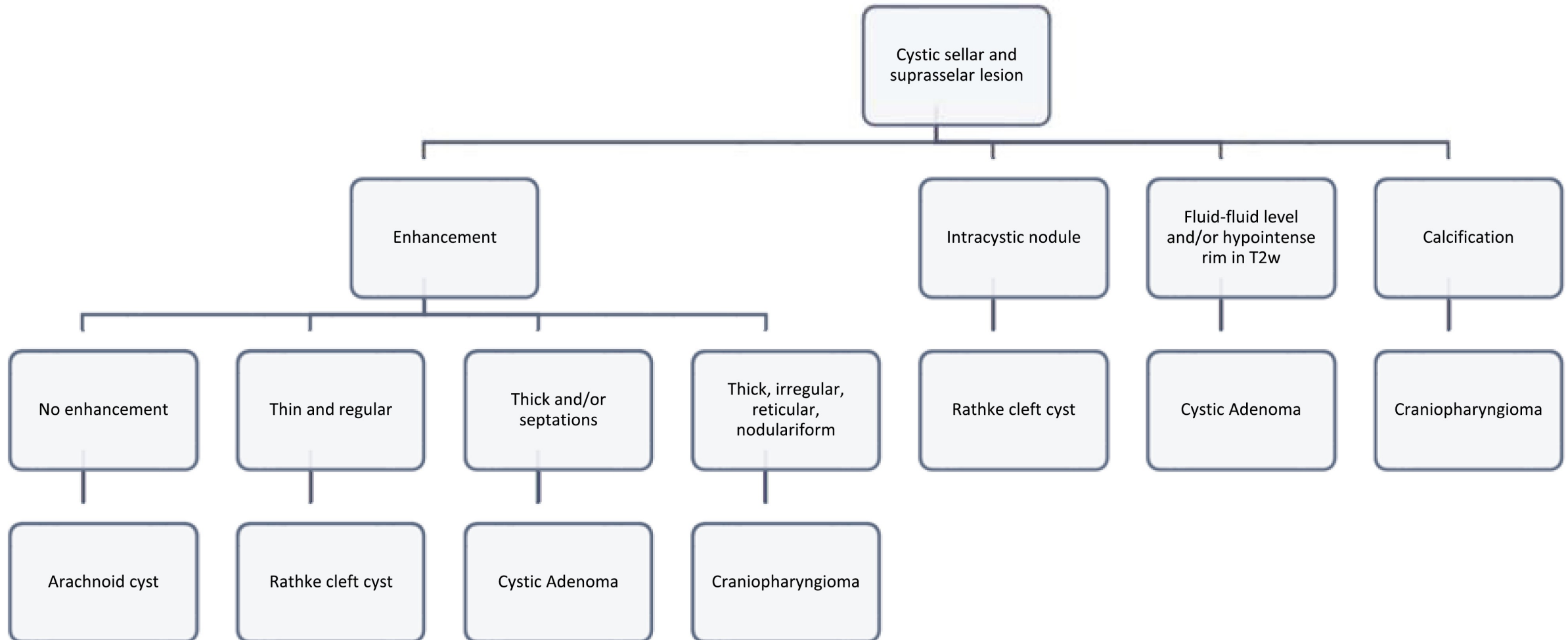
---



- Cystic lesions of the sellar region are considered to be any predominantly fluid-containing lesion
  - Fluids can vary from CSF, bleeding, necrosis, and high protein or oily contents and are present as non-enhancing components on postcontrast MRI sequences



# Differential Diagnosis of Cystic Sellar Lesion

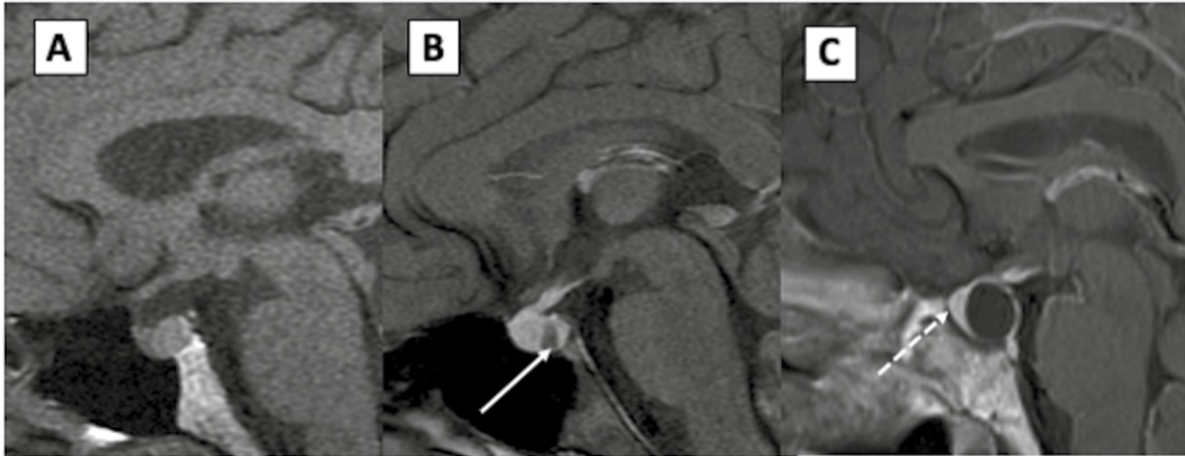




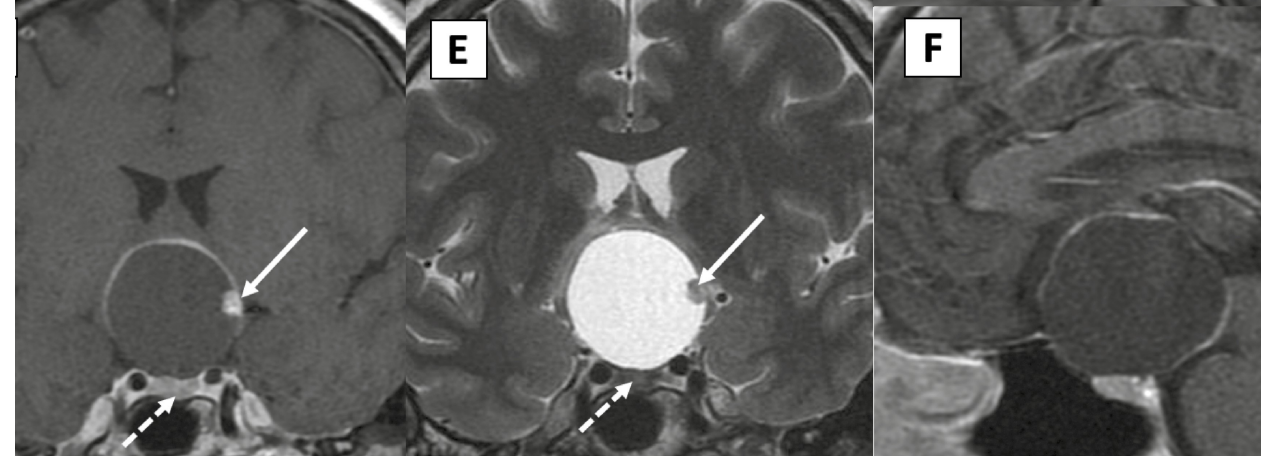
# Differential Diagnosis of Cystic Sellar Lesion



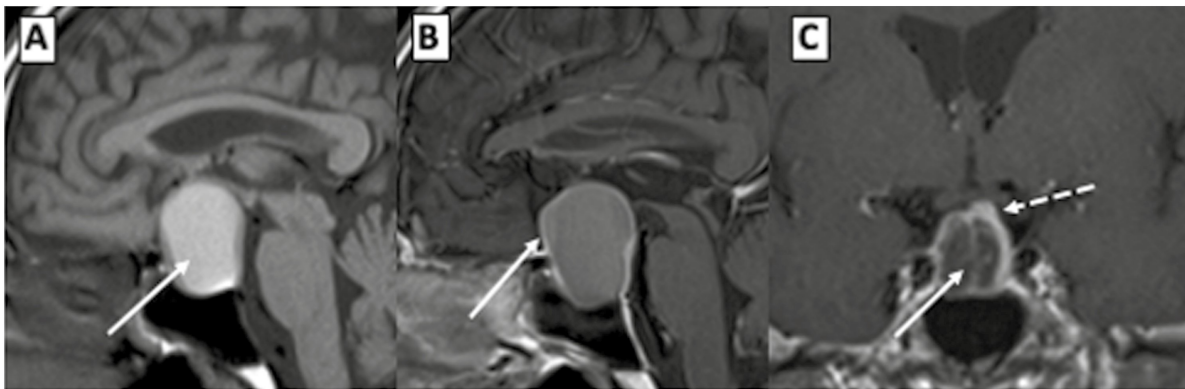
Rathke's Cleft Cyst



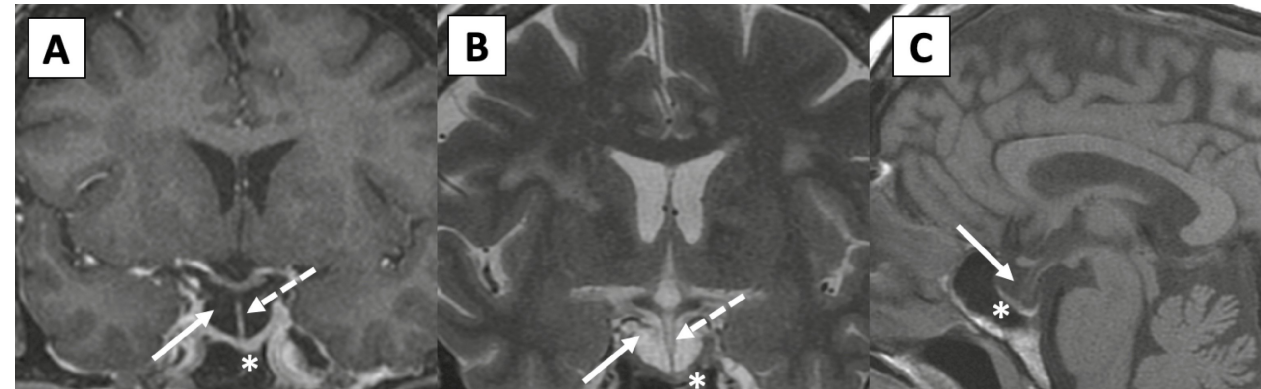
Craniopharyngioma



Cystic Pituitary Adenoma



Arachnoid Cyst





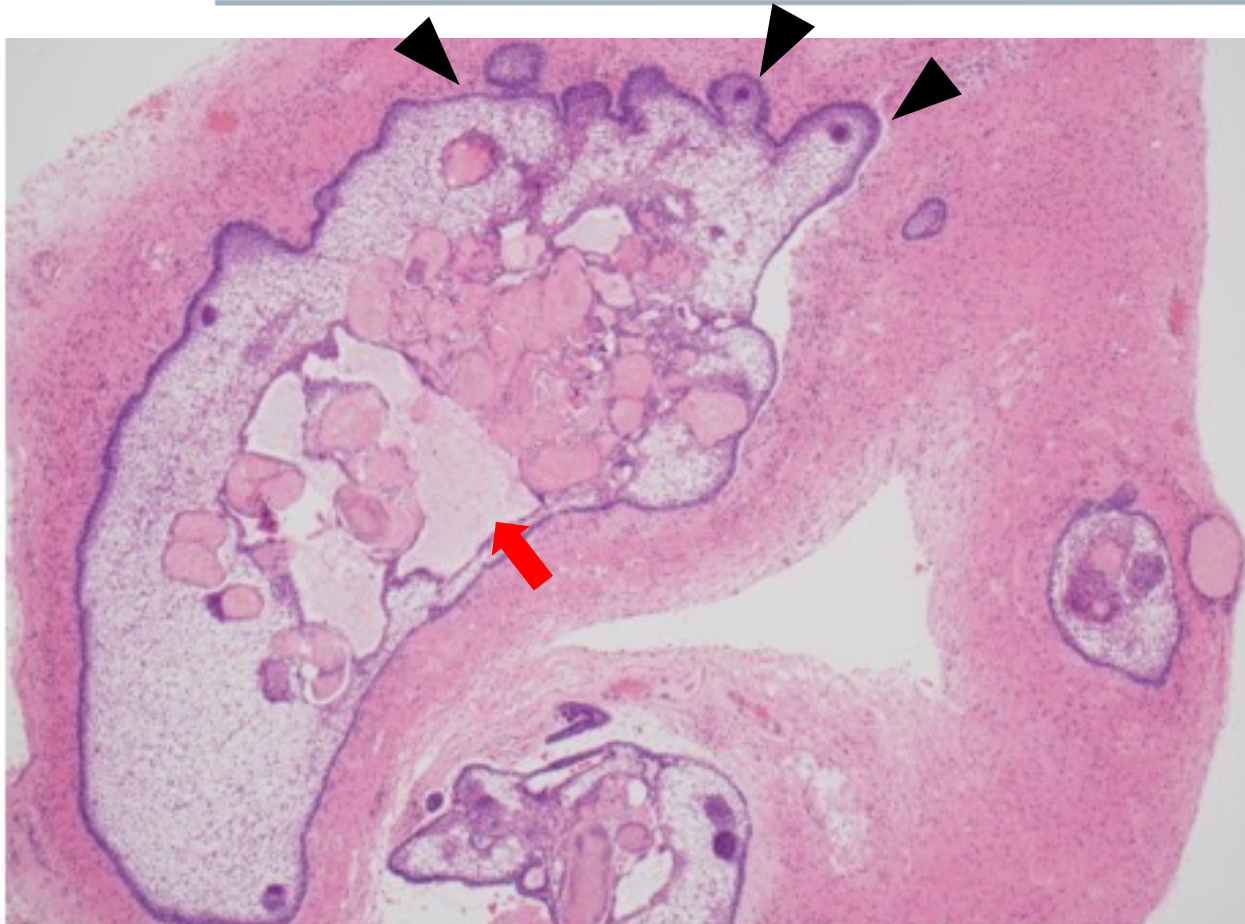
# Craniopharyngioma



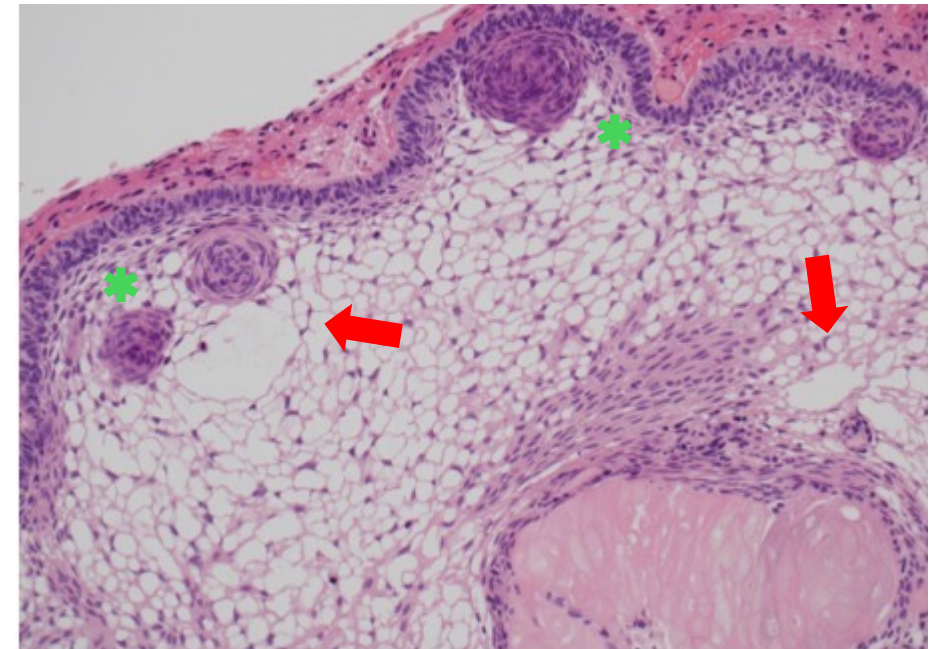
- Craniopharyngioma (CP) is a rare intracranial tumor arising from the epithelial remnants of Rathke's pouch, most frequently originating in the sellar/parasellar region
- Constitutes 1–3% of all primary intracranial tumors in adults and 5–10 % of intracranial tumors in children
- Histologically, CP is a benign low-grade tumor with 2 distinct phenotypes:
  - Adamantinomatous CP (ACP)
  - Papillary CP (PCP)



# Adamantinomatous craniopharyngioma (ACP)

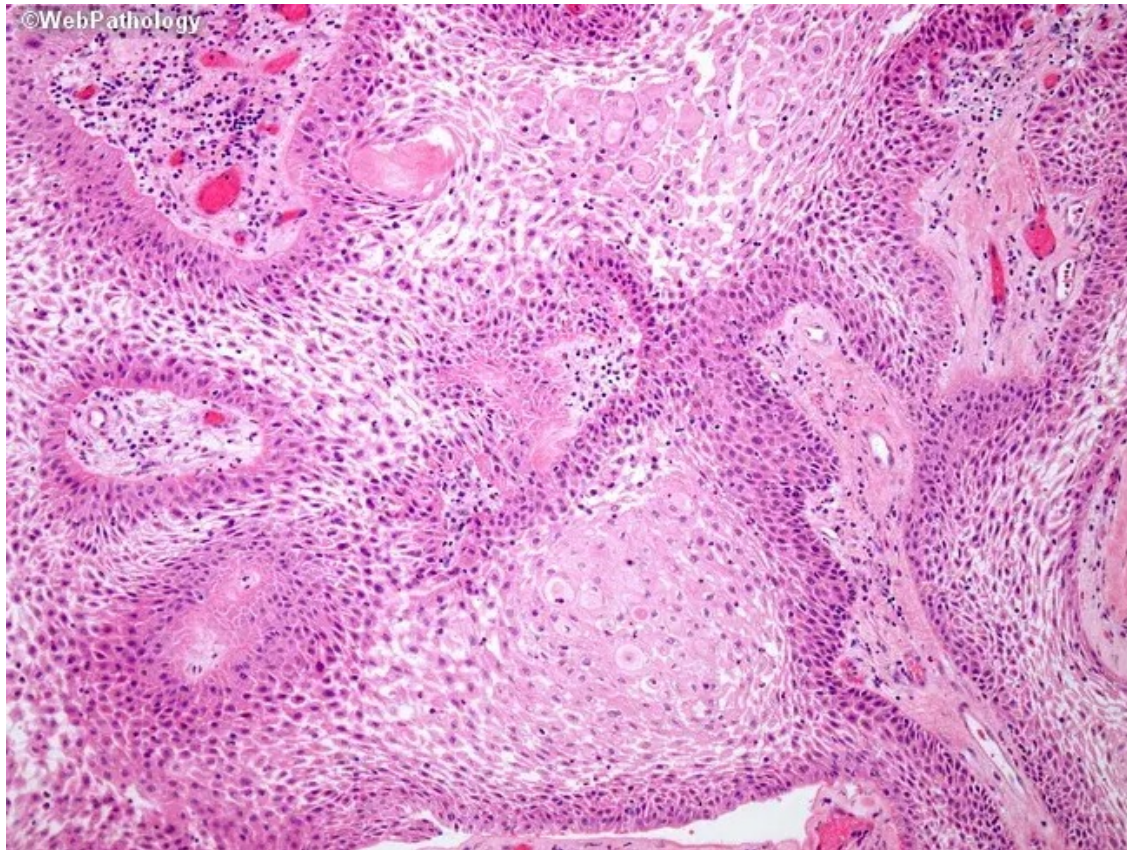


- Finger-like protrusion into surrounding tissue ▲
- Peripheral palisading, nodular whorls \*
- Satellite reticulum ↑





# Papillary craniopharyngioma (PCP)



- Sheets of well-differentiated **non-keratinizing squamous epithelium** surrounding the fibrovascular cores.
- Pseudopapillary appearance.



# Craniopharyngioma


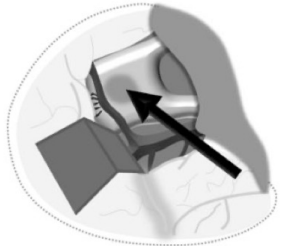
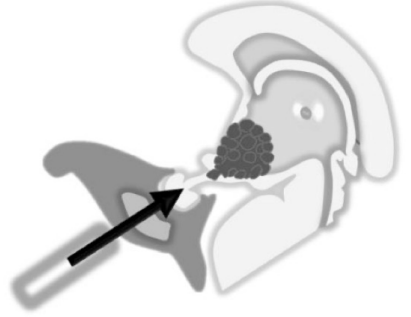


|                       |              | PCP   | ACP   |
|-----------------------|--------------|---|---|
| <b>Epidermiology</b>  | Gender       | Male predominance   | Male = Female                                 |
|                       | Age          | Adults<br>(mean age 45 Y/O)                                   | <b>Bimodal distribution</b>                   |
| <b>Clinical</b>       | Hypothalamic | <b>Frequent</b>   | Rare  |
|                       | Psychiatric  | <b>Frequent</b>   | Rare  |
|                       | Visual       | <b>Common</b>   | <b>Frequent</b>                               |
|                       | Endocrine    | Unusual   | <b>Frequent</b>                               |
| <b>Area of origin</b> |              | Midline at infundibulum to<br>3 <sup>rd</sup> ventricle floor | Midline at pituitary stalk to<br>infundibulum |

|                          |                        | <b>PCP</b>  | <b>ACP</b>   |
|--------------------------|------------------------|---|--|
| <b>Neuroimaging</b>      | Distribution           | <b>Mostly involving the 3<sup>rd</sup> ventricle</b>  | <b>Children: mostly sella</b><br>Adults: mostly not-strict 3 <sup>rd</sup> ventricle |
|                          | Shape                  | <b>Mostly round</b>                                   | <b>Typically multilobulated of elliptical</b>  |
|                          | Consistency            | <b>Mostly pure solid, but also cystic-cauliflower</b> | <b>Mostly mixed with solid and cystic components</b>                                 |
|                          | Basal duct-like recess | Half of cases<br>(pathognomonic sign)                 | Absent   |
|                          | Calcification          | <b>Rare</b>   | <b>Children 90%, adult 40%</b>   |
|                          | MRI signal             | Enhancement of the cyst wall or solid portion         |  |
| <b>Other Macroscopic</b> | Cystic content         | Clear to yellow (when cystic)                         | Machinery-oil like rich in cholesterol clefts  |

|                             |                                       | <b>PCP</b>                                     | <b>ACP</b>         |
|-----------------------------|---------------------------------------|--|--------------------|
| <b>Microscopic features</b> | Epithelium                            | <b>Well-differentiated stratified squamous</b> | Odontogenic        |
|                             | Stellate reticulum (microcystic area) | Absent   | <b>Present</b>     |
|                             | Keratinization                        | <b>Exceptional</b>                             | <b>Wet nodules</b> |
|                             | Keratohyaline granules                | Rare   | Absent             |
|                             | Goblet cells                          | Rare   | Absent             |
| <b>Molecular genetics</b>   | BRAF (V600E) gene mutation            | <b>Present</b>                                 | Exceptional        |
|                             | CTNNB1 gene mutation                  | Exceptional                                    | <b>Present</b>     |

- **Surgery**
- **Adjuvant therapy**
  - Radiotherapy
    - No consensus regarding the optimal timing of RT for residual or recurrent PCPs or the prefer modality
  - *Targeted therapy: BRAF/MEK inhibitor*

| Operative corridor   | Advantages   | Disadvantages   |
|--|--|---|
| Transcallosal<br>                     | <ul style="list-style-type: none"> <li>• Early control of hydrocephalus</li> <li>• Good view of the upper intra-3V portion of the tumor</li> </ul>   | <ul style="list-style-type: none"> <li>• Risk of injury to the fornices and deep venous structures</li> <li>• Poor view of the basal tumor attachment to the 3VF</li> </ul>   |
| Pterional trans-lamina terminalis<br> | <ul style="list-style-type: none"> <li>• Shortest approach to the chiasm-parasellar region</li> <li>• Good view of the ipsilateral optic nerve and carotid artery</li> <li>• Good view of the tuber cinereum/infundibulum, the most common area of PCP attachment</li> </ul>   | <ul style="list-style-type: none"> <li>• Risk of brain retraction injury to the frontal/temporal lobes</li> <li>• Poor view of the optic chiasm undersurface and hypothalamic perforating vessels</li> <li>• Poor view of the ipsilateral hypothalamus</li> </ul> |
| Endoscopic endonasal approach<br>    | <ul style="list-style-type: none"> <li>• Offers the best aesthetic results and avoids brain retraction</li> <li>• Good midline panoramic view of the pituitary stalk, 3VF and optic chiasm undersurface</li> <li>• Good control of tiny hypothalamic perforators and superior hypophyseal artery branches to the chiasm</li> <li>• Good view of tumor ring-like attachment to the infundibulum/tuber cinereum</li> <li>• Higher rates of radical resection and better patient visual outcomes</li> </ul> | <ul style="list-style-type: none"> <li>• Poor control of the tumor portions extending beyond the carotids</li> <li>• Poor view of the upper portion of the 3VF</li> <li>• Risk of CSF leak/meningitis</li> </ul>  |



# Targeted therapy in PCP



- Newly diagnosed PCP population (N = 16)
  - Histologically proven *BRAF* V600E–mutant papillary craniopharyngioma
- Vemurafenib 960 mg p.o. b.i.d. for 28 days in combination with cobimetinib 60 mg p.o. o.d. for 21 days
- Patients would receive definitive therapy with radiation or surgery after treatment with vemurafenib–cobimetinib for 4 cycles

## ORIGINAL ARTICLE

### BRAF–MEK Inhibition in Newly Diagnosed Papillary Craniopharyngiomas

P.K. Brastianos, E. Twohy, S. Geyer, E.R. Gerstner, T.J. Kaufmann, S. Tabrizi, B. Kabat, J. Thierauf, M.W. Ruff, D.A. Bota, D.A. Reardon, A.L. Cohen, M.I. De La Fuente, G.J. Lesser, J. Campian, P.K. Agarwalla, P. Kumthekar, B. Mann, S. Vora, M. Knopp, A.J. Iafrate, W.T. Curry, Jr., D.P. Cahill, H.A. Shih, P.D. Brown, S. Santagata, F.G. Barker II, and E. Galanis

**Table 2. Objective Response at 4 Months.\***

| Assessment   | Value (N = 16) |
|--|----------------|
| <b>Volumetric response according to central radiologic review</b>  |                |
| Complete or partial response — no. (%)                             | 15 (94)        |
| 95% confidence interval  | 70–100         |
| Nonresponse — no. (%)  | 1 (6)          |
| <b>Bidimensional response according to local radiologic review</b> |                |
| Complete or partial response — no. (%)                             | 15 (94)        |
| 95% confidence interval  | 70–100         |
| Nonresponse — no. (%)  | 1 (6)          |



# Spontaneous Rupture of Craniopharyngioma



- Spontaneous rupture of a cystic craniopharyngioma is an extremely rare event, which was first described by Worster-Drought et al in 1927
- The pathophysiology of spontaneous CP rupture is yet to be fully elucidated, but it seems to involve weakness of the cystic wall caused by cystic growth
- It may present with the sequelae of chemical meningitis or with symptoms of neural compression or asymptomatic.
- Diagnosis is generally suggested by an altered CSF analysis (pleocytosis and high protein levels, high cholesterol content in cyst) with negative culture



| Author/Y                                   | Age(y)/gender | Clinical presentation   | CSF findings                        |                 |                                | Histological subtype | Management                                 |
|--|---------------|---|-------------------------------------|-----------------|--------------------------------|----------------------|--|
|  |               |   | Chemical abnormalities (ChoC, ChoL) | Protein (mg/dL) | Cells (cells/mm <sup>3</sup> ) |                      |  |
| Worster-Drought et al 1927 <sup>1</sup>    | 19/F          | Headache and vomiting   | Fat globules                        | 12              | 267                            | NA                   | NA   |
| Russell and Pennybacker, 1961 <sup>2</sup> | 67/F          | Fever and neck stiffness  | NA                                  | NA              | 500                            | NA                   | Antibiotics + hydrocortisone               |
| Patrick et al, 1974 <sup>3</sup>           | 21/M          | Headache and neck stiffness   | Fat; ChoL (175 mg/dL)               | 7.500           | 23.700                         | NA                   | Dexamethasone                              |
| Lloyd and Belchetz, 1977 <sup>4</sup>      | 29/F          | Headache, vomiting, fever, drowsy, and neck rigidity                    | NA                                  | 1.420           | 320                            | NA                   | Dexamethasone                              |
| Martin and Kleinman, 1980 <sup>5</sup>     | 60/M          | Nuchal rigidity, headache, confused, fever                              | NA                                  | 365             | 132                            | NA                   | Antibiotics + methylprednisolone + surgery |
| Krueger and Larsson, 1988 <sup>6</sup>     | 73/M          | Recurrent fever, headache, chills, mild confusion                       | NA                                  | NA              | 270                            | NA                   | Antibiotics + steroids + tumor surgery     |
| No authors listed, 1993 <sup>7</sup>       | 51/M          | Headache, nausea, vomiting, photophobia, stiff neck, fevers, and chills | NA                                  | 97              | 400                            | PCP                  | Antibiotics + surgery                      |
| Satoh et al, 1993 <sup>8</sup>             | 25/M          | Headache, nausea  | ChoC                                | 400             | 35                             | NA                   | NA   |
| Satoh et al, 1993 <sup>8</sup>             | 36/M          | Fever, neck stiffness   | No ChoC                             | 93              | 3.070                          | ACP                  | Steroids + surgery                         |
| Satoh et al, 1993 <sup>8</sup>             | 54/M          | High fever, consciousness disturbance                                   | ChoL (39mg/dL)                      | 855             | 54                             | PCP                  | Surgery                                    |
| Maeda et al, 1993 <sup>9</sup>             | 20/F          | Headache, vomiting, fever, and neck stiffness                           | NA                                  | 386             | 2029                           | NA                   | Surgery (3 mo)                             |
| Shinohara et al, 1997 <sup>10</sup>        | 8/F           | Fever, headache, visual disturbance, and lassitude                      | No ChoC or ChoL                     | NA              | NA (no pleocytosis)            | NA                   | Steroids                                   |
| Kulkarni et al, 2000 <sup>11</sup>         | 38/F          | Acute deterioration in sensorium  | ChoL (8mg/dL)                       | 133             | 410                            | NA                   | Steroids + anticonvulsants + surgery       |
| Hadden and Allen, 2004 <sup>12</sup>       | 34/M          | Sudden generalized headache, fever                                      | NA                                  | NA              | NA                             | NA                   | Antibiotics and hydrocortisone             |
| Rajput et al, 2012 <sup>13</sup>           | 17/F          | Headache and vomiting   | ChoL (11mg%)                        | NA              | 650                            | PCP                  | Steroids                                   |
| Rajput et al, 2012 <sup>13</sup>           | 16/M          | High fever, headache and vomiting                                       | ChoL (8mg%)                         | 17              | 5                              | PCP                  | Steroids + surgery                         |

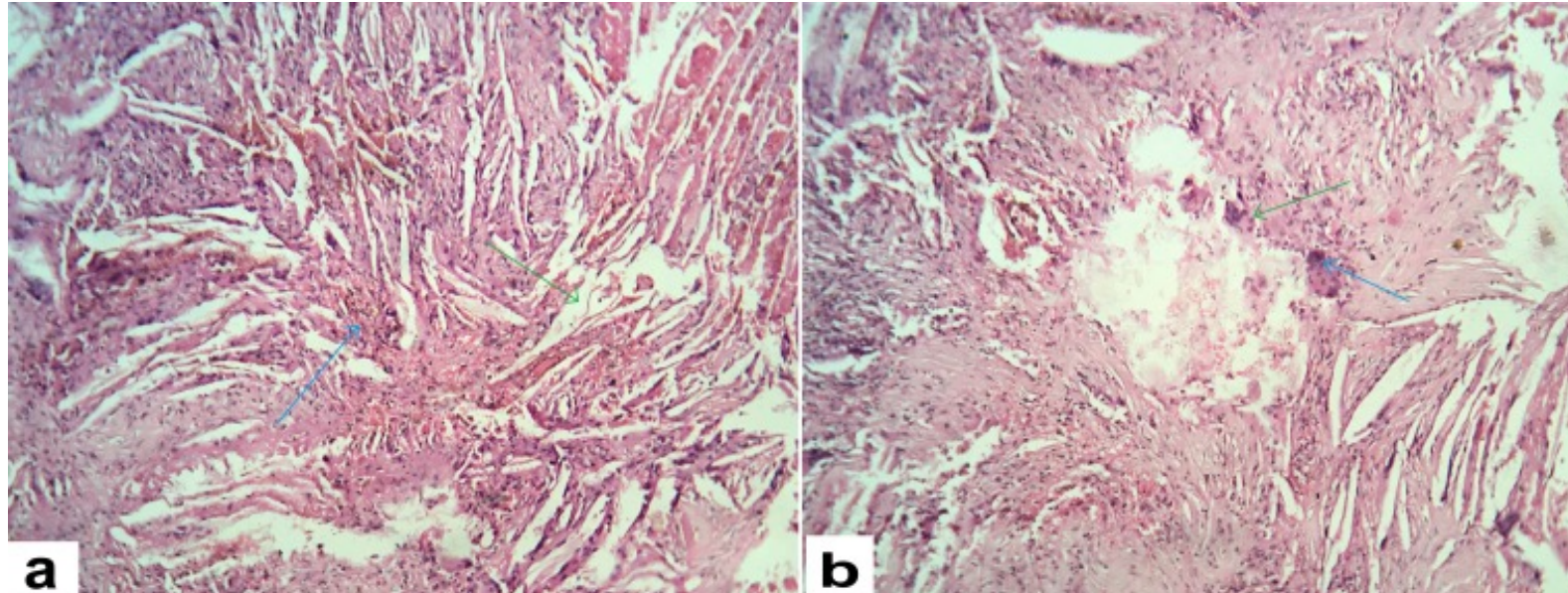


# Spontaneous Rupture of Craniopharyngioma



## Hallmark Findings

- Cholesterol crystals or elevated cholesterol levels on CSF analyses
- Cyst reduction on subsequent imaging





# Spontaneous Rupture of Craniopharyngioma



## Management

- Treatment is straightforward with IV steroid administration
- Surgery is reserved for maintained mass effect tumors or cyst regrowth after rupture
  - Hydrocephalus
  - Endangered vision
- Surgical technique:
  - Direct surgical approach
  - Aspirate cyst fluid with or without placing an intracystic catheter in case of a cystic lesion



โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล  
RAMATHIBODI HOSPITAL, MAHIDOL UNIVERSITY

Thank You