Case 5: Hiding in plain sight...

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Dr. Maria Martinez-Lage declares she has no conflict of interest to disclose.

Case presentation

- 9 year old girl with polyuria and polydipsia
- Negative initial work up
- Months later she developed headaches and visual changes
- Biochemical panhypopituitarism

MRI: T1 post-contrast images

Coronal view

Sagittal view

Histopathology images
Lymphocyte-rich intracranial mass lesions
- Sellar/midline lesions
- Hemispheric/other lesions
- Children
- Young adults
- Older adults

Lymphocyte-rich lesions of the sella
Non-neoplastic: Hypophysitis
- Primary
  - Infectious (rare)
  - Inflammatory:
    - Lymphocytic
    - Granulomatous
    - Xanthogranulomatous
- Secondary (due to systemic autoimmune disorders including sarcoidosis, IgG4, and treatment with checkpoint inhibitors)

Lymphocytic hypophysitis
- Initially attributed to young women in the postpartum state
- Affects both men and women over a large age range
- Inflammatory infiltrates are focal or diffuse, with varying degrees of gland destruction
- Can involve adenohypophysis or neurohypophysis

IgG4-related hypophysitis
- Can be associated with hypertrophic pachymeningitis
- Most frequently seen with systemic disease (retroperitoneal fibrosis and salivary gland involvement)
- Maybe more common in men
Granulomatous hypophysitis

- Primary
- Secondary
  - Sarcoidosis
  - Granulomatosis with polyangiitis (Wegener’s)
  - Tuberculosis

Lymphocyte-rich lesions of the sella

Neoplastic conditions

- Histiocytosis
  - Langerhans Cell Histiocytosis (50%)
  - Non-LCH (Erdheim-Chester disease)
- Germ-cell tumors: germinoma
- Lymphoma (not a common site)

Germinoma

A malignant germ cell tumour histologically characterized by the presence of large primordial germ cells with prominent nuclei and variable cytoplasmic clearing. (WHO 2016 definition)

- Most common CNS germ cell tumor
- Affects children, adolescents and young adults
- Extremely sensitive to radiotherapy – long term survival >90%
- Midline location: pineal > suprasellar > others
- More frequent in isolation, can be seen in mixed germ cell tumors

Germinoma

- Tumor cells show round, vesicular nuclei with prominent nucleoli and clear cytoplasm
- Frequent lymphocytic and occasional granulomatous inflammation
- Isolated syncytiotrophoblastic elements are allowed
- POSITIVE IHC MARKERS
  - Nuclear OCT4, Sall4
  - Cytoplasmic/membranous PLAP
  - Membranous/Golgi CD117/Kit
  - Membranous D2-40
  - LIN28A, NANOG, ESRG

Lymphocytic infiltrates in CNS neoplasms (other locations outside of the sella/midline)

- Ganglion cell tumors (gangliocytoma and ganglioglioma)
- Pilocytic astrocytoma
- Pleomorphic xanthoastrocytoma
- Subependymal giant cell astrocytoma/tumor
- Chordoid glioma
- Astrocytomas
- Lymphoplasmacytic rich meningioma
- Hematolymphoid derived neoplasms
- Histiocytosis (LCH and non-LCH)
- CNS lymphoma and related conditions
- Germinoma and other germ cell tumors

Chordoid glioma of the third ventricle

A slow-growing, non-invasive gial tumour located in the third ventricle, histologically characterized by clusters and cords of epithelioid tumour cells expressing GFAP, within a variably mucinous stroma typically containing a lymphoplasmacytic infiltrate. (WHO 2016 definition)

- Rare (about 100 cases reported)
- Most cases occur in adults
- Involves the anterior portion of the third ventricle
- Clinical presentation with increased intracranial pressure, visual changes, or hypothalamic/hypophyseal dysfunction
- WHO grade II
Chordoid glioma of the third ventricle
- Clusters and chords of epithelioid cells in a myxoid background
- Lymphoplasmacytic infiltrate
- Other patterns include solid, spindle cell, and fibrosing
- POSITIVE IHC MARKERS
  - GFAP
  - TTF-1
  - Others: vimentin, CD34, variable S100 protein, EMA, and cytokeratin

Back to our case
- After the biopsy she was diagnosed with neurosarcoidosis
- Treated with steroids, mass decreased in size
- Due to side effects she was transitioned to adalimumab (Humira) with >90% reduction in the mass
- Due to mass growth Humira was discontinued and she was started on methotrexate
- Months later, she developed episodes concerning for TIA, and MRI showed progression

Chordoid glioma of the third ventricle
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- POSITIVE IHC MARKERS
  - GFAP
  - TTF-1
  - Others: vimentin, CD34, variable S100 protein, EMA, and cytokeratin

Back to our case
- She was placed on leflunomide (Arava) for two years, then she had another episode aspirin was added
- She then developed steatohepatitis and she was switched to infliximab (Remicade) and when an MRI showed progression the dose was increased and monthly steroid pulse was added
- After several months her baseline poor vision had worsened significantly and she was admitted for a biopsy (8-9 years after initial symptoms)
CASE 5: HIDING IN PLAIN SIGHT

Final Diagnosis: Germinoma

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