

# Neuroendocrine Disturbances as The Initial Manifestation of Leptomeningeal metastasis due to Breast Cancer. -

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## BACKGROUND

Leptomeningeal metastasis (LM) is defined by the presence of malignant cells in the leptomeninges or cerebrospinal fluid (CSF) distant from the site of the tumor.

Usually represents an advanced stage of cancer. Recently, **LM has become more prevalent** due to improved advanced-stage survival in many cancer patients, as well as the increased use of highly sensitive neuroimaging studies.

LM can present with a variety of manifestations making diagnosis oftentimes **challenging**.

## CASE PRESENTATION

A recently relocated 60 year old female presented to the hospital reporting 4-weeks of rapidly progressing symptoms including a 20 pound unintentional weight loss, fatigue, polydipsia, polyuria, poor appetite, and right-gaze diplopia. Patient reported she was **up-to-date in malignancy screening**, and denied recent travel, drug abuse, or hospitalization.

Physical exam: her vital signs were notable for a blood pressure of 100/50 mmHg and mild tachycardia (HR 104), but otherwise her physical exam was unrevealing, including neurologic evaluation.

### Notable initial labs

<b>CBC</b>	Hgb(10.3), Plat (122)
<b>CMP</b>	Na (143), Ca (12)
<b>Endo</b>	PTH (214), Cortisol (2.5)

## DIAGNOSTIC WORK UP – HOSPITAL COURSE

- Day 3**
  - ACTH stimulation test showed appropriate response. Cortisol therapy started.
  - Pt developed hypernatremia: **central DI**
  - MRI brain: leptomeningeal enhancement in the basal structures of the brain, specifically in the posterior pituitary gland. **Concern for Neuro Sarcoidosis.**
- Day 7**
  - LP: RBC wnl, WBC 13 (94%), Prot (185), Glu (60). Negative cytology. Plan to start steroids, but needs to get tissue first.
  - CT C/A/P: Mottled appearance of the osseous structures. Negative for masses or adenopathy.
- Day 7 14**
  - NM gallium scan: Physiologic uptake in lacrimal glands, nasopharynx, liver, bone marrow, and colon.
  - Parathyroid biopsy: Hypercellular parathyroid gland bilaterally.
  - BMBx: Rare atypical cells. Rule out breast cancer was recommended.
- Day 14 21**
  - 2<sup>nd</sup> MRI brain: Nodular leptomeningeal enhancement involving cerebrum and cerebellum, including the optic chiasm and thalami.
  - Mammography: mass with spiculated micro calcifications and retracted nipple BIRADS 0.
- Day 27**
  - Breast biopsy: Invasive lobular carcinoma, HER2 positive, estrogen receptor-positive, and progesterone receptor-negative

## DIFFERENTIAL DIAGNOSIS

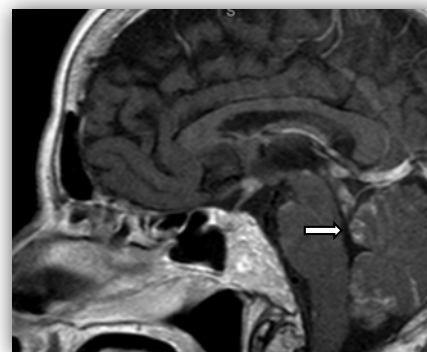
- Neuro Sarcoidosis
- Leptomeningeal metastasis
- Histocytosis X

## OUTCOMES

- Patient was discharged to continue treatment with Oncology.
- Patient continues therapy with Oncology so far.



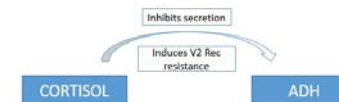
No enlarged pituitary



Leptomeningeal enhancement in posterior fossa

## DISCUSSIONS

- Leptomeningeal metastasis is a rare and devastating manifestation of advanced malignancy. Multifocal involvement is the **hallmark** of the disease.
- Solid tumors (mainly **breast**, lung, and melanoma), and hematologic cancers are the main etiologies.
- Diagnose is made by imaging and positive cytology in CSF.
- DI and secondary adrenal insufficiency are most commonly seen in pituitary metastasis which are also associated to breast cancer. Was interesting that there was no pituitary masses in the patient.
- Central DI was worse after by cortisol replacement which is explained by its close physiologic relationship.



- Posterior lobe involvement that lead to DI is associated with metastatic disease given its arterial supply and anatomical position that facilitates malignant spread.
- Central DI and diplopia are independent predictors of metastatic disease.

## TAKE HOME MESSAGES

- LM has multifocal involvement.
- LM can be the initial manifestation of cancer.
- Presence of neuroendocrine manifestations should rise concern for underlying malignancy.
- Always remember the relationship between the cortisol and ADH.