A patient with hyponatraemia and hyperprolactinaemia with pituitary and ventricular lesion.

A 48-year-old female patient with a long medical history of primary focal segmental glomerulosclerosis and renal insufficiency in 1985, kidney transplantation in 1991, chronic vascular rejection with restart of dialysis in 2005, followed by multiple liver and spleen abscesses, development of diabetes mellitus, then removal of the transplanted kidney in 2007, in 2009 second kidney transplantation with again borderline rejection of the kidney and continuous immunosuppressive medication, is admitted to a smaller hospital (where she also works as a nurse) because of progressive fatigue, nausea and muscle weakness that started after she underwent cataract surgery. After that surgery she developed a pneumonia and sinusitis that was treated with amoxicillin. The fever disappeared but the nausea remained and she started to vomit, several times a day. She lost 8 kg of weight in the last four weeks. A hyponatraemia is found (125 mmol/L, normal value 135-145 mmol/L) with a normal potassium (4.7 mmol/L, normal value 3.5-4.7 mmol/L) and for further diagnostic work-up she is transferred to the department of internal medicine at our university hospital. Further lab testing shows hypogonadotropic hypogonadism (very low levels of LH and FSH) with increased prolactin level of 1600 mE/L (normal value <500 mE/L) and the patient has indeed an amenorrhoea since 5 months. The endocrinologist has seen the patient and he now asks the neurosurgeon to evaluate a MRI scan that had been performed in the other hospital 6 weeks earlier (but without Gadolineum contrast) for signs of a pituitary lesion and he asks if there are any neurosurgical explanations for her hyponatraemia and hyperprolactinaemia.

1. What is the differential diagnosis of the continuous nausea and vomiting?
2. What is the differential diagnosis of prolonged hyponatraemia?
3. What kind of neurosurgical lesions can cause hyperprolactinaemia?
4. What is your advice to the endocrinologist?

Differential diagnosis of nausea and vomiting in this patient with prolonged history of renal insufficiency, kidney transplant with rejection and second transplant with many years of immunosuppressive therapy, could be a malignancy (colon, pancreas, ovaries), it could be secondary to the hyponatraemia, it could be gastroparesis with the diabetes mellitus or adrenal insufficiency. The hyponatraemia could be due to SIADH, cerebral salt wasting or from a renal source, could be caused by adrenal insufficiency (although potassium is not elevated) or secondary to hyperglycaemia (but glucose is only slightly elevated).
The differential diagnosis of hyperprolactinaemia is quite extensive (including pregnancy, a nonfasting blood sample, excessive exercise, a history of chest wall surgery or trauma, renal failure, cirrhosis, hypothyroidism, and a wide array of drugs like dopamine-receptor antagonists (eg, phenothiazines, butyrophenones, thioxanthenes, risperidone, metoclopramide, sulpiride, pimozide), dopamine-depleting agents (eg, methyldopa, reserpine) and others (eg, isoniazid, danazol, tricyclic antidepressants, monoamine antihypertensives, verapamil, estrogens, antiandrogens, cyproheptadine, opiates, H2-blockers [cimetidine], cocaine), but neurosurgical lesions that can cause hyperprolactinaemia are (micro)prolactinoma, Rathke’s cyst with stalk compression and other suprasellar tumors with stalk compression.

Advice to the endocrinologist was to repeat the MRI scan without and with Gadolineum with focus on the pituitary region.

MRI was repeated and showed the following:

5. Describe the findings on the MRI (coronal and sagittal T1 with Gd).

There is an area of low intensity on the left side in the pituitary gland. There is also contrast enhancement of the ependyma of the third ventricle and both lateral ventricles.
6. Describe the findings on the MRI (axial and coronal T1 with Gd).

Enlarged ventricular system with loculated right temporal horn and densely enhancing choroid plexus of lateral, third and fourth ventricle. This imaging is typical for choroid plexitis caused by Cryptococcus.

Clinical course.

A lumbar puncture was performed, 7 cc of dark yellow, viscous CSF was aspirated. Lab testing was positive for Cryptococcus antigen, and culture was positive for Cryptococcus neoformans. Because of progressive confusion and persistent nausea and vomiting, an external ventricular drainage was inserted. The opening pressure however was low (6 cm H2O). She was treated with amfotericine B and flucytosine. After two weeks she underwent endoscopic septostomy and fenestration of loculated parts of the ventricular system and slow improvement of her clinical condition.

Discussion of this case.

Central nervous system cryptococcal infection usually manifests as meningitis, meningoencephalitis, encephalitis or ventriculitis, depending on the patient's immunity and inflammatory response. Choroid plexus involvement, with trapping of the temporal horns, is a rare manifestation of this infection. Cryptococcus neoformans is a fungal pathogen that causes invasive infection of the CNS (and is particularly important in the era of the HIV/AIDS epidemic). The encapsulated yeast-like fungus was first isolated from fruit juice by San Felice in 1894 and was shown to be present in natural sources such as milk. Various types of soil contaminated with pigeon excreta provide an environmental source of this widely prevalent organism.

Infection occurs through inhalation of a small diameter (<10 µm) yeast-like organism, which enters the respiratory passage but then remains dormant depending on the host reaction. The mode of spread to the CNS is through haematogeneous dissemination from the lungs. Subsequently, the fungus spreads to the CSF to cause meningitis, encephalitis and
ependymitis; it is this leptomeningeal spread that is responsible for the clinical manifestations, rather than choroid plexitis alone, which is often asymptomatic. The CNS is the preferred site for cryptococcal infection, as the soluble anticyeptococcal factors present in serum are absent from CSF. In addition, the inflammatory response evoked is minimal, as the polysaccharide capsule of the fungus hinders phagocytosis and impairs leukocyte migration.

The spectrum of radiological findings includes dilated perivascular spaces, gelatinous pseudocysts, intraparenchymal cryptococcomas, miliary nodules, meningeal involvement, intraventricular/choroid plexus masses and hydrocephalus. As the infection spreads, mucoid gelatinous material produced by the capsule of the fungus gets enmeshed with budding cryptococci, resulting in the formation of cysts, called gelatinous pseudocysts. These are thought to be an “unreactive” form of meningoencephalitis, preferentially located in the basal ganglia, thalamus, midbrain and dentate nuclei. Gelatinous pseudocysts are non-enhancing lesions and appear similar to CSF on all imaging sequences.

Gelatinous pseudocysts and cryptococcomas in the choroid plexus are relatively specific for CNS cryptococcosis. A unilateral or bilateral enlargement of the choroid plexus that enhances on contrast is a relatively rare manifestation of cryptococcal infection. Choroid inflammation can progress to ependymitis, intraventricular synechiae, loculation or enlargement, and entrapment of the temporal horn owing to the obstruction of flow by cryptococci, as seen in this case. Contrast enhancement may not occur in the presence of impaired immunity. The choroid plexus, which lies at the interface between the CSF and the systemic circulation, forms an important portal for entry. The papillary fronds of the choroid plexus which protrude into the ventricle have an external epithelial lining that is continuous with the ependyma and encloses a vascularised mesenchymal core. It is thus an important site for initial dissemination for many infections such as tuberculosis, cytomegalovirus, cryptocoecosis, bacteria and parasites, as well as non-infectious processes such as sarcoidosis, xanthogranulomas and rheumatoid nodules. Similarly purulent ventriculitis and neoplastic lesions, such as lymphomas and germinomas, can cause ventricular enhancement by virtue of their subependymal location.

The imaging findings differ between immunocompetent and immunodeficient individuals. MR findings of intraparenchymal cryptococcomas and enhancement are noted in the former whereas, in the latter, MR can be normal or show mildly dilated Virchow-Robin spaces, cortical atrophy and rarely meningeal enhancement. Meningeal involvement is often inferred from progressive ventriculomegaly in sequential images, but neither is specific for cryptococcosis. Therefore, diagnosis frequently depends on the identification of cryptococci in CSF through the Indian ink preparation or on the detection of cryptococcal antigen in CSF to complement the imaging findings. The former is useful when >10 colony forming units (CFU) ml−1 of yeast are present. Other than Indian ink, Alcian blue and mucicarmine are the stains used to detect the polysaccharide capsule of yeast in tissue.

The choice of antifungal treatment depends on the site of infection and the immune status of the patient; options include polyene-amphotericin B (Amp B), azoles (fluconazole, itraconazole) and flucytocine. Serially preformed lumbar punctures or external ventricular drainage may serve to reduce headache in a patient with raised intracranial pressure.
References:


