BRAIN TUMOUR (FIRST PRESENTATION)

Introduction

First presentations of brain tumor (primary or secondary) will not uncommonly present to the ED.

The most common presentations are:

1. **Headache.**

2. **First seizures.**

3. **Unexplained and persistent nausea and vomiting.**

Less commonly there may be:

4. Alterations of higher cerebral functioning: in cognitive ability / in behaviour.

5. Focal neurological signs

Pathophysiology

Neural cell types:

There are two types of cells that make up the nervous system: **neurons and neuroglia**.

Neuroglia, also known as glial cells, are non-neuronal cells that provide support, protection, nutrition, help maintain homeostasis for neurons and form myelin for neurons. The glia are estimated to outnumber neurons by about 10 to 1

Types of **glial** cells include:

1. Microglia:

    - Specialized cells capable of phagocytosis.

2. Macroglia:

    CNS:

    - Astrocytes, (the most abundant glial cells)

- Oligodendrocytes (coat axons and produce myelin sheaths)
- Ependymal cells
- Radial glia

Peripheral nervous system:

- Schwann cells (similar in function to oligodendrocytes, but provide myelin sheaths for the peripheral nervous system neurons)
- Satellite cells

A primary brain tumor that develops from glial cells is called a glioma and most primary brain tumors arise from these cells. Gliomas, meningiomas, and embryonal tumors account for over 95 percent of **primary** intracranial neoplasms.

Gliomas are divided into subgroups depending on the origin of the glial cells. The most common type of glioma is an astrocytoma, (which arise from astrocytes)

Classification

Brain metastases (single or multiple) are the most common brain tumours, and are ten times more common than primary brain malignancies

Brain metastases will develop in up to 20% of cancer patients.

The commonest causes are:

- Lung cancer
- Breast cancer
- Malignant melanoma

A number of histological classifications exist for **primary brain tumours** (see appendix 1 below) but these are of limited **clinical value**.

The WHO classification is more useful from a clinical and prognostic point of view.

The World Health Organization (WHO) classification

In contrast to tumors originating elsewhere in the body, differentiating primary brain tumors into benign and malignant is of relative and limited clinical value, since many histologically “benign” tumors will still grow by infiltration of healthy surrounding brain tissue and some, in time, may transform into more malignant forms.

True *benign* intracranial tumors arise mainly from the meninges (meningiomas), pituitary gland (adenomas) and myelin sheath tumors (neuromas)

The World Health Organization (WHO) classification of nervous system tumors incorporates a number of variables including histology, molecular and genetic markers and immunologic markers in an attempt to construct a classification that is universally applicable and **prognostically valid.**

It establishes a "malignancy scale" based on these variables.

The WHO grades are listed below in appendix 2.

Clinical Features

There are 3 classic or hallmark presenting symptoms with respect to a **space occupying** lesion:

1. **Headache**

2. **Unexplained and persistent nausea and vomiting**

3. **Seizures**

Patients who have a space-occupying lesion essentially present with non specific features of raised intra-cranial pressure or neurological symptoms and signs.

Presenting symptoms may therefore include:

Signs of raised intra-cranial pressure:

1. New onset headache that is persistent over weeks or even months especially if in the early morning is a common presenting symptom.

2. Unexplained and persistent vomiting.

Unexplained neurological symptoms and signs:

1. **First seizure.**

2. Central features:

    - Confusion, altered conscious state

    - Less commonly alteration of "higher functions", personality, emotional or cognitive changes.

3. Focal neurological signs:

- Visual disturbances
- Unilateral Weakness
- Unilateral Paraesthesia
- Speech disturbances

4. Loss of balance/ coordination.

    - This may be due to cerebellar involvement, but may also be due cerebral involvement, particularly in cases of multiple metastases.

The clinical setting is also important:

1. **All oncology patients need to be considered to be at risk of cerebral metastases. Threshold for investigation must be low in these patients.**

2. Fever and altered conscious state of rapid onset, is suggestive of cerebral abscess as the cause.

3. The rate of development of symptoms may also provide clues to diagnosis.

    - A gradual onset of symptoms (weeks to months) suggests tumour.
    - An intermediate onset of symptoms (days to weeks) suggest tumour or subdural.
    - A rapid onset of symptoms (hours to days) and fever suggest an infective cause, such as abscess or a bleed from a previously asymptomatic tumour.

Investigations

Blood tests

1. FBE
2. U&Es/ glucose
3. Consider serum calcium if the lesion is likely to be secondary.

CT scan brain

Any patient suspected of having a space occupying lesion of the brain must have a CT scan, (or MRI) before leaving the department.

Besides the lesion itself found on a CT scan, the following important features will also need to be looked for:

- Whether there are signs of cerebral edema.
- Whether there are signs of raised intra-cranial pressure.
- Whether the lesion alters with contrast.

Cerebral Edema

Cerebral edema is often classified as vasogenic or cytotoxic.

Vasogenic Cerebral Edema:

The blood brain barrier is disrupted and the edema is predominantly extracellular.

On CT fluid is seen to accumulate predominantly within the white matter, and there is good **preservation of the grey-white matter interface.**

Causes include:

1. Tumours.
2. Infection, (abscess).
3. Contusions.
4. Radiation.

Cytotoxic Cerebral Edema:

The blood brain barrier is intact and edema is predominantly intracellular.

On CT scan there is **blurring of the grey-white matter interface.**

Causes include:

1. Hypoxia
2. Ischemia, (including infarction)
3. Toxins, including encephalopathies.

Features of Raised Intra-cranial Pressure:

These include:

1. Effacement of sulci.

2. Midline shift.

3. Obliteration of the ventricles.

4. Obliteration of the quadrigeminal plate

    - This is the basal cistern, the subarachnoid space surrounding the midbrain.
    - Its normal appearance is the so called “smiley face”.

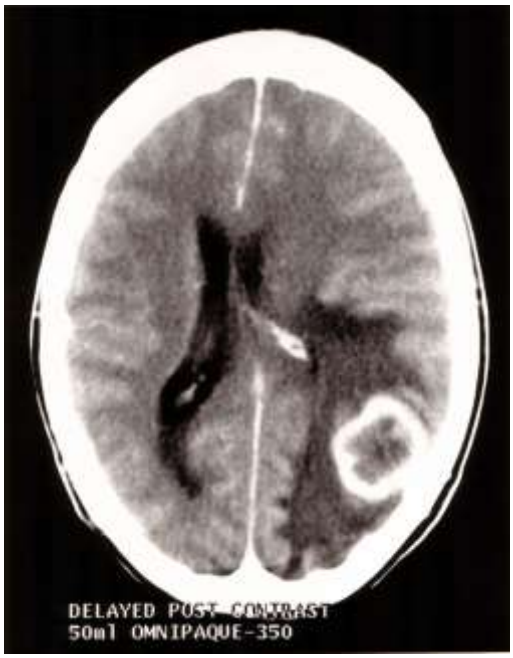
CT Scan with IV contrast:

IV contrast will often need to be given to further define a suspicious lesion.

Important findings seen with IV contrast include:

- **The ring enhancing lesion**
- **The mass enhancing lesion**

Causes of Ring Enhancing Lesions on CT include:



Classic appearance of a ring enhancing lesion on IV contrast CT scan, there is also mass effect and vasogenic edema.

These causes of a ring enhancing lesion on CT scan include:

1. Malignancy:

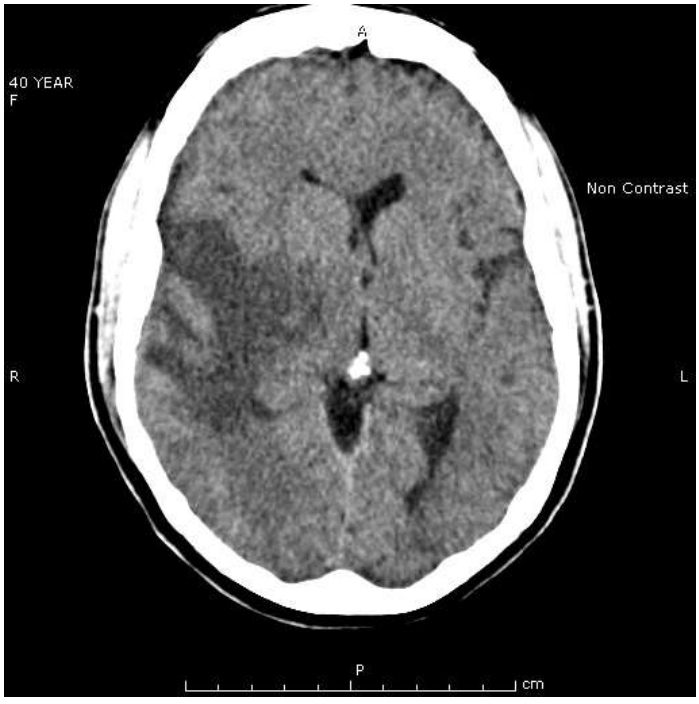
- Primary
- Secondary metastases
- Lymphoma, (in HIV infected patients)

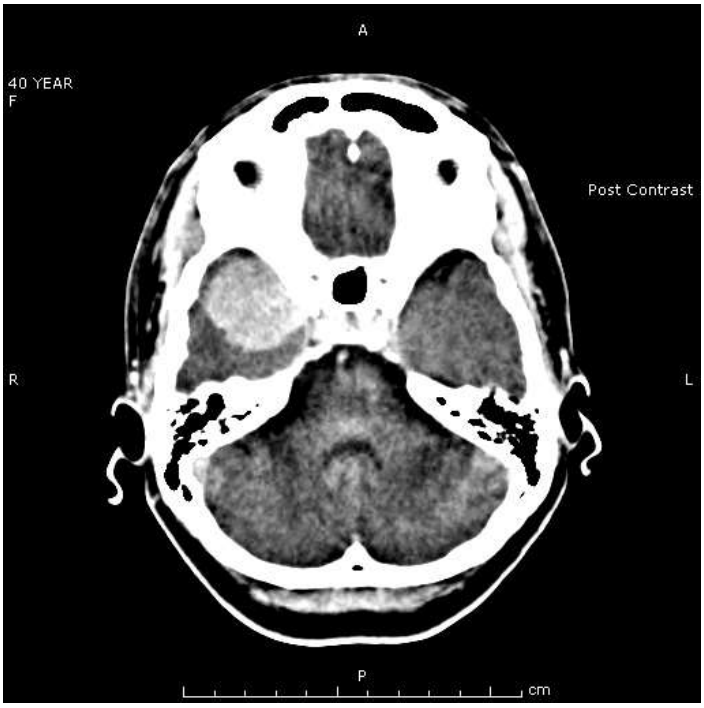
2. Abscess:
   - Bacterial
   - Toxoplasmosis, (in HIV infected patients)

Less commonly:

3. Demyelination, (active)
4. Infarction.
5. Resolving hematoma
6. Radiation necrosis

Mass enhancing lesions:





Left: CT scan without contrast of a woman who presented with a first seizure. There is a low density lesion in the right parietal region, with a large amount of vasogenic edema, (note preservation of the gray-white interface) as well as some mass effect.

Right: Following IV contrast a large vividly enhancing mass is seen attached to the wing of the sphenoid bone, which was not apparent on the initial plain CT scan. The impressive amount of edema can be associated with very large meningiomas, such as this woman had.

MRI

- This is the best imaging investigation for cerebral tumours. It is the most sensitive and the most specific investigation.
- This will usually be done to more clearly define a suspicious or equivocal lesion detected on initial CT scan.
- It does not need to be routinely done in the ED when there is a clear lesion on CT and it is evident that patient will require transfer to a neurosurgical unit.
- It is a better imaging option when ionizing radiation is best avoided (eg in children, or pregnant women) or when there is a history of IV contrast allergy or poor renal function.

Further Investigations

These will be determined according to the index of suspicion for any given pathology, in the context of the observed cerebral lesion seen on imaging.

Considerations may include:

1. CXR
    - For a possible primary malignant source
2. Serological testing, (with respect to differential diagnoses):
    - HIV
    - Toxoplasmosis.
3. CT scan abdomen
    - To search for a primary lesion, (this will rarely be necessary from the ED however).

Management

In cases of new diagnosis of brain tumor (or possible brain tumor) in the ED, issues that may need addressing will include:

1. Headache:

   - Analgesia should be given as clinically indicated. Severe symptoms may require narcotic analgesia.

   - Steroids (**IV dexamethasone)** should be given if there is edema seen on CT scan.

     This will help reduce symptoms such as headache and vomiting due to raised intra-cranial pressure.

2. Seizures:

   - Prophylactic anticonvulsants are controversial, they are not usually routinely given.

   - IV phenytoin should be given if the presenting problem was seizure.

3. Nausea and vomiting:

   - Symptoms can be severe, stemitil, maxalon or ondansotron may be given.

4. Raised intracranial pressure:

   - This is the predominant cause of the nausea, vomiting and headache.

   - It should be treated initially with **10 mg IV dexamethasone.**

   - Mannitol is not usually given. It may be considered in severe cases with an altered conscious state.

5. Communication:

   - Good communication with patient and family is very important.

   - The usual scenario will be the need to explain to the patient/ family that a "lesion" has been detected on CT/ MRI that is most likely the cause of the symptoms. Specific diagnoses, (even "best guesses") should in general be avoided in the first instance however.

   - Prognostic predictions should similarly be avoided.

   - Patients should be told that the lesion could represent a range of possibilities, in *lay terms*, (infection, old scarring, cysts, and tumour, and that a neurosurgical referral will need to be made to establish the exact nature of the lesion and that this may involve operation and tissue biopsy

- Patients themselves may then ask more questions and honest answers should be given, but again stressing that *definitive* diagnosis cannot be given in the first instance. It can be stressed that even if the diagnosis is a "tumour" that there is a whole range of prognoses for these depending on the exact type of tumour it is.

6. Definitive management:

   - This will naturally depend on the exact nature and extent of the lesion, together with consideration given to age and any co-morbidities of the patient.

   - Modalities include surgery, chemotherapy, radiotherapy and steroids.

Disposition:

- All patients with suspected brain tumour must be referred to the neurosurgeon on call.

- Most patients will then be transferred to a neurosurgical unit for further assessment and investigation, particularly if the lesion is likely to be malignant and/ or there have been significant symptoms such as severe headache or seizures that require ongoing management and observation.

- If the lesion is likely benign and the patient does not otherwise have significant symptoms, outpatient follow-up may be appropriate, but again neurosurgical consultation will be necessary in the first instance, before a patient is discharged.

- All patients who are to be transferred should be so via ambulance.

Appendix 1

Histological Classification

Astrocytic

- Pilocytic astrocytoma (WHO grade I astrocytoma)
- Astrocytoma (WHO grade II astrocytoma)
- Anaplastic astrocytoma (WHO grade III astrocytoma)
- Glioblastoma multiforme (WHO grade IV astrocytoma)

Oligodendroglial tumors

- Oligodendroglioma, (WHO grade 2)
- Anaplastic oligodendroglioma, (WHO grade 3)

Ependymal tumors

- Myxopapillary ependymoma (WHO grade 1), Ependymoma, (WHO grade 2) / Anaplastic ependymoma (WHO grade 3)

Mixed gliomas

- Oligodendroglioma-astrocytoma, (WHO grade 2)
- Anaplastic oligodendroglioma-astrocytoma, (WHO grade 3)

Choroid plexus tumors

- Choroid plexus papilloma (WHO grade 1)/ Choroid plexus carcinoma, (WHO grade 3)

Neuronal and mixed neuronal-glial tumors

- Gangliocytoma, (WHO grade 1-2)
- Dysembryoplastic neuroepithelial tumor
- Ganglioglioma
- Anaplastic ganglioglioma
- Central neurocytoma, (WHO grade 2)

Pineal parenchymal tumor

- Pineocytoma, (WHO grade 2) / Pineoblastoma, (WHO grade 4)

Embryonal tumors

- Medulloblastoma (WHO grade 4)/ Primitive neuroectodernal tumors (PNETs), (WHO grade 4)

Meningeal tumors

- Mengingioma (WHO grade 1) and other rarer variants with variable WHO grades.

Germ-cell tumors

- Germinoma / teratoma and others.

Tumors of the sellar region

- Pituitary adenoma/ Pituitary carcinoma
- Craniopharyngioma

Metastatic (or secondary) tumors

WHO Classification of Brain Tumours

WHO Grade I

This includes lesions with low proliferative potential, a frequently discrete nature, and the possibility of cure following surgical resection alone.

WHO Grade II

This includes lesions that are generally infiltrating and low in mitotic activity but recur. Some tumor types tend to progress to higher grades of malignancy.

WHO Grade III

This includes lesions with histologic evidence of **malignancy**, generally in the form of mitotic activity, clearly expressed infiltrative capabilities, and anaplasia.

WHO Grade IV

This includes lesions that are mitotically active, necrosis-prone, and generally associated with a rapid preoperative and postoperative evolution of disease.

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