Tumours of the central nervous system

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Abstract

Tumours of the central nervous system can be metastatic or primary in origin, and can affect all age groups. The WHO grading system is most widely used to classify these tumours. CT and MRI imaging guide initial management and tissue diagnosis can be sought via open or image guided procedures. Prognosis depends on the type and location of the tumour, patient age and baseline characteristics. This article provides an overview of different tumour types, grading systems, clinical presentations, imaging techniques and management options.

Keywords CNS tumours; glioblastoma; meningioma; brain metastasis; astrocytoma; ependymoma

Introduction

Central nervous system (CNS) tumours represent 2% of deaths from malignant neoplasms annually. Different pathologies predominate in different age groups. The most common adult CNS tumours are metastatic followed by gliomas such as glioblastoma. In the paediatric population CNS tumours are second only to haematopoietic malignancies, such as leukaemia, in presentation. In infants and children under 2 years brain tumours are rare and mostly congenital such as teratoma.

Overall, 65% of primary CNS tumours are gliomas. About 10% of patients present with meningioma and 10% with vestibular schwannoma. In adults 70% of intracranial tumours present in a supratentorial location compared to paediatric tumours of which 70% present infratentorially. Unlike other malignancies the CNS neoplasms rarely metastasize outside the craniospinal axis. CNS tumours are more common in certain neurocutaneous syndromes (e.g. neurofibromatosis).

Classification

CNS tumours can be divided based on histology, location or malignant potential. They can also be divided into intra-axial (e.g. astrocytoma) or extra-axial (e.g. meningioma).

To understand the behaviour and clinical presentation of tumours all these factors need to be considered.

The grading of tumours is the single most important prognostic factor in the longer term prognosis of patients following surgical treatment. The World Health Organization (WHO) grading system is most widely used and divides tumours into the following grades:

- **Grade I:** Slow growing with the potential for cure with resection alone.
- **Grade II:** Relatively slow growing with risk of recurrence.
- **Grade III:** Tumours are malignant with increased growth rate and are infiltrative. They have increased nuclear atypia and mitotic activity.
- **Grade IV:** Rapidly growing and aggressive malignant tumours.

As an example astrocytic tumours are graded as follows (Figure 1).

The growth and grading of tumours is assessed based on the level of the Ki67 antigen. It is expressed only during mitosis and can be assessed in fresh frozen specimens as a proxy to the rate of mitosis.

Other grading systems exist, such as the Kernohan grading system for astrocytoma, however they are not well recognized internationally.

The current classification used is the WHO classification based on the histological origin with grades as shown in Box 1. In this classification pituitary adenomas were not included.

The terms benign and malignant are generally not used to describe CNS tumours. In part this is due to the rarity of true metastatic spread beyond the CNS, but more importantly because tumour location and presence or absence of mass effect is more significant in determining clinical impact.

Tumour-markers can be used to identify CNS tumours. Glial fibrillary acidic protein (GFAP) is present in tumours of astroglial origin. S100 is present in melanomas and Schwann cells, and cytokeratin in metastatic carcinomas. Germ cell markers are used to identify various germ cell tumours discussed under germ cell tumours.

Clinical presentation

Age at presentation gives a clue towards tumour type as discussed previously.

CNS tumours can cause symptoms by causing compression, invasion or irritation of CNS structures. Additional cerebral oedema can worsen the mass effect caused by the tumour bulk. Oedema formation is related to neovascularization of surrounding tissues and break down of the blood–brain barrier. It is common in infiltrative tumours.

The most common presenting symptom is progressive neurologic deficit followed by headache and then seizures.

Neurologic deficit is related to the location of the tumour (Figure 2) and thorough understanding of anatomy and neurological examination is the key in picking up early tumours clinically. CNS tumours can present with motor weakness, dysphasia, visual disturbance or change in mental state depending on tumour location.

Frontal lobe tumours usually present with personality change. Temporal lobe tumours can present with seizures. Occipital lobe tumours present with visual deficit or alexia. Cerebellar tumours present with hydrocephalus and/or ataxia.

Tumour-associated headaches tend to be worse in the morning and are often exacerbated by straining or bending forward. The aetiology of headache may be due to raised intracranial

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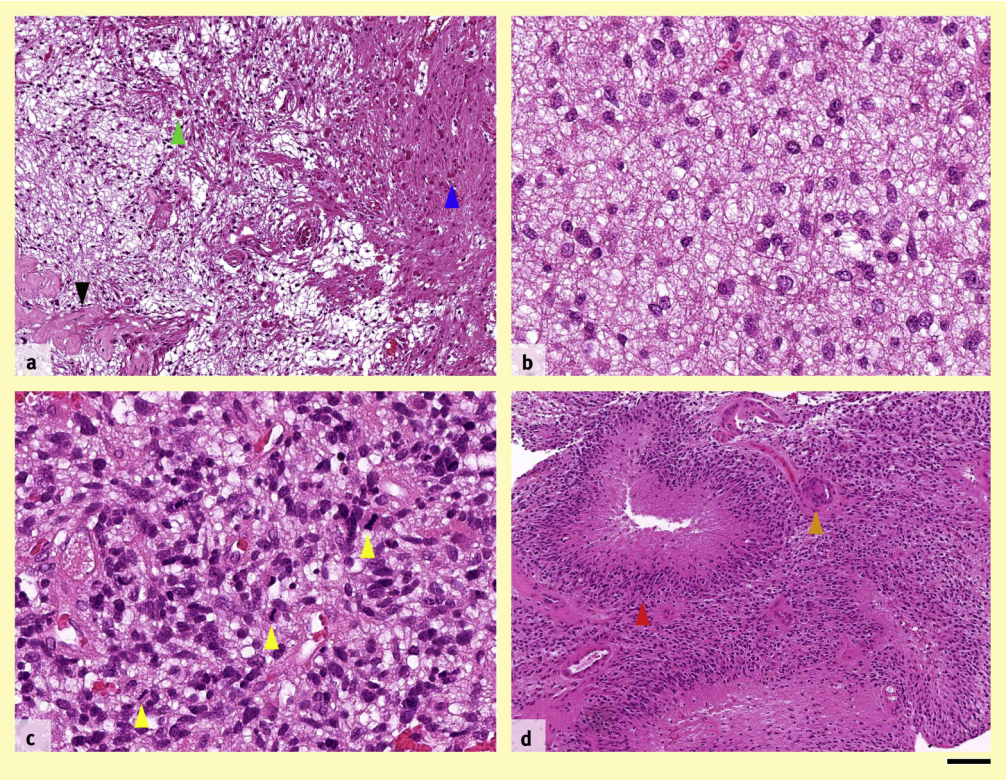

Figure 1 Haematoxylin and Eosin (H&E) stained sections of a pilocytic astrocytoma, WHO grade I (**a**), diffuse fibrillary astrocytoma, WHO grade II (**b**), anaplastic astrocytoma, WHO grade III (**c**) and glioblastoma, WHO grade IV (**d**). Pilocytic astrocytoma, WHO grade I (**a**) comprises astroglial cells with hair-like morphology and often shows a biphasic growth pattern with densely fibrillary fascicular areas admixed with loosely organized cystic regions. Rosenthal fibres (blue arrowhead), eosinophilic granular bodies (green arrowhead) and hyalinised blood vessels (black arrowhead) is a frequent finding. In diffuse fibrillary astrocytoma, WHO grade II (**b**), anaplastic astrocytoma, WHO grade III (**c**) and glioblastoma, WHO grade IV (**d**) the tumour cells of variable pleomorphism show diffusely infiltrative growth pattern in the surrounding neural parenchyma. In diffuse astrocytoma, WHO grade II (**b**) the cell density is only mildly increased, mitotic activity is inconspicuous and there is no microvascular endothelial proliferation or necrosis. In anaplastic astrocytoma, WHO grade III (**c**) there is brisk mitotic activity (yellow arrowheads) and often markedly increased cellularity, but no evidence of microvascular endothelial proliferation or necrosis. In glioblastoma, WHO grade IV (**d**), in addition to hypercellularity and frequent mitoses, there is microvascular endothelial proliferation (orange arrowhead) and/or tumoural necrosis of either pseudopalisading (red arrowhead) or ischaemic-coagulative type. Scale bar: 100 μm in **a** and **d**; 25 μm in **b** and **c**.

pressure secondary to mass effect, or invasion of the dura which is supplied by the trigeminal nerve.

Classic presentation of different tumours is described with individual types.

Diagnosis

The availability of CT scans in every A&E department has made the early diagnosis of these tumours possible. If there is any clinical suspicion a plain CT scan should be performed initially, followed by a contrast enhanced CT scan. These images can pick up most intracranial tumours and differentiate from a haemorrhagic stroke or intracranial bleed, key differentials in acute presentations. While differentiating CNS tumours the algorithm shown in Figure 3 can be used.

The age and location of a tumour are key to interpreting scans. To further delineate the tumour characteristics and shorten the differential an MRI scan with and without contrast with special algorithms is used (Figure 4).

In Table 1 three common paediatric tumours are presented with clinical characteristics and imaging findings.

Multiple tumours tend to be metastatic tumours. If metastatic disease is considered in the differential then a CT of the chest, abdomen and pelvis is also performed to stage the primary disease.

Ependymomas have a propensity to disseminate via the cerebrospinal fluid (CSF) pathways and managing these patients requires MRI of the whole neuro-axis to rule out drop metastases, especially in the lumbosacral area.

With the emergence of new techniques and modalities, the role of MRI is gradually expanding and helps in more accurate diagnosis preoperatively. MR spectroscopy is increasingly used to detect certain electrolytes, for example choline which is present in high concentrations in tumours, while creatine reflects the energy stores. A choline:creatine ratio of more than 2, is indicative of tumour. It is used increasingly to differentiate a neoplasm from abscess and especially in patients suffering with AIDS differentiating toxoplasmosis from a CNS lymphoma.

Functional MRI is another form of imaging using the BOLD (blood oxygen level dependent) technique. It is used preoperatively in mapping brain areas. The areas of the brain performing a task (e.g. speaking) have different oxygen

