Brain tumours in adults and children

1. Brain tumours in adults and children

> Brain tumours can cause devastating physical, psychological and social problems, not only for the patient but also for their loved ones and dependants. Both patients and clinicians worry about headaches as a symptom of an undiagnosed tumour. The trouble is, no symptom helps us that much!
>
> They are also relatively uncommon; a full-time clinician might see around 3 cases of primary brain tumour in their lifetime.

Only around 2% of brain tumours are diagnosed via the suspected cancer pathway, more commonly presenting in other outpatient settings or as emergencies.

No individual symptom has a PPV >1%, so this is really hard.

1.1. Role of primary care

A BMJ Clinical Update considered brain tumours, and specifically glioblastomas (BMJ 2021;374:n1560). It suggested that the role of primary care was:

- Refer as soon as possible if a brain tumour is suspected.
- Provide psychological support after diagnosis.
- Manage supportive care towards the end of life, and support bereaved relatives.

1.2. NICE guidance

Referral guidance by NICE was issued in 2015 and is summarised in the table below (NICE 2015 NG12).

It illustrates how non-specific the presentation can be:

Brain and CNS cancers (NICE 2015, NG12)

Urgent investigation:

- Consider urgent direct-access MRI brain scan in adults with progressive subacute loss of CNS function.

Urgent referral:

- Consider a very urgent (within 48h) referral for children and young people with newly abnormal cerebellar or other CNS dysfunction.

NICE recommended an urgent scan for adults because it anticipated this would increase speed of diagnosis (rather than the more typical neurology referral, wait for imaging, then neurosurgery referral if imaging is positive).

There are no specific recommendations if you do not have access to direct MRI – a discussion with neurology or the cancer referral pathway is likely to be most appropriate.

In Scotland, NHS Scotland recommends an urgent specialist referral, e.g. to a neuro-oncologist who will arrange imaging if required.

1.3. Brain tumour presentation: adults

Can anything help us to spot brain tumours earlier in adults?

The largest ever case–control study to examine a wide range of symptoms associated with a diagnosis of both primary and secondary brain tumours in adults in UK primary care was published in 2019 using data from the CPRD. All coded presentations within 6 months were included (though free text

entries were not included, which may be a significant limitation (BMJ Open 2019;9:e029686).

The study found that:

- No feature alone was strongly predictive of a brain tumour in absolute terms.
- Almost half the cases were metastatic secondary cancers.
- No single symptom reached the 'magic' PPV 3% threshold that is used for NICE referral.
- The most predictive symptoms with PPV 1.4–1.6% were:
    - Seizure (remember, this requires urgent investigation in its own right along the first seizure pathway).
    - Weakness.
    - Confusion.
- Unsurprisingly, headache alone was NOT discriminatory (PPV 0.2%), but the study did identify that the concept of 'headache PLUS' and 'cognitive symptoms PLUS' may be useful. In the 6 months prior to diagnosis:

Symptom combination	PPV
Headache + cognitive symptoms	5.9%
Headache + weakness	4.4%
Cognitive symptoms + headache	7.2%
Cognitive symptoms + weakness	9.6%

The authors of the CPRD study acknowledge that this remains very difficult,

and concluded that we could:

- **Remember 'headache +' and 'cognitive +' and actively seek out other neurological symptoms in people with these presentations.**
- **Have a lower threshold for referral in people with a past history of cancer** *(remember, in people with breast cancer, metastases can present even as long as 10 years after initial treatment).*
- Look back over the previous 6 months in the notes when seeing patients to spot these '+' symptoms.

Note that specific use of MMSE or other cognitive assessments is not recommended when considering a diagnosis of brain tumour as they lack sensitivity to spot these subtle neurocognitive defects (BMJ 2021;374:n1560).

What is meant by 'cognitive symptoms'?

The CPRD study grouped these symptoms together but included things such as changes in cognition, concentration and confusion.

In addition, a qualitative study interviewed patients within 2 weeks of diagnosis with a primary brain tumour to assess their experience of 'symptoms'. It also interviewed their families (BJGP 2019;69(681):e224). The study included 39 patients (which is quite big for a qualitative study of a rare event).

Key themes were that patients had noticed the following changes in the 6 months prior to seeking help:

- Multiple subtle changes in cognition, "like their brain wasn't working properly", e.g. speaking, writing, comprehension, memory, concentration.

- Change in balance, sensations and senses.
- 'Head feelings' such as dizziness or "that is not me."
- Changes in sleep.

Family members reported that:

- The person "wasn't quite themselves."
- There were changes "out of character", e.g. more sensitive, irritated or angry, low mood, awkward or initiating more stressful interactions.

This is interesting, and the authors plan to validate in a larger cohort.

We appreciate this is vague but, now and again, we have a consultation a bit like this, don't we? We often end up thinking about delirium or dementia, but I have to confess, brain tumour might not have made it to my list of differentials. Perhaps this information may be helpful just to spike our senses when these consultations occur? We might think about safety-netting and using a symptom diary with planned follow-up if we are not planning to refer?

Headaches and brain tumours

Headaches are common in patients with brain tumours; they are reported in 10% of records of adults and 20% of records of children in the year before diagnosis.

BUT headaches are very common in the general population, and this is what makes the PPV of headache as a symptom very low, around 1%. This means that for every 1000 people presenting to primary care with headache, only 1 to 2 in 1000 will have a brain tumour (Family Practice 2015;32(6):618).

The pattern of headache in people subsequently diagnosed with a brain tumour may be migrainous or tension-like. Specific features of headache

that suggest raised intracranial pressure should make us more concerned (BMJ 2021;374:n1560). These include:

- Headache worsens on lying down.
- Precipitated or exacerbated by coughing or Valsalva manoeuvre.
- Increasing in frequency or severity over time.
- Presence of neurological or cognitive symptoms.
- Accompanied by vomiting without obvious cause.
- Past history of malignancy known to metastasise to the brain.

1.4. Brain tumour presentation: children

Only one-third of children diagnosed with a brain tumour will have a red-flag symptom recorded in the preceding 12m, and only 2% of childhood cancers are diagnosed through the cancer referral pathway!

Some children are at higher risk (genetic syndromes such as neurofibromatosis and history of cerebral radiation treatment).

A BMJ article reminds us that the presentation can be quite varied, depending on age of the child and tumour location (BMJ 2013;347:f5844).

Studies suggest that at initial symptom onset, children tended to have one symptom or sign, but by the time the diagnosis was made, they had six!

Red-flag symptoms

Unfortunately, none of the red-flag symptoms are highly specific. The most predictive red-flag symptoms for brain tumours in children were:

- Abnormal movements.
- Visual symptoms.
- Vomiting.
- Headaches.
- Seizures.

The likelihood of these symptoms leading to a diagnosis of brain tumour is increased in children with frequent primary care presentations, so the authors suggest that the presence of any red-flag symptom and repeat (3 or more) consultations should be referred for investigation. *Trust your gut and use your GP sixth sense!*

Brain tumour presentation according to age

The RCPCH and RCGP Headsmart tool is helpful (accessed January 2022). Two or more of these features should prompt urgent referral.

Preschool (<5y)	Primary school (5–11y)	Secondary school (12–18y)
Persistent or recurrent vomiting. Problems with balance/coordination/walking. Abnormal eye movements. Behaviour change, esp. lethargy. Fits or seizures. Abnormal head position, e.g. head tilt, wry neck, persistent stiff neck. Increasing head circumference (if fontanelle still open). Unexplained nausea/vomiting lasting >2 weeks.	As per preschool + Complaints of persistent or recurrent headache.	As per primary school + Delayed or arrested puberty or slow growth.

There is now a useful online decision support tool that offers an approach to assessing and referring each of these symptom clusters. A link can be found in the useful resources.

Headsmart reminds us of the pitfall of failing to make a complete reassessment when there is a change in headache type of a known sufferer of migraine or tension headache.

What should I do if I suspect a brain tumour in a child?

Sick children

- Children with symptoms of raised intracranial pressure (persistent headache, vomiting, confusion, drowsiness, impaired consciousness) should be referred to paediatrics on the same day for urgent admission and imaging.

Well children

- Examine the nervous system – remember, visual assessment in young children can be difficult and you may need to refer to community orthoptics/optometry; children should be seen within 2w.
- If findings are specific enough to raise concern, refer urgently to paediatric outpatients for consideration of imaging.
- If findings are non-specific, a period of watchful waiting with careful safety-netting may be appropriate because symptoms and signs tend to evolve with time in children with brain tumours. Review within 2w.

1.5. Types of brain tumour

A diagnosis of a brain tumour is a rare event in primary care, and we are likely to look after a handful of these patients over our professional lifetime. A Lancet Seminar offered some information which may be helpful if you are caring for a patient with a brain tumour (Lancet 2018;392:432).

The table below is intended as a quick reference:

Histological type	Gliomas (glioblastoma oligodendroglioma, astrocytoma)	Meningiomas	Metastatic

Incidence	60% of primary brain tumours.	30% of primary brain tumours.	Increasing due to improved cancer survival.
Origin	Arise from glial cells (brain tissue).	Arise from meninges.	Mainly lung and breast.
Diagnosis	MRI scan.	MRI scan. CT scan (if bone invasion suspected).	MRI scan.
Clinical picture	May be high or low grade. Genetic profile indicates prognosis.	Slow growing. 'Benign' but can cause significant morbidity. Very long-term follow-up needed.	Symptoms with or without past cancer diagnosis.
Management	Active monitoring (including MRI imaging). Surgery. Chemotherapy/radiotherapy.	Active monitoring. Surgery. Radiotherapy.	Surgery. Stereotactic radiotherapy. Rarely whole brain radiotherapy.
Prognosis	Depends on genetic type and whether high or low grade. Varies from months to >12y!	Grade 1: >10y. Grade 3: 1–5y. Recurrences:	With active treatment, 2–6 months. With supportive

		months.	care only, week to months.

Glioblastoma

A JAMA review reminds us that glioblastoma is the most common malignant primary brain tumour (JAMA 2023;329(7):574). Incidence rises from age 40y, and peaks at age 75–84y. It is usually treated with resection and chemotherapy, and is invariably recurrent, with median progression-free survival of 7 months. Median survival from diagnosis is under 2 years, and only 7% of patients will survive to 5 years or beyond.

If you are actively supporting a patient with glioblastoma, you may find the full BMJ Practice article a useful resource (BMJ 2021;374:n1560).

1.6. NICE on primary care management of brain tumours

In 2018, NICE made more detailed recommendations for diagnosis and management of brain tumours (NICE 2018 (NG99)). This is mainly directed at specialists, but there are some points of interest for us in primary care. NICE reminds us of specific issues relating to brain tumours:

- Prognosis is highly variable, ranging from days to years depending on tumour type/location and stage.
- Treatment options and outlook are changing as genetic and molecular understanding grows.
- Brain tumours often cause psychological and cognitive impairment.

This can make it harder for the individual to participate in their own management decisions and may affect sense of identity.

- NICE recommends that neurological rehabilitation should be considered and offered more frequently as a standard part of care to aid maximal recovery after treatment.
- NICE reminds us to remember late effects of treatment, including fertility issues, secondary cancers and endocrine sequelae. These are likely to be of greater significance for children with brain tumours than adults.
- Children treated with chemo-radiotherapy often have a degree of cognitive impairment, especially in processing information. This will have educational impact, especially if unrecognised.

Living with and beyond a diagnosis of brain tumour

People treated for primary brain tumours are at risk of late effects of treatment, often after many years.

NICE (2018 NG99) recommends that patients have a written treatment summary at the end of their initial treatment which includes advice on risks.

We should have access to these and ensure our records highlight this information for future clinicians who will be seeing the patient. This table highlights some of the main issues to consider (BMJ 2018;362:k2924):

Late effects	Causes/timescale	Actions
Cataracts	>10y after radiotherapy.	Refer for extraction if meet criteria.

Cavernoma	Vascular malformation >5y after radiotherapy. May bleed, presenting as headache or stroke.	Refer back to team/acutely depending on presentation.
Cognitive decline	Radiotherapy.	Refer back to team. Neuropsychology assessment and rehabilitation may be helpful.
Epilepsy	Higher risk with radiotherapy and reduced seizure threshold in epilepsy.	Refer back to team.
Hearing loss	Local radiotherapy effect.	Audiology assessment.
Hypopituitarism	Radiotherapy: patient may need blood test monitoring.	Shared care between neurosurgery team/endocrinology.
Infertility	Chemotherapy or cranial irradiation.	Refer to fertility services.
Neuropathy	Chemotherapy-related.	May be sensory, motor or autonomic – manage symptomatically where possible.
Secondary tumours	Radiotherapy-induced: estimated as 1% in 10–20y.	New/recurrent symptoms = referral.
SMART	Stroke-like migraine attacks usually >4y after radiotherapy.	Seek specialist advice.
Stroke	Due to radiation vasculitis.	Manage risk factors,

	Usually >4y after treatment.	particularly if longer prognosis.

Brain tumours

- Brain tumours can be difficult to spot: trust your gut!
- Think about 'headache +' and 'cognitive +'.
- Children with brain tumours present with symptoms and signs depending on age and location of the tumour. If concerned, we should speak to a paediatrician.
- Prognosis varies from days to years depending on type of tumour.
- Patients may present acutely to primary care with late effects of treatment.

Do a significant event analysis on the last 2–4 cases of brain tumour diagnosed at your practice. Reflect on the presentation, whether there was any diagnostic delay and what safety-netting strategies were used. Discuss this with the primary care team.

Useful resources:

Websites (all resources are hyperlinked for ease of use in Red Whale Knowledge)

- HeadSmart (this charity website groups together useful information, e.g. symptom cards to give parents if safety-netting headaches, and copies of the RCPCH quick reference guideline on diagnosing brain tumours. There is also a great e-learning module)
- Headsmart decision support tool

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