Pineal tumours

See also separate articles Brain Tumours in Children, Brain Tumours in Adults and Meningiomas.

The pineal gland is centrally placed in the brain and is concerned with secretion of melatonin. Melatonin production is controlled by an endogenous circadian timing system and is also suppressed by light. Melatonin is therefore involved in our circadian cycle. Other properties of melatonin include:[1]

- Mild hypotensive and hypothermic effects.
- It is a powerful antioxidant with oncostatic properties.
- It may have a role in control of reproductive activities (elevated melatonin levels in both men and women with hypogonadism and/or infertility) but its precise role is not fully understood
- There is an emerging body of evidence suggesting that melatonin has an immuno-protective effect.

Pineal tumours are a rare and heterogeneous group of primary central nervous system neoplasms, including:[2] [3]

- Germ cell tumours, which account for >50% of pineal tumours. They arise from the neoplastic transformation of residual primordial tissue derived from ectoderm, mesoderm, or endoderm. These are more commonly found in children.
- Teratomas, which are found almost exclusively in males and tend to present in the second decade of life with hydrocephalus ± Parinaud's syndrome (see 'Presentation', below) and, rarely, a chemical meningitis resulting from tumour rupture with release of their contents into the subarachnoid space.

- Non-germ cell tumours: pineal parenchymal tumours (pineocytomas, pineal parenchymal tumours of intermediate differentiation and pineoblastomas) are derived from pineal parenchymal cells and surrounding tissue. Pineoblastomas are primitive and pineocytomas are well-differentiated.
- Some tumours arising from the supporting tissues/adjacent structures of the pineal gland, including astrocytomas, ependymomas, meningiomas and haemangiopericytomas.
- Primary melanomas of the pineal region; these are very rare and may be difficult to diagnose.[4] [5]

Cysts may also occur in the pineal gland. They are benign, normal variants and have a tendency to calcify peripherally. They are increasingly diagnosed due to increased MRI imaging for unrelated reasons where they are found incidentally. Other non-neoplastic tumours found in this region include arachnoid cysts, cysticercus cysts and vein of Galen malformation.

Epidemiology[3]

- They account for 0.4-1% of adult intracranial tumours.
- They make up 3-8% of childhood intracranial tumours, with most occurring between the first and second decade of life.
- There is evidence of a much higher incidence of intrinsic pineal tumours, glial tumour and non-germinomatous germ cell tumours in North America and Europe than in Japan and Korea, where germinoma is much more common.[6]

Presentation

Their clinical presentation is one of a space-occupying lesion:[7] headache (persistent and often worse in the morning), and nausea and vomiting caused by aqueductal compression. If there is a secondary hydrocephalus which is not relieved, then progressive lethargy and death may ensue. Other features relating to these tumours include:[3]

- Parinaud's syndrome - vertical gaze palsy ± pupillary or oculomotor nerve paresis.

- Further tumour growth leads to mydriasis, convergence spasm, pupillary inequality, and convergence or refractory nystagmus.
- Motor impairment (eg ataxia and dysmetria) if there is cerebellar involvement.
- If the thalamus is involved, there may be unilateral paraesthesia.
- Childhood tumours can present with endocrine dysfunction such as diabetes insipidus, precocious pseudopuberty, secondary amenorrhoea or an abnormally slow growth rate.
- Rarely, bleeding into the tumour can result in pineal apoplexy causing sudden neurological deterioration.

Differential diagnosis

Other causes of space-occupying lesions, raised intracranial pressure and pituitary hormone dysfunction.

Investigations

- High-resolution MRI scan of the head with gadolinium is the principle investigation.
- This should be backed up by serum and CSF tumour markers (eg melatonin and S antigen, although these are less valuable than their germ cell counterparts such as alpha-fetoprotein (AFP) and beta human chorionic gonadotrophin (beta-hCG).
- Evaluation of pituitary function tests if endocrine abnormalities are suspected.
- An ophthalmological assessment including visual fields should be carried out if there is superior colliculus involvement leading to Parinaud's syndrome or if there are other ocular features.

Biopsy

- Tissue diagnosis has traditionally been a vital part of management of patients with pineal region tumours.[6]

- Stereotactic biopsy is one approach, particularly useful in obtaining a tissue diagnosis in certain situations such as widely disseminated disease, clearly invasive malignant tumours, and patients with multiple medical problems.
- More recently, the need for a histological diagnosis has been questioned and, increasingly, patients are treated based on clinical and nonsurgical investigative findings (serum and CSF markers combined with imaging).[7] [8]
- However, there is always a small group of patients needing surgical confirmation, particularly where germ cell tumours are involved, as neuroimaging cannot distinguish these adequately from other tumours.[7]

Management[3]

Radiotherapy

Although this is an important treatment option, particularly for nonresectable tumours and those highly sensitive to radiation (such as germinomas), it has many side-effects (see 'Complications', below) and is a particular issue with young children in whom there may be long-term significant cognitive effects. Treatment may be focal or over a larger area, or a combination of both.

Chemotherapy

This is used to reduce tumour size prior to radiotherapy or surgery, particularly in young children where radiotherapy side-effects are significant. A number of different agents have been used.

Stereotactic radiation

Involves the use of a single high-dose (or sometimes smaller, multiple doses) of radiation beams that converge on to the tumour, guided by three-dimensional computer-aided planning software. Its use in the treatment of pineal tumours is still novel but early evidence looks promising, particularly in children.

Surgery

- Open resection may be curative for benign lesions and a helpful debulking adjunct to alternative therapy in malignant lesions. However, the risks of this type of surgery are greater.
- Ultimately, the surgical approach is guided by the tumour type and histology and, to a lesser extent, the operating surgeon's personal preferences.
- Many patients develop hydrocephalus and need third ventriculostomy or ventriculoperitoneal (VP) shunt prior to biopsy or resection.

Complications

- **From the tumour** - effects relating to space-occupying lesions in the CNS.
- **From radiation therapy** - hypothalamic and endocrine dysfunction, cerebral necrosis, secondary tumourigenesis and progression of disease.
- **From surgery**:[3]
    - Extraocular movement dysfunction, ataxia and altered mental status. However, many of these features significantly improve or resolve altogether over time.
    - Non-neurological complications include postoperative haemorrhage and venous infarction.
    - Where there has also been surgery for hydrocephalus, shunt malfunction, ventriculostomy closure and aseptic meningitis have all been described.

Prognosis

The response of tumours to various treatment modalities depends on the tumour subtype.[3]

- Generally, intracranial germinomas have an excellent prognosis on account of their sensitivity to radiotherapy (the five-year overall survival rate being >90%).[7]

- Recurrent germ cell tumours have been shown to respond to chemotherapy, as have some pineal cell tumours, although to a lesser degree.
- The use of adjuvant chemotherapy has improved survival rates in non-germ cell tumours and so, whilst they have a poorer prognosis, it is improving.[9]
- Microsurgery has changed the outcome dramatically, reducing the mortality rate of 90% in the early 20th century to 0-8% (with a morbidity rate of less than 12%) today.[3]

Other factors influencing prognosis include:

- Age.
- General medical condition of the patient.
- The extent and severity of brain involvement.

Further reading

- Service guidance for improving outcomes for people with brain and other central nervous system tumours, NICE (2006)

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