Medulloblastoma

Medulloblastoma is the most common malignant brain tumour of childhood and makes up approximately 20% of all brain tumours in children. It mostly occurs in young children, with a peak incidence between the ages of five and nine years, but also occurs both in both infants and young adults. Medulloblastoma one of a group of tumours referred to as embryonal tumours. It arises from primitive foetal tissue within the brain, with a point of origin that usually lies within the cerebellum. The cerebellum is located in the base of the brain (the posterior fossa) and its function is to control balance and co-ordination. Medulloblastoma is closely related to other embryonal brain tumours such as supratentorial PNET tumours and pineoblastomas. While these three embryonal tumours look very similar under the microscope, and are often treated with very similar forms of therapy, they have been shown to be genetically distinct and to respond differently to treatment.

Signs and symptoms

Children with medulloblastoma often have symptoms for several weeks or months before the tumour is diagnosed. Some symptoms occur due to the tumour blocking the drainage of fluid from the brain, resulting in a build up of pressure within the brain. These symptoms include severe, persistent headaches (often worse at night or early morning, and exacerbated by straining or coughing); persistent vomiting; sleepiness or drowsiness; and in some cases blurred vision. Other symptoms may be due to the direct effect of the tumour on the cerebellum. This can result in disturbed balance; a wide based, unsteady gait; a tremor that gets worse when pointing; and flickering eye movements (nystagmus).

Diagnosis and work-up

The initial step in diagnosing medulloblastoma is to perform imaging of the brain with a CT scan or MRI scan. Surgery is performed in order to obtain a biopsy and establish the diagnosis, and to attempt to remove as much tumour as is safely possible. As medulloblastomas are sensitive to both chemotherapy and radiotherapy it is not necessary to surgically remove every last bit of tumour. Medulloblastoma has the potential to spread throughout the brain and spinal cord, (and very rarely into other parts of the body), therefore once the diagnosis is established further investigations are performed to determine how widespread the tumour is. These investigations may include an MRI of the spine, a lumbar puncture to obtain spinal fluid, and a bone marrow biopsy or bone scan. Areas of tumour that have spread to distant sites are known as metastases. Medulloblastoma metastases are graded using the Chang classification system as follows:

M0: No metastases

M1: Tumour cells seen in spinal fluid

M2: Tumour spread to other parts of the brain

M3: Tumour spread to spinal cord

M4: Tumour spread to other parts of the body (eg bone or bone marrow)

Medulloblastoma is generally divided into two groups of tumours: average risk and high risk. Tumours are regarded as high risk if there is evidence of metastatic disease (M1 - M4), there is a large amount of residual tumour that cannot be removed surgically, or, in some cases, if the tumour has an aggressive appearance under the microscope (anaplastic or large cell histology). Working out the risk group is important for deciding on the most appropriate treatment options.

Treatment

Treatment for medulloblastoma generally consists of surgery, radiation therapy and chemotherapy. The aim of surgery is to remove as much tumour as possible while minimising damage to the normal brain. Radiation therapy is used to treat the area in which the tumour was located, as well as a lower dose to treat the entire brain and spinal cord. Recent studies have incorporated chemotherapy as well as radiation therapy and the results have shown further improvements in cure rates. Many different chemotherapy regimens have been tested around the world, resulting in similarly high cure rates. Some centres use protracted courses of chemotherapy for over 1 year, while others have used short intensive chemotherapy courses using stem cells to 'rescue' the normal bone marrow cells from the chemotherapy effects. Overall the majority of children with medulloblastoma are now able to be cured, with cure rates ranging from 60-90% depending on the risk factors present.

Infants with medulloblastoma

Medulloblastoma commonly occurs in children less than the age of three years. Infants of this age need special consideration when deciding on their treatment due to their young age and the susceptibility of the brain to the effects of treatment. Radiation to the whole brain and spine can be particularly problematic in this age group due to the potential to cause severe long term damage to the developing brain. In most cases treatment protocols will aim to use chemotherapy alone and avoid radiation therapy altogether, or at least delay it until the child is more than three years of age. In some cases a focal dose of radiation therapy may be used to treat the site of the tumour while avoiding the whole brain and spine. Some infants have a type of tumour that is classified as 'desmoplastic' based on its appearance under the microscope. These tumours seem to have a particularly good prognosis with very high cure rates, even without the use of radiation therapy.

Late effects of treatment

Children who have been successfully treated for medulloblastoma are usually continually monitored for long term side effects of their treatment. Radiation therapy in particular can cause health issues which need to be monitored for as the child grows older. These include hormone deficiencies (especially growth hormone), learning difficulties, second tumours, hearing impairment, short stature (from the effect on growth hormone and spinal growth), and a risk of stroke. Chemotherapy can cause infertility, hearing impairment and, rarely, second cancers such as leukaemia.

Future directions

Over the last few years dramatic inroads have been made into understanding the genetic changes that cause medulloblastoma to occur and drive the tumours to grow and spread. Identifying different genetic markers within each tumour will allow us to more accurately identify which tumours are more aggressive, and may need more intensive treatment, and which tumours are less

aggressive and in which treatment may able to be reduced. In addition, drugs are currently in development that may be able to more effectively target the genetic perturbations within the tumour and avoid damaging normal tissue and thus limiting treatment side effects. Ultimately these advances will be made through the conduct of large, international clinical trials.