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ORIGINAL PAPER

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Noninvasive diagnosis of brain tumours in children

He, that thinks he's got all the answers
right is the silliest fool ever.
Pirandello

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Abstract The author reviews the progress made during the last 25 years in noninvasive diagnosis of brain tumours in children. MRI has replaced all other modalities available at that time. The diagnosis is still based on a precise anatomical analysis of the lesion rather than on other specific findings. New techniques, such as spectroscopy and diffusion, may help to characterise further brain tumours in children preoperatively.

Keywords Children · Brain · Tumour · MRI

Introduction

In his introduction to the milestone book by my friend and master Derek Harwood Nash, Bernard J Reilly, a dedicated violin player, wrote of the design of the new paediatric neuroradiology department in Toronto in 1976: "[T]hree large special procedures rooms were planned, one for pneumoencephalography and ventriculography and two for arteriography. Two rooms for skull radiography and one for polytomography were immediately adjacent. ..., when CT scanning hove on to the horizon one of the angiography rooms had to be torn apart. ... CT head scanning is now an integral part of neuroradiology and is, as yet in its infancy."

Earlier days

The neuroradiological approach to mass lesions of the brain in 1976 consisted in the following steps:

1 Establish whether a mass lesion exists
2 Provide correct and precise localisation (geography of the lesion)
3 Demonstrate the lesion's effect on the cerebral vasculature

In 1976, Derek Harwood Nash stated that a summation of these factors would define the geography of the mass, might make it clear whether the mass was neoplastic, and might enable the examiner to suggest the probable histological content (together with reasonable alternatives) of the mass.

In those days the techniques available were:

1 Standard skull radiographs. They have almost gone out of use now. They were mandatory at that time.
2 Computed tomography
3 Cerebral angiography
4 Ventriculography
5 Radionuclide scanning

Twenty-three years ago, a precise analysis of the skull anomalies and of the presence or absence of calcifications was the characteristic diagnostic approach adopted by a well-trained radiologist working in neuropaediatrics. The expertise of the neuroradiologist was actually based more on epidemiological knowledge than on morphology.

Developments

Little has changed. The techniques have improved dramatically, but the rationale for the diagnostic approach to brain tumours in children has changed very little.

The present situation

In most cases the patient comes from another hospital, where a CT scan or an MRI has been performed.

MRI has replaced virtually all the examinations that were still performed in 1976. The steps recommended by Derek Harwood Nash can be replaced by the following:

1 CT scan if MRI is not available
2 MRI and MRA

In our institution MRI can answer all the preoperative questions that the neurosurgeon asks himself:

1 Is there a tumour?
2 Where is the tumour?
3 Will this tumour bleed?
4 Is there any metastases?
5 How can I approach this tumour?
6 Should a 3D acquisition be performed to allow me to use neuronavigation?

In some cases, mostly for preoperative stereotactic 3D acquisition, general anaesthesia is necessary. About 700 general anaesthetic procedures are performed in the radiology department each year.

Another indication for general anaesthesia is the preoperative work-up of medulloblastoma, because the procedure is lengthy (brain and spine) and is painful for the patient.

MR angiography can be performed during the same session if it is anticipated that the tumour is hypervascular (choroid plexus tumour, meningioma).

Angiography is now reserved exclusively for patients in whom it is thought that an embolisation could be useful prior to surgery, such as patients with highly vascular tumours, e.g. choroid plexus lesions.

In conclusion, the role of neuroradiologists has undergone little change. The equipment available, on the other hand, has given rise to new techniques: neuronavigation, minimally invasive neurosurgery, stereotactic radiotherapy.

New medical treatment, and in particular new chemotherapy regimens, has also changed the prognosis of brain tumours in children. New challenges are ahead.

There is more and more need for a precise histological diagnosis prior to surgery. Morphologic techniques such as MRI will never enable us to make a precise histological diagnosis preoperatively. Functional images may offer some hope of this.

Another challenge is the diagnosis of recurrence. MRI is now available postoperatively in most paediatric neurosurgery centres. It is clearly the technique of choice for assessing the completeness of the surgical resection.

The diagnosis of recurrence late after surgery is a completely different matter. It is very difficult to determine the nature of a small lesion in the ponto-cerebellar cistern of a patient who has earlier been operated upon for an ependymoma. The differentiation between a recurrence and a gliotic scar is highly problematic. This challenge is not yet answered.

It is not our intention to describe the precise morphologic features of all neoplasms in children; the reader can consult the textbooks and papers listed at the end of this paper. However, we will emphasise some features and some limitations of morphologic diagnosis of brain tumours in children.

Infratentorial tumours

Brain stem gliomas

Cranial nerves are frequently involved, in contrast to the absence of such an involvement in other posterior fossa tumours.

Several classifications have been published [4, 6] in attempts to correlate the clinical and MRI features with outcome. It has to be said that despite those classifications it is almost impossible to establish a prognosis in a given individual. The best prognostic factor that can be observed is the resectability of the tumour. Diffuse pontine gliomas have the worst prognosis.

One word of caution should be emphasised. Some gliomas may present acutely because of an intratumoral bleed. A great mimic of pontine glioma is pontine cavernoma, which can also bleed. In this case MRI and MRA, by showing the blood clot and the associated venous anomaly, can orient the diagnosis towards a nontumour pathology.

Another rare condition is the postimmune encephalitis that can involve the brain stem and the basal ganglia, mimicking a brain stem glioma. CSF analysis and follow-up will help in the diagnosis.

Cerebellar astrocytomas

These are the most typical tumours, although cystic medulloblastomas and ependymomas do exist. However, the presence of a large, partially cystic tumour of the vermis or the cerebellar hemisphere with an enhancing nodule after gadolinium injection is virtually diagnostic of carcinoma.

MRI has a role to play postoperatively, as the prognosis is excellent if removal has been complete.

Primitive neuroectodermal tumours (medulloblastomas)

The work-up of a primitive neuroectodermal tumour (PNET) has very recently been the subject of passionate discussion.

As new chemotherapeutic treatments become available it is increasingly necessary and desirable that a specific diagnosis be made preoperatively. As ever, 90% of medulloblastomas are easily recognised because they are midline lesions growing in the IV ventricle and enhancing homogeneously after gadolinium injection. However, some solid astrocytomas and some ependymomas can mimic a PNET. On the other hand, some medulloblastomas can be off the midline and partially cystic. It is not yet known whether other imaging modalities can differentiate medulloblastomas from ependymomas.

The presence of mestastases in the CSF spaces means that profound modifications of the treatment are needed. The challenge is important as:

1 MRI of the spine should be performed prior to any injury to the CSF spaces, surgery or even a lumbar tap. Indeed, even a lumbar tap can produce subtle enhancement of the lumbar CSF spaces, mimicking subarachnoid mestastases.

Spinal MR is technically difficult to perform in a 5-year-old boy or girl who is already in pain.

It is our opinion that a complete MRI study should be performed at the time of diagnosis. This requires general anaesthesia and at least 1 h of machine time.

Ependymomas

The heterogeneity of the tumour, with its tendency to produce exophytic portions through the Magendie and Luschka foramina, helps to orient the diagnosis. It usually enhances heterogeneously.

The very low incidence of spinal metastasis does not require a systematic spinal MRI. But it is important to make sure that the tumour is not a PNET.

Local recurrence are usually followed up by MRI after surgery or stereotactic radiosurgery. We now rely on the volume and enhancement behaviour of the residual lesion during follow-up.

Supratentorial tumours

Choroid plexus tumours

Choroid plexus tumours are not uncommon in children. The prognosis is completely different with different histological characteristics. Choroid plexus carcinomas have a poor prognosis, and the prognosis of choroid plexus papilloma and meningioma is better.

It is not essential that the diagnosis should be made preoperatively, as all these tumours should be operated on. Preoperative embolisation, if possible, helps to reduce the blood loss during surgery.

Optic/hypothalamic astrocytomas

Patients with NF1 are frequently affected by such tumours, but 50% of them arise in otherwise normal children.

The problems with these lesions are manifold.

In patients with NF1 it is a problem to decide what to do in a patient in whom the tumour is discovered by a systematic MRI. No answer is readily available. Follow-up MRI and visual field testing seem to be the appropriate medical protocol.

Histology of these tumours is almost invariably the same as that of pilocytic astrocytomas. Imaging has a role in isolated optic nerve gliomas, which can be resected in toto if the patient has a blind eye on the same side.

It is essential to assess the exact extent of the tumour and its posterior boundaries relative to the chiasm. Vascular complications such as aneurysms and moyamoya disease are not uncommon, especially in patients with NF1 and after radiotherapy.

Tumours of the cerebral hemispheres

Although not the commonest brain tumours in children, tumours of the cerebral hemispheres, including basal ganglia tumours, do occur and are difficult for the neuroradiologist. The hints provided by histology are almost invariably wrong, as most tumours do not have a typical behaviour.

Classical signs of aggressivity, such as rapid growth, peritumoral oedema and hypervascularity, may be lacking. On the other hand, benign astrocytomas may enhance, be affected by oedema and bleed.

Nowadays the exact characterisation of these tumours is obtained through a biopsy performed under stereotactic conditions. If lesions are found to be benign the tumour is resected and the patient followed up by means of MRI.

In the case of malignant lesions the problem is the follow-up of these patients. It would be useful to develop special techniques to assess the response of the lesion after treatment.

Radionecrosis, oedema, and viable tumour are difficult to differentiate on morphologic MRI only.

Perspectives

Future techniques may help to differentiate neoplastic from nonneoplastic brain tissue and to classify neoplastic lesions in malignant versus benign lesions.

Single photon emission computed tomography (SPECT) has been showed to differentiate low- versus high-grade gliomas.

Positron emission tomography (PET) has showed promising results in other field of oncology. Experience is limited in brain tumours in children owing to the very low availability of this technique.

MR spectroscopy gives the radiologist a biochemical insight into brain tumours in children. It may show the degree of malignancy and help to differentiate tumorous from nontumorous conditions. It may help to monitor the tumour response to treatment. More experience is obviously needed.

Conclusion

Nowadays MRI is the key examination to diagnose, localise, and monitor the follow-up of children with brain tumours. The radiological approach is still based an the concepts established by Derek Harwood Nash 25 years ago.

The histological diagnosis can be approached in approximately 80% of cases on the following criteria:

Where does the tumour come from?
What is its aggressivity on the surrounding parenchyma?
What is its rate of growth?
What is its enhancement pattern?

MRI helps the surgeon in the planning and localisation of the lesion (neuronavigation).

MRI helps the oncologist in following up the treated tumour.

In an ideal world noninvasive characterisation of the tumour would be useful. It has to be bear in mind that this will be useful for only 20% of the patients seen in a given institution.

It has to be known that histological classification is itself not a 100% perfect technique. Some tumours are difficult to classify even with modern histological techniques. I tend to call them “never-seen-that-beforomas” as our neuropathologist does.

MR spectroscopy and MR diffusion will only visualise part of the unknown. Much basic sciences work is needed to look for specific markers, either genetic or histological, before we can advance along this path. It will not be long before specific markers will be injected into the patient and looked for by MRI. It is not inconceivable that with MRI we will be able to assess some histological and genetic markers in vivo.

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