UPDATE

Review and update about medulloblastoma in children

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Abstract Medulloblastoma is the most common malignant CNS tumor in children. Although all medulloblastomas are classified as grade IV lesions, the wide histological and molecular variation among these tumors means that the risk and prognosis involved also vary widely. Imaging studies are important not only because the initial diagnostic evaluation indicates what type of surgery will be performed and has prognostic value, but also because it influences the postoperative treatment approach, providing, among other details, information about the dissemination of disease and remnants of the tumor after surgery, which are both risk factors in medulloblastomas. Improvements in our understanding of the biological and molecular characteristics of medulloblastoma promise a dramatic change in the accuracy of staging and treatment of this tumor in the near future that are sure to bring about further improvements in survival.

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PALABRAS CLAVE
Medulloblastoma; Pediatría; Tumores del SNC; Resonancia magnética

Medulloblastoma pediátrico, revisión y puesta al día

Resumen El medulloblastoma es el tumor maligno más frecuente del SNC en pediatría. Presenta una variabilidad histológica y molecular tan importante que hace que, aunque todos los tipos de medulloblastoma se clasifiquen como grado IV, el riesgo y el pronóstico de los mismos sean muy amplios. Las pruebas de imagen son importantes no sólo porque la valoración diagnóstica inicial indica el tipo de cirugía a realizar, que presenta un valor pronóstico, sino para el planteamiento terapéutico posterior, teniendo en cuenta que determinan, entre otras, la diseminación y el resto tumoral posquirúrgico, factores de riesgo en este tumor. Una mejor comprensión de las características biológicas y moleculares del medulloblastoma promete un cambio dramático hacia la precisión en la estadificación y el tratamiento tumoral en un futuro próximo, favoreciendo aún más la actual mejora de la supervivencia.

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Introduction

Medulloblastoma is the most common pediatric central nervous system (CNS) malignancy. It occurs more frequently in males (ratio 1.5:1) and usually before 10 years of age. Although much less common, the disease may also occur in adults, usually in the 3rd and 4th decades of life. This condition was initially described as cerebellar glioma until Bailey and Cushing named it medulloblastoma in 1925. Now it is included in the group of embryonal tumors (grade IV) of the World Health Organization (WHO) classification.

Clinical characteristics

Clinical manifestations depend on patient's age and extension of the disease, local or disseminated, and are usually brief—less than three months—reflecting the aggressive biologic behavior of the tumor. Clinical signs include headache, vomiting, papilledema, irritability, diplopia, nistagmus, and increased head perimeter in younger infants, and are due to increased intracranial pressure related to hydrocephalus secondary to tumor obstruction.

Clinical signs are also related to the vermian location of the tumor that results in ataxia, frequently accompanied by spasticity, and gait instability. A laterally located mass, more common in older children and adults, manifests as limb ataxia and dysdiadochokinesis. In older children, the first symptoms are usually headaches that worsen in the supine position, start in the morning and may improve after vomiting. Pressure from the hydrocephalus on the dorsal brainstem may result in Parinaud's syndrome, vertical gaze palsy and pupils reactive to accommodation, but not to light. Abducens nerve palsy is common and may result from compression of the partially exposed nucleus of the VI cranial nerve along the anterior margin of the IV ventricle, or from traction or pressure of this nerve in its course along the cranial base.

Manifestations of disseminated disease are related to metastatic location and include signs and symptoms of spinal cord compression resulting from spread to the spinal canal or convulsions when there is hemispheric spread.

Associated syndromes

Medulloblastoma is associated with nevoid basal cell carcinoma (Gorlin-Gotz syndrome), Turcot syndrome -type 2-, Li-Fraumeni syndrome, neurofibromatosis types 1 and 2, Rubinstein-Taybi syndrome, Fanconi anemia and Nijmegen syndrome. Part of the information on the molecular pathways related to medulloblastoma comes from the study of two syndromes associated with a constitutional predisposition to medulloblastoma—Gorlin syndrome and Turcot syndrome.

Radiological findings

Medulloblastomas arise from the midline vermis, the most common location, and grow into the IV ventricle. Cerebellar hemispheric location is more common in adults and older children. These variations in location may be explained by the different cellular origins of medulloblastoma, by the different progenitor cell pools of the cerebellum, and by the cellular signaling pathways that control its development that probably represent different compartments from which the various types of medulloblastoma arise. In addition, initially the migration of the origin cells starts from the posterior medullary velum toward a superior location, close to the midline, giving rise to tumors centered in vermis. Later in life, the cells migrate laterally so in older patients the tumor appears in the hemisphere. Less common locations include the IV ventricle (3%) and supratentorial compartment (2%). Computed tomographic (CT) appearance is hyperattenuating due to its high cellularity. Calcium is present in a low percentage (22%) and peritumoral edema is variable (fig. 1). The initial CT may demonstrate tumor complications including the degree of hydrocephalus secondary to obstruction and signs of intracranial hypertension.

MRI appearance is hypointense on T1-weighted sequences and hypo- to isointense on T2. This tumor is predominantly homogeneous, with little necrotic, hemorrhagic or calcific component. Enhancement is usually homogeneous after contrast administration; however, poor and heterogeneous enhancement has also been described (fig. 2).

Brainstem infiltration is common (33% of 144 cases published by Park et al) and complicates complete tumor resection. Although uncommon, foraminal extension with involvement of the cerebellopontine angle cistern, cisterna magna or other cisternal compartments may occur. It has been reported that signal heterogeneity on T2 sequences with “honeycomb” pattern is associated with anaplastic medulloblastoma with a sensitivity of 100%, but lower specificity. Similarly, a “grape-like” appearance has been described in the medulloblastoma with extensive nodularity (fig. 4). Since this subtype has neuronal differentiation, so it was previously called “cerebellar neuroblastoma”, some studies have reported higher uptake of iodine- 123-metaiodobenzylguanainid in this variant compared to other subtypes.

The presence of diffusion restriction is usually found, appearing as high signal on b1000 images and low signal on the apparent diffusion coefficient (ADC) maps. This is due to the high intrinsec cellularity of the tumor, decreased extracellular space and high nucleus/cytoplasm ratio. Given the fact that the higher the cellularity, the more histological aggressiveness, the ADC map may be used for tumor grading. In this respect, low signal on ADC map in pediatric patients is very characteristic of high grade embryonal tumors including medulloblastoma (fig. 2d and e).

Diffusion imaging is helpful in the initial definition of the tumor and in the assessment of the progression of those neoplasms that do not enhance with contrast before or after treatment. Chemotherapy increases the signal on the ADC map since the cellularity decreases and the extracellular space increases, but the coefficient decreases again in case of recurrence. Thus, diffusion imaging provides complementary data for monitoring tumor response to therapy. Pretreatment diffusion values may predict the tumor response to radiotherapy and may differentiate radiation-induced lesion from recurrence.
MR spectroscopy shows elevated choline (Cho) levels, higher than those of other posterior fossa masses, indicative of high turnover of tumor cells. There is also a marked decrease of N-acetyl aspartate (NAA), resulting in a high Cho/NAA ratio; and a marked increase of Cho/creatine (Cr) ratio and significant decrease of NAA/Cr. 23,24 Sometimes, lipid resonance indicative of necrosis is present in rapidly proliferating tumors, including malignant embryonal tumors, although not specifically in medulloblastoma. 24,25

It should be noted the significantly elevated taurine concentrations compared to other tumors. 21,23,25-27 The hypotheses that explain the presence of taurine include the aggressiveness of medulloblastoma, an active metabolite associated with increased cellular proliferation and the loss of differentiation of tumor cells. 26 Taurine is detected at a frequency of 3.36 (3.4) ppm. Although there are few studies published, taurine is observed at lower concentrations in the desmoplastic/nodular variant than in more aggressive subtypes of medulloblastoma. 23,26

Perfusion assesses hemodynamic changes in the cerebral microcirculation. Its main application in neoplasms is preoperative tumor grading. 24 Relative cerebral blood volume (rCBV) is significantly higher in high-grade than in low-grade tumors—secondary to tumor neovascularization—irrespective of the degree of integrity of the blood-brain barrier (BBB). This information is not provided by conventional contrast-enhanced MR imaging, in which the presence and degree of enhancement correlate with both vascular hyperplasia and BBB status. 13,24 This explains why the degree of enhancement does not correlate with tumor grading. For example, a low-grade tumor such as the pilocytic astrocytoma enhances intensely, whereas a high-grade tumor such as medulloblastoma may not enhance as intensely but may show high perfusion with increased rCBV. In addition, perfusion has the potential to identify disease progression, characterized by increased rCBV values in comparison with stable lesions whose rCBV does not change significantly over time. 13,24

Increased 18F fluorodesoxyglucose (FDG) uptake is observed on PET scans of the brain and spinal cord in disseminated medulloblastomas. 29 Cerebrospinal fluid (CSF) dissemination has to be ruled out at the initial evaluation, as medulloblastoma is the pediatric tumor with the highest rate of neuraxis dissemination. 30 Metastatic spread is present in about 30% of patients at diagnosis, with higher probability in younger children. 12 This examination has the highest sensitivity and specificity in the perioperative period, before oncologic treatment planning. Current diagnosis of dissemination is performed by:

1. Spinal RM imaging, preferably preoperative or two weeks after surgery. If no preoperative spinal study was performed, it is important to delay the spinal MRI two weeks to reduce false positives caused by subarachnoid blood and postsurgical irritation. 31

**Figure 1** Presence of calcium within the tumor. a) Unenhanced CT scan shows small scattered calcifications within the tumor mass corresponding to a medulloblastoma in a 10-year-old patient. In a pediatric patient, this type of calcifications must not be confused with those that appear in the plexus of the IV ventricle at later ages. Increased density of medulloblastoma in relation to the surrounding parenchyma. Signs of hydrocephalus secondary to compression, like development of temporal horns. b) Gradient echo MRI sequence for evaluating the presence of calcium. A different patient with millimetric signal-void areas in the tumor periphery. (Image provided by Dr. Elida Vázquez Méndez, Hospital Vall d’Hebron).
CSF cytologic analysis via lumbar puncture approximately 15-20 days after surgery. In previous years, the site of CSF sampling, lumbar or cranial (through previously placed catheters for hydrocephalus) was a subject of much discussion; lumbar sampling is currently preferred. MRI of the neuraxis has greater diagnostic accuracy than CSF cytologic analysis in the detection of medulloblastoma; in this respect, statistical studies have proven that CSF cytology does not show disseminated tumor when MRI of the neuraxis is negative. MRI of the neuraxis generally includes T1 sequences with gadolinium gadopentate dimeglumine (Gd-DTPA), with or without fat suppression, depending on the institution and protocol, but excellent results have been published for diffusion imaging, which seems to be more sensitive than contrast imaging in the detection of disseminated medulloblastoma. Images showing intradural extramedullary spread usually correspond to linear pial lesions, but also to isolated subarachnoid nodules and drop metastases in the caudal region of the spinal canal, or to actual tumor masses occupying the canal, all showing contrast enhancement or restricted diffusion (fig. 7).

Although extraneural metastases of CNS tumors are rare, they are characteristic of medulloblastoma with a prevalence close to 7%, with bone marrow location (77%) followed by lymph nodes (33%).
Differential diagnosis

The main differential diagnoses of pediatric posterior fossa masses include medulloblastoma, astrocytoma pilocytic and ependymoma. Atypical teratoid-rhabdoid tumors (ATRT) also need to be considered in certain instances.

Consideration of medulloblastoma within the differential diagnosis mandates an aggressive surgical approach as residual tumor is one of the prognostic factors. If medulloblastoma is suspected, preoperative imaging must include the neuroaxis given the high propensity to disseminate. For this reason, differentiation with the above-mentioned tumors is important, with a different pre- and postoperative imaging approach.

Unlike medulloblastoma, ependymoma, pilocytic astrocytoma and ATRT generally occupy cerebellopontine angle and adjacent cisterns. Ependymoma and pediatric medulloblastoma are usually midline tumors, whereas astrocytoma and ATRT are usually eccentric.

Figure 3 Although it may happen, foraminal extension involving the cerebellopontine angle cistern, cisterna magna or other cisternal compartments is unusual in medulloblastoma, allowing differentiation from ependymoma, an infratentorial midline tumor that shows this feature. a) Axial T2 MRI fast sequence shows tumor extension into the prebulbar cistern (short arrow) and foramina of Lushka and Magendie (long arrows). b) Axial T2 MRI shows a medulloblastoma partially occupying the left cerebellopontine angle cistern (arrow).

Figure 4 Relation between imaging findings and histological findings. a) Contrast-enhanced T1 MRI sequence shows a medulloblastoma with nodular, “grapelike” appearance. No dissemination is observed. The diagnosis of extensive nodularity variant was considered, but this patient was 7-year-old and this condition usually appears in younger children. Pathologic results demonstrated desmoplastic/nodular subtype. b1, T2 MRI sequence; b2, Contrast-enhanced axial T1 MRI; b3, Contrast-enhanced T1 MRI with magnification along the sagittal plane. Patient with medulloblastoma with marked heterogeneity on T2 sequences (small cysts, internal areas of necrosis and heterogeneous signal of the solid component of the tumor) as well as an enhancement pattern that may be considered as “honeycomb”. Consideration was given to the possibility of an aggressive variant. In addition, the lesion showed other features of poor prognosis including leptomeningeal dissemination at the time of diagnosis. The diagnosis of anaplastic medulloblastoma was considered and subsequently confirmed by pathologic examination.
The most likely alternative consideration for a hyperattenuated midline mass due to the presence of calcium is an ependymoma. In contrast to medulloblastomas, ependymomas typically show more calcification and display a “plastic” morphology, extending and conforming from the IV ventricle through the foramina of Luschka and Magendie into the cerebellopontine angle cistern.\textsuperscript{2,3,13}

Diffusion MRI shows some similarities among the three types of tumors, particularly in their pathological variants, including the lower restriction of desmoplastic medulloblastoma compared to other subtypes of the tumor,\textsuperscript{15} the increased restriction in two thirds of anaplastic ependymomas (WHO grade III) and 50% of classic ependymomas (WHO grade II), or the restriction described in a considerable percentage of solid nodules of pilocytic astrocytoma.

Although diffusion is a useful modality for the assessment of pediatric posterior fossa tumors (evident restricted diffusion of medulloblastoma compared to other tumors), additional features (age, location, 

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Figure 5  Hydrogen MR (1.5 Tesla). a) Single-voxel acquisition with short TE (23). b) Multivoxel acquisition. Horizontal arrow: choline (3.22 ppm). Short arrow: creatine (3.04 ppm). Long arrow: NAA (2.02 ppm). Thick arrow: taurine (3.36 ppm). Each figure corresponds to a different medulloblastoma, but both spectra show elevated choline peaks, marked reduction of NAA and decreased creatine. The presence of taurine is observed in the second study, corresponding to a desmoplastic/nodular variant, which exhibits lower taurine peaks than the most aggressive variants of medulloblastoma.

Figure 6  Vermian medulloblastoma in a 7-year-old patient that shows intense and homogeneous enhancement at T1 MRI with Gd-GPDM (a) and elevated rCBV at contrast-enhanced perfusion imaging (b), indicative of loss of BBB integrity and increased tumor angiogenesis, respectively. (Images provided by Dr. Elida Vázquez Méndez, Hospital Vall d’Hebron).
morphology, dissemination) are needed for tumor differentiation.\textsuperscript{18,19}

Differentiation between some midline pilocytic astrocytomas with significant solid component, heterogeneity and intense contrast enhancement, and medulloblastomas would be difficult if it were not for diffusion imaging, which depicts medulloblastomas with no restriction and intense brightness on ADC maps.\textsuperscript{5,36} On MR spectroscopy, the presence of taurine in the medulloblastoma helps distinguish from cerebellar astrocytoma, which shows no taurine.\textsuperscript{25,27}

Although both ATRT and medulloblastoma are embryonal tumors, ATRT presents earlier (mean 1.3 years) with a remarkably more aggressive course and lower response to treatment; its differentiation is thus relevant for prognosis. Despite their similar neuroimaging features, the typical infratentorial location of ATRT is in the cerebellopontine angle (more hemispheric and less centric than medulloblastoma) and exhibits more intrallesional hemorrhage than medulloblastoma. Diffusion imaging is not useful for differential diagnosis since both tumors are hypercellular; therefore, showing marked restricted diffusion.\textsuperscript{18} In short, if a posterior fossa mass in a young child displays marked heterogeneity, restricted diffusion and cerebellopontine angle location, ATRT is the first diagnostic consideration.\textsuperscript{36}

**Pathologic characteristics**

The 2007 WHO classification of tumors recognizes medulloblastoma, primitive neuroectodermal tumor (PNET) of the CNS and ATRT as embryonal tumors; all grade IV lesions.\textsuperscript{7,8}

Two new histological variants with different clinical behavior have been incorporated: medulloblastoma with extensive nodularity, associated with a favourable prognosis; and the anaplastic type, with poor prognosis. Other subtypes previously described are classic, desmoplastic/nodular and large cells.\textsuperscript{7,8,37} Medulloblastoma with extensive nodularity is related to the desmoplastic/nodular subtype, but the former has better prognosis, appears earlier, whereas the latter occurs in older children, and tends to hemispheric location. Both tumors are histologically more favourable than the other variants. The anaplastic subtype shows the highest degree of atypia. Large cell variant also carries poor
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prognosis and shows similar cytologic features than the anaplastic form.\textsuperscript{1,7,18}

Prognostic factors

Identifying the pathobiological correlation of clinical behavior or the therapeutic response currently represents the key for medulloblastoma research.\textsuperscript{4}

The diagnostic factors that have been considered to date are:

1. The degree of surgical resection. Complete surgical resection is considered the best prognostic factor. Macroscopic tumor excision is defined as absence of residual lesion at the first postoperative (48-72h) MRI\textsuperscript{39} (fig. 8).

2. Presence of metastasis at diagnosis, based on radiological findings and CSF analysis\textsuperscript{29}. Staging is done according to the modified Chang classification: M0, no dissemination, and M1 to M4, disseminated disease.\textsuperscript{40}

3. Age. Children under three have poorer prognosis, probably due to the extension of the tumor that makes excision more difficult and to the difficulty of giving radiotherapy at this age.\textsuperscript{1}

According to these parameters patients are divided into two risk groups:\textsuperscript{6,41-43}

1. Average-risk patients, with the following features: older than three years, non-metastatic disease at diagnosis (M0) and total or nearly total resection (residual tumor < 1.5 cm\textsuperscript{2}).

2. High-risk patients present at least one of these features: younger than three years, metastasis at diagnosis or residual tumor > 1.5 cm\textsuperscript{2}.

Histopathologic and molecular profiles are incorporated into the three classic clinical parameters of risk since many current studies consider that these profiles may be evaluated for risk stratification and, thus, influence the biological behaviour and response to treatment.\textsuperscript{12,44}

A major drawback is that the classification according to the classic parameters does not differentiate high- from low- histological risk patients within the same clinical stage.\textsuperscript{12} It is a noted fact that patients with the same clinical stage, receiving similar treatment, may show widely disparate outcomes, depending on the biological differences within the tumor. In addition, two different studies, the German trial HIT’91\textsuperscript{45} and the Children’s Cancer Group 921,\textsuperscript{46} established that overall survival was not significantly different between children staged M0 and M1. It has been even proven that brainstem invasion, previously regarded as a high-risk indicator, does not affect prognosis. These are only two of the many examples showing the impact of tumor biology on prognosis.

The histological factors currently included in the determination of the outcome are:\textsuperscript{12,44,47-49}

1. Histopathological variant: desmoplastic and extensive nodularity subtypes show better outcome than anaplastic and large cell subtypes. The classic form has intermediate risk.

2. Extent and degree of nodularity: only medulloblastoma with extensive nodularity is associated with better survival.

3. Anaplasia: the most aggressive biological feature. Presence and degree of anaplasia are associated with the poorest outcome.

Molecular and cytogenetic factors considered for prognostic assessment are:\textsuperscript{44,47}

1. Chromosomal abnormalities: the most common is loss of genetic material of chromosome 17p, which corresponds to the location of a suppressor gene, so its deletion leads to tumor expresion.\textsuperscript{49} Sometimes this deletion occurs as a component of 17q, forming an isochromosome (i17q). 17p loss and isochromosome 17q are more frequent in classic and anaplastic subtypes than in the desmoplastic one.

2. Genetic alterations: amplification of c-myc and N-myc is considered a very unfavorable factor usually associated with the anaplastic and large cell subtypes.

3. Embryonic development and oncogenesis: mutation in the PTCH gene, involved in the SHH (sonic Hedghog) pathway, is essential for the development of the cerebellar granular layer. PTCH mutation is identified in the Gorlin syndrome, but also in 10-15 % of sporadic medulloblastomas.\textsuperscript{50}

4. Abnormalities in cellular signal pathways: research studies are investigating the role of the expression of neurotrophins such as Trk C and their role in neuronal development, the expression of the epidermal growth factor receptor (ErbB2) as well as the involvement of the SHH/PTCH signals and Wnt/Wg pathways among others.

Other chromosomal abnormalities and molecular aberrations have been described but are beyond the scope of this work. Readers are referred to specialized literature.\textsuperscript{4,43,47,48,51-53}

Treatment

Treatment is based on three mainstays: surgery, chemotherapy and radiotherapy. Significant variations are managed in relation to the different risk factors above mentioned.

There are several ways of grouping patients in order to include them into the different treatments. The proposal of some authors is:\textsuperscript{12,54}

1. Average-risk medulloblastoma in children older than three years. Craniospinal irradiation and radiation boosts of the posterior fossa in conjunction with different chemotherapy regimens depending on the protocol into which the patient is enrolled or the protocol in process (the last protocol was the HIT-SIOP PNET 4, CNS 2003 05, now closed).\textsuperscript{54} A significant percentage of these patients are curable.\textsuperscript{1}

2. High-risk medulloblastoma in children older than three years. Intensified radiotherapy and chemotherapy with modified regimens compared to the previous group.
3. Medulloblastoma in infants younger than three years. These protocols are continuously under review due to the relative rarity of this tumor in this age group, and multicenter prospective trials are needed in this respect. 55-58 Although radiotherapy presents particularly adverse effects in these patients, they seem to benefit from proton radiotherapy. 55

Treatment of recurrence usually depends on the age, extent of the recurrent disease and type of treatment received after initial diagnosis. 1,58,59

Follow-up imaging studies

Follow-up imaging studies are intended to identify early relapses, so secondary therapies may potentially improve the outcome. In addition, medulloblastoma follow-up may be considered as part of the treatment given its high recurrence rate. 39 Recurrence is the major cause of death in patients with medulloblastoma. 2,60

Medulloblastoma is a very aggressive malignancy with a high rate of local recurrence associated with incomplete tumor resection that results in significantly reduced time to recurrence. 39 Most common sites of recurrence are the posterior fossa, followed by spinal and supratentorial locations 61 (fig. 9); infrequently, systemic spread (bone and lymph nodes) may also occur 34. This makes necessary the follow-up of these children until adulthood, although most recurrences appear two years after the initial diagnosis 1,2,63. The longest latency period reported is 19 year after diagnosis. 64

There are numerous follow-up imaging protocols. The present work describes the one implemented at the GOSH of London, result of an extensive and detailed neuroimaging study on medulloblastoma follow-up. 39,65 This protocol includes a postoperative cranial MRI acquired within 24-48h (in other centres 72h). MRI is repeated at 2-3 months during the first year and then every 6-8 months in the following years (after six but before 7.5 years) or until a recurrence appears or the child is discharged. Equivocal results require closer follow-up (every 2 or 3 months).

Initially, MRI of the neuraxis was performed only in case of dissemination at diagnosis or detection of recurrence. In the current protocol, all the imaging studies include complete evaluation of the neuraxis because, although they found no children with spinal recurrence if there was not intracranial recurrence—in other words, neuraxis relapse does not appear isolated—, they believe that imaging the neuraxis at every follow-up entails more benefits than drawbacks 39,66. Other protocols propose different timing for neuraxis follow-up.

Sequelae

Most sequelae correspond to neuropsychological disorders and neurocognitive deterioration, 57,68 more severe in younger children. 57 Many medulloblastoma survivors have severe sequelae secondary to the tumor or the treatment. 69

Patient’s age at the time of craniospinal radiation and radiation dose are known neurotoxic factors. Endocrine follow-up is important due to the risk of endocrine disorders secondary to holocranial irradiation.

An interesting trial has tried to determine by diffusion tensor MR imaging the loss of white matter anisotropy caused by radiotherapy, concluding that the mean value of white matter anisotropy is potentially useful to evaluate neurotoxicity. 70

Secondary tumors are also described in medical literature as side-effects of radiotherapy, as well as vascular malformations and white matter lesions. 2,68,69,71
Conclusions

Five-year survival rates for patients with medulloblastoma have improved dramatically from the ‘70s (2-30%) to the present (50-85%).

Imaging plays a prominent role in the assessment of the prognostic factors since the degree of tumor resection and the presence of dissemination at the time of diagnosis are evaluated by imaging techniques. The use of diffusion sequences in the study of leptomeningeal spread represents an advance of the technique that helps in tumor staging and follow-up.

Imaging follow-up is essential given the high recurrence rate, so much so that some authors call it “treatment protocol” instead of “follow-up protocol”. A significant change has been introduced into the prognostic evaluation, so in addition to clinical factors (metastasis, residual tumor, age), biological parameters (histologic variant, degree of anaplasia and nodularity extent) as well as molecular and cytogenetic parameters have been included, although still under research but with a very promising future for the assessment of tumor prognosis and treatment. It seems unjustified to include all medulloblastomas, highly aggressive neoplasms, into WHO grade IV. The new trend is to consider medulloblastoma not as a single entity, but as a complex group of tumors biologically different but with morphological similarities, which entails individualization of the treatment in order to increase survival rates and reduce long-term toxicity and morbidity.

Authorship

Dr. Martinez León takes responsibility for the integrity, conception, design, analysis and interpretation of the data, as well as for the bibliographical research, drafting of the manuscript and approval of the final version.

Conflict of interest

The author declares no conflict of interest.
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