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CASE REPORT

Natural history of a medulloblastoma: 30 months of wait and see in a child with a cerebellar incidentaloma

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Abstract
Introduction With the increasing use of neuroimaging studies, the discovery of incidental neoplastic lesions is becoming more frequent. However, standard procedures are lacking, and little is known about their optimal management.
Case Report We here present the case of a boy with a cerebellar mass incidentally discovered on a CT scan performed after head trauma. In another scan performed after another incident of head trauma 14 months earlier, the lesion could be seen after retrospective examination. In view of the asymptomatic clinical and stable radiological status and the presumed diagnosis of a low-grade glioma, a watch-and-wait strategy was elected. After clinical and radiological progression was observed, the tumour was resected, 2½years after the initial imaging study. Histological evaluation revealed a WNT pathway-activated classical medulloblastoma.
Discussion To our knowledge, this is the first description of such a long natural history and pre-symptomatic period of a medulloblastoma. The long period of stability followed by a period of accelerated tumour growth is compatible with increasing biological aggressiveness, possibly related to the stepwise accumulation of genetic changes.

Keywords Medulloblastoma · Brain neoplasms · Incidental findings · Child · Cancer · Radiology

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Introduction

Due to increasing use of neuroimaging studies, the number of neoplastic incidentalomas, i.e. incidentally discovered abnormal findings unrelated to the purpose of the examination, has been rising, with an overall prevalence ranging from 0.1 to 1 % [13, 16]. After the detection of a lesion, standard procedures are lacking, and little is known about the optimal management. In many instances, the neuroimaging features are not diagnostic, and histopathologic diagnosis comprises a diverse spectrum of entities. Here, we present the case of a boy with a cerebellar incidentaloma, which was resected after 2½years of observation and, surprisingly, yielded the diagnosis of medulloblastoma (MB).

Case report

After sustaining a minimal head trauma in April 2006, a 6½-year-old boy underwent a cranial CT scan in another institution, which at that time was judged as normal. Fourteen months later, during the investigation of a similar head trauma, another CT scan was performed, which showed a circumscribed, mainly hyperdense vermian mass with a diameter of 2 cm without any evidence of obstructive

hydrocephalus (Fig. 1). Retrospectively, the identical finding was identified on the first scan. The patient was then referred to our institution for neuropaediatric evaluation, where a MRI showed an inhomogenously contrast enhancing lesion without perifocal oedema with an inhomogeneous hypo- and hyperintense signal in T2 and FLAIR sequences, and a larger proportion showing no diffusion restriction with a correspondingly elevated ADC value. The patient complained of headache, tiredness and dizziness, which could not be explained by the lesion, and which subsequently resolved spontaneously. The neurological examination was normal. Since the presumptive diagnosis was a low-grade glioma, a wait-and-see strategy was chosen. A follow-up MRI in December 2007 showed discrete signs of progression, with increased contrast enhancement and extension of the tumour into the right foramen of Luschka and left cerebellar grey matter. Despite radiographic evidence of progression, the patient remained asymptomatic. An MRI performed 4 months later was unchanged when compared to the previous MRI. At that time, the patient complained of blurred vision, loss of balance and coordination deficits. On neurological examination, moderate truncal ataxia, bilateral dysmetria, right-sided dysdiadochokinesis, and nystagmus were noted. In addition, right monocular double vision and visual acuity that fluctuated between 0.3 and normal were documented; however, not all of the findings could be explained by the tumour. Clinically, fatigue and gait disturbance persisted, and a subsequent MRI in December 2008 showed further tumour progression. Accordingly, the tumour was partially resected in January 2009, with the histological diagnosis of a classical MB (Fig. 2). The MIB-1 proliferation index was 10 %, and more than 10 % of tumour cells showed strong nuclear immunoreactivity for beta-catenin. A CTNNB1 mutation (S37P) was found, corresponding to medulloblastoma of the WNT subgroup [15]. Immunohistochemical analyses for hedgehog target genes as well as genomic and immunohistochemical analyses for c-myc amplification and target genes were negative. There was no evidence of micro- or macroscopic CNS metastases. The patient received craniospinal radiotherapy with concomitant vincristine followed by eight chemotherapy cycles with cisplatin, lomustine, and vincristine, and has stable residual disease for more than 3 years.

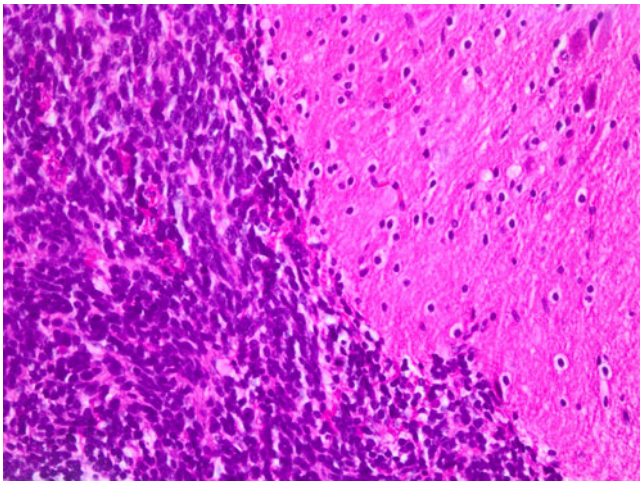

Fig. 2 Medulloblastoma: cerebellar cortex infiltrated by densely packed monomorphous tumour cells with moderate nuclear pleomorphism and scant cytoplasm

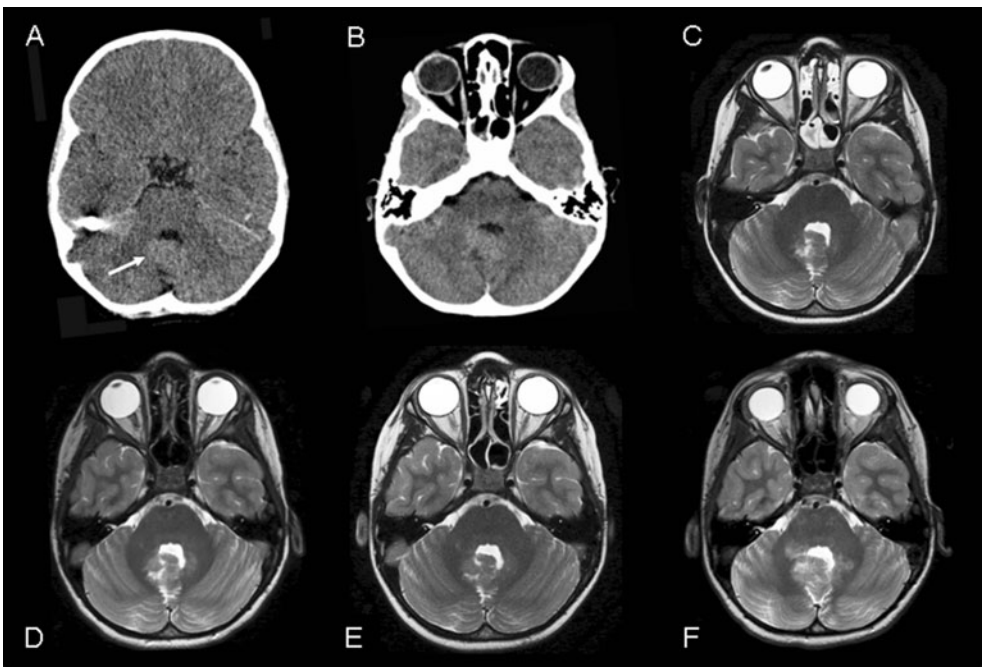

Fig. 1 **a**–**f** Serial images illustrating the natural growth behaviour with a prolonged period of stability followed by progression of a medulloblastoma initially discovered as an incidentaloma (*arrow*). **a** CT scan, April 2006; **b** CT scan, June 2007 (stable disease); **c** MRI (T2), July 2007 (stable disease); **d** MRI (T2), December 2007 (progressive disease); **e** MRI (T2), April 2008 (stable disease compared to 1D); **f** MRI (T2), December 2008 (progressive disease)

Discussion

To our knowledge, this is the first description of such a long natural history and pre-symptomatic period in a patient with an untreated MB that was incidentally discovered on imaging. Due to the incidental nature of its discovery, the stable size during the 14-month interval between the first and the second CT scan and the lack of neurological signs or symptoms (and despite an unequivocal hyperdensity on unenhanced CT, which is suspicious for a tumour with increased cellular density), the working diagnosis was low-grade glioma, which prompted a wait-and-see approach. Surgery was only performed after clear clinical and radiological progression, altogether 2½years after the first CT scan.

In most instances, the appearance of neurological symptoms precedes the radiological diagnosis of a posterior fossa tumour, followed by immediate surgical extirpation. Therefore, in contrast to the reported case, the kinetics of tumour growth before the appearance of the first symptom(s) are unknown. Accordingly, only the length of the prediagnostic symptomatic interval (PSI) can provide some indirect evidence regarding the kinetics of tumour growth: Not only are differences documented between different types of brain tumours, with malignant tumours (e.g. MBs) having shorter PSIs than low-grade tumours [4, 10, 12, 17, 19], but considerable variability is seen within the patient group with MB [2, 8]: In a large prospective series, we found PSIs ranging from 0 to 24 months, with a median of 2 months. Interestingly, the group of patients with the longest PSIs had lower-stage disease at diagnosis and a better overall survival probability than that with shorter PSIs [6]. The likely explanation for these results probably lies in the broad spectrum of biologic behaviour within the whole group of MB [3, 15]. The present tumour can be classified histologically as WNT pathway-activated MB. This MB subtype is associated with a favourable prognosis [5, 15]. One could speculate that the tumour acquired a stepwise accumulation of genetic aberrations over time, which—after a relatively stable phase—resulted in accelerated growth. This hypothesis is consistent with the findings of an accumulation of such aberrations in relapsed medulloblastoma when compared to their corresponding primary tumours [9].

Due to the more frequent use of neuroradiologic imaging, the number of neoplastic incidentalomas has been steadily rising [13, 16]. While for a definitive histological diagnosis of a posterior fossa tumour a neuropathological examination is needed, neuroimaging can offer a certain diagnostic guidance, notably regarding the distinction between a high and a low cellularity. In the case of this patient, due to the long-lasting constant size and the lack of clinical symptoms, a low-grade tumour was suspected, even if on the basis of the increased CT density this working diagnosis would have to be doubted. Low-grade gliomas are tumours with a low cellularity and therefore exhibit low CT density values [11], while the typical CT appearance of medulloblastoma is hyperdense before contrast medium application [14, 18]. CT density still remains a very good tool to differentiate between lesions with low and high cellular density [1]. In magnetic resonance imaging, comparison of apparent diffusion coefficient parameters revealed distinctive values in different entities of posterior fossa tumours in single-centre reports [7, 20].

Conclusion

This is the first description of MB with such a long natural history diagnosed as an incidentaloma that was followed according to a wait-and-see approach. During the long period of clinical and radiological stability preceding the radiological and clinical progression, the working diagnosis was low-grade glioma, despite a nonfitting hyperdensity of the tumour on CT. We suspect an accumulation of genetic aberrations over time leading to a change of growth behaviour. However, as the tumour was not biopsied at the time of radiological detection, this remains speculative.

There are no evidence-based guidelines for the management of neoplastic CNS incidentalomas. Not only a precise histological diagnosis can often not be made on radiological grounds, but also a neoplastic incidentaloma might clinically behave differently compared to a lesion of the same histology diagnosed on the basis of symptoms. Whereas a delay in treatment in some patients may have negative consequences, unnecessary surgical exploration may also be associated with considerable morbidity (e.g. CNS lesions, haemorrhage). Therefore, a case-by-case evaluation by an interdisciplinary tumour board is recommended, with the consideration of parameters such as the radiological nature of the lesion, the differential diagnosis, the evolution and the clinical state of the patient.

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