CASE REPORT

Early diagnosis in a case of atypically located germinoma: $^1$H-MR-spectroscopy as a decision tool

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Abstract

CNS germinoma is a malignant germ cell tumor with a high potential for curative treatment. In MRI it mainly appears as contrast enhancing mass in the midline structures of the brain but it can also occur atypically located in the basal ganglia. We present the case of a 21-year-old patient suffering from psychiatric symptoms and a mild, right-sided hemiparesis. A MRI scan solely showed diffuse T2/FLAIR hyperintensity and mild atrophy around the left basal ganglia. As excessive diagnostics remained insignificant, $^1$H-MR-spectroscopy was performed. Considering the previous diagnostics, increased choline, decreased NAA and increased Myoinositol suggested a malignant disease. Consequently, brain biopsy was performed, revealing a germinoma. In comparable, published cases a lack of evidence for a neoplastic disease usually leads to a severely delayed diagnosis. Our report shows for the first time, that this evidence can be obtained early with MR-spectroscopy and discusses the possibility of specific metabolic patterns.

INTRODUCTION

Although rare (incidence rate 0.2/1 000 000), germinoma is the most common subtype of germ cell tumors in the CNS. They predominantly affect young males (m:f 3–15:1), with more than 60% being diagnosed below the age of 20 years [1]. Compared to all other malignant brain tumors, germinoma has a high potential for curative treatment (5-year survival rate $\approx 90\%$) [1].

More than 90% of all germinomas are located in the midline structures of the brain (pineal gland $>$ suprasellar). More rarely they appear in the basal ganglia or other brain regions. The common MRI appearance on either site is a uni- or multifocal, contrast enhancing, solid mass, with sometimes additional cysts and low ADC values [2, 3]. After histologic diagnosis irradiation, if suitable combined with chemotherapy, is the treatment of choice [1].

CASE REPORT

A 21-year-old male patient was initially admitted for minor traumatic brain injury. Upon first examination depressive symptoms and behavioral problems where noticed and the patient was admitted to a psychiatric ward. He had an at least 4-week history of mild spastic hemiparesis and right-sided hypesthesia. MRI revealed left-hemispheric, diffuse T2/FLAIR hyperintensity and mild atrophy around the left basal ganglia. As excessive diagnostics remained insignificant, $^1$H-MR-spectroscopy was performed. Considering the previous diagnostics, increased choline, decreased NAA and increased Myoinositol suggested a malignant disease. Consequently, brain biopsy was performed, revealing a germinoma. In comparable, published cases a lack of evidence for a neoplastic disease usually leads to a severely delayed diagnosis. Our report shows for the first time, that this evidence can be obtained early with MR-spectroscopy and discusses the possibility of specific metabolic patterns.
infectious inflammation, a vasculitis or vasculopathy or a specific tumor entity (including β-HCG and AFP levels in cerebrospinal fluid) could be obtained. As a result, the differential diagnostic spectrum still included a degenerative, inflammatory or neoplastic cause. Proton MR-spectroscopy showed on both 2D chemical shift imaging (TE 140 ms, 16 × 16 matrix, voxel size 7.5 × 7.5 × 20 mm) (Fig. 2) and single voxel spectroscopy in a temporomesial and a basal ganglia volume (TE 140ms/30ms, voxel size 24 × 20 × 22 mm) a decrease of N-acetylaspartate (NAA, neuronal marker, NAA/Creatine quotient 1,41 in the lesion and 1,81 in the contralateral tissue) and a slight increase of Choline (Cho, reflecting cell membrane turnover, Cho/Creatine quotient 1,32 in the lesion and 1,15 in the contralateral tissue) in comparison to the contralateral tissue (NAA/Cho quotient 1,07 in the lesion and 1,59 in the contralateral tissue). In addition, a marked increase of Myo-inositol (MI, among other things glial marker) in the affected tissue with a concentration reaching up to 13–14 mM in the temporomesial region was noticed in the spectra at short TE (Fig. 3). The MI levels well exceeded the range for degenerative or inflammatory diseases. Additionally, a slight increase of mobile lipids was distinguishable in the temporomesial volume. In the absence of inflammatory CSF changes, the metabolic profile overall strongly indicated an active neoplastic process. Brain biopsy was recommended and the temporomesial spectroscopy volume was selected as biopsy site. Neuropathologic examination revealed a highly cellular tumor without significant areas of necrosis, composed of dense lymphocytic infiltrates (positive for CD45) and tumor cells with round nuclei and often prominent nucleoli as well as abundant eosinophilic or clear cytoplasm. Tumor cells showed a specific expression pattern (Oct 3/4+, PLAP+, c-Kit+ and no staining for alpha-fetoprotein, beta-hCG, CD30) supporting the diagnosis of a germinoma (Fig. 4). Treatment based on the SIOP CNS GCT II protocol (platinum-based chemotherapy with irradiation) was initiated shortly after. Upon treatment the hemiparesis improved markedly. Follow up MRI after 4 cycles of chemotherapy and irradiation remained stable.

Figure 1: FLAIR (a) and correlating T2 (b, d) weighted MRI images, showing left hemispheric hyperintensity and atrophy in the basal ganglia, insular and temporomesial region. There was no correlating contrast enhancement. Also, contrast enhanced T1 images (c) showed no pathologic enhancement in the pituitary or pineal gland.
Figure 2: Placement of the 2D chemical shift imaging with voxels corresponding to the spectra in (b) and (c) marked in red (a). Spectrum for the lesion (c) and normal spectrum for the contralateral region (b).

Figure 3: Placement of the temporomesial single voxel in coronal T2 (a) and axial FLAIR (b). The corresponding spectrum for TE 30 ms (c) demonstrates very high MI peaks (at 3.6 ppm) and elevated Cho (at 3.2 ppm), which exceed the NAA peak (at 2.0 ppm). In the TE 140 ms spectrum (d) MI almost disappears due to short T2 relaxation time and spin dephasing, but the increase of Cho and reduction of NAA is still prominent in comparison to the creatine −CH2 and −CH3 peaks (at 3.9 and 3.0 ppm, respectively). The additional single voxel spectroscopy of the left basal ganglia is not shown due to redundant results.
DISCUSSION

A small number of case reports describing germinoma of the basal ganglia appearing only as unilateral diffuse FLAIR/T2 hyperintensities, with basal ganglia and cerebral crus atrophy have been published. Likely this is an early form of presentation, with patients developing contrast enhancing solid masses and cystic lesions as the tumor progresses [4]. The symptoms described in our case report are fairly common in this context, but also unspecific. Thus, in all but two published cases [5, 6], follow up MRI instead of a biopsy was recommended since no neoplastic disease was evident. As already recognized by Phi et al. [4] the diagnosis was then established upon tumor progression into a contrast enhancing mass, on average almost one year later. The late diagnosis was identified as risk factor for tumor progression and likely worse clinical outcome, especially with regards to the motor function [4]. The problematic delay depicts the need for additional diagnostic tools. As a promising approach to identify neoplastic diseases, $^{11}$C-methionine PET imaging has been proposed. It demonstrated significantly increased tracer uptake in the tumor region, prompting brain biopsies in the two cases without delayed diagnosis [5, 6]. Current MR-spectroscopy studies on germinoma mostly focus on typically located, contrast enhancing lesions and describe high lipid peaks/lactate as main characteristic [2, 7]. Comparable results have been published for basal ganglia germinoma, sharing the main imaging features of low ADC values, contrast enhancement and formation of a tumor mass [8, 9]. To the best of our knowledge there is no published case including MR-spectroscopy in a CNS germinoma showing solely atrophy and T2 hyperintensity. However, in a report by Rossi et al. [9] both the cystic lesion and the adjacent and contralateral T2 hyperintensities were analyzed by $^1$H-MR-spectroscopy. Whereas the cystic lesion mostly contained a high lipid concentration consistent with necrosis, the adjacent region showed markedly increased MI, a slight reduction of NAA, an increase of Cho and near normal Creatine, much resembling our own measurement. As in our report, biopsy of the tissue correlated the metabolic abnormalities with pathologically altered tissue containing tumor cells and the typical inflammatory infiltration. If these distinct pathological features account for a more distinct metabolic profile (e.g. dens inflammatory infiltration accounting for very high MI levels) and if this profile could be distinguishable from differential diagnosis like a diffuse glioma showing a pattern of gliomatosis cerebri [10] can only be hypothesized.

In conclusion our case report shows that even at an early stage and with a lack of typical morphologic tumor features on MRI, diffuse germinoma could potentially show pronounced metabolic abnormalities strongly indicating an active and, in the context, likely neoplastic disease. Excessive MI concentrations might be of additional diagnostic value and could be of interest in further studies. In otherwise uncertain cases additional $^1$H-MR-spectroscopy could be considered, as it might give additional information that could prompt an earlier biopsy.

CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

FUNDING

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ETHICAL APPROVAL

Written and informed consent was obtained. Ethics committee approval was not applicable.

PATIENT CONSENT

The patient gave written and informed consent for the publication of this case report.

GUARANTOR

Eike Steidl.

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