SEPTUM PELLUCIDUM HAMARTOMAS IN NEUROFIBROMATOSIS TYPE 1

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SUMMARY

Septum pellucidum hamartomas have not been reported previously in neurofibromatosis type 1 (NF1). In a retrospective study of 86 cases with NF1 we found three patients with septum pellucidum hamartomas (frequency = 3.4 %). These could be detected on especially fluid attenuated inversion recovery and proton density-weighted images on MRI. With respect to proton spectroscopy in a patient, a low Cho level with a normal NAA peak was found, excluding a neoplasm. MR spectroscopy findings resulted in a very high NAA/Cho ratio (= 2.91), and a low Cho/Cr ratio (= 0.53) compared to a control group of 8 normal age-matched individuals. In this control group, mean NAA/Cho ratio was 1.86, and mean Cho/Cr ratio was 0.78.

Key words : neurofibromatosis, hamartomas, brain, MR studies, neurofibromatosis type 1, proton MR spectroscopy.

INTRODUCTION

Neurofibromatosis has two types; type 1 and type 2. Neurofibromatosis type 1 (NF1) is far more common than neurofibromatosis type 2 (NF2) that more than 90 % of cases belong to this group [1-3]. In the recent literature, new imaging findings in NF1, as well as its associations with different diseases or syndromes have been reported [4-11]. To the best of our knowledge, septum pellucidum hamartomas have not been reported previously in NF1.

SUBJECTS AND METHODS

We recently studied a patient with NF1, and a septum pellucidum hamartoma on a 1.5 Tesla unit. After this, we reviewed the records of previous 5,000 cranial MR imaging examinations in pediatric patients, and noted 86 patients with NF1. (Ages ranged from 3 to 17 years, and there were 47 males and 39 females). We retrospectively studied the MR imaging examinations of these 86 patients with respect to uncommon findings in NF1.

MR imaging examinations were performed by either GE Vectra (General Electric, USA) operating at 0.5 Tesla, or on a 1.5 Tesla MR unit, Magnetom, Vision (Siemens, Erlangen, Germany). In most of the patients MR images were available in two or three orthogonal planes. In the only patient studied on the 1.5 Tesla MR unit, proton MR spectroscopy was also performed. Spectroscopy images were acquired using the single-voxel mode with spin-echo point resolved spectroscopy (PRESS). The volume of interest of the spectroscopic study covered both a right-sided globus
Results

In these 86 cases with NF1, there were three patients with septum pellucidum hamartomas (frequency = 3.4%). In a 15-year-old girl the septum pellucidum hamartoma (approximately 1 cm in diameter) was clearly seen on the FLAIR (fluid attenuated inversion recovery) images as a high-signal lesion (Figure 1a), and no enhancement was noted after administration of contrast medium. MR spectroscopy revealed an apparently decreased Choline (Cho) peak compared to NAA (N-acetyl aspartate) and Creatine (Cr) peaks. This resulted in a very high NAA/Cho ratio (= 2.91), and a low Cho/Cr ratio (= 0.53) compared to the control group (to 8 normal age-matched individuals). In this control group, mean NAA/Cho ratio was 1.86, and mean Cho/Cr ratio was 0.78. On the other hand, the NAA/Cho ratios were similar both in the NF1 patient and in the control group. With respect to the integral values in the hamartoma the following were noted: NAA = 35.41 ; Cr = 21.72, and Cho = 6.21 (Figure 1).

In the other two patients with septum pellucidum hamartomas, a 13-years-old girl, and a 3-years-old girl, respectively, the hamartomas were best appreciated on proton-density weighted images on the 0.5 Tesla unit, and they had high signal (Figures 2a, 3a). Both had an approximately 1 cm diameter, and did not show enhancement after administration of contrast medium (Figures 2b, 2c, 3b, 3c). The 3-years-old girl had, in addition, an enhancing hypothalamic hamartoma.

There were globus pallidus hamartomas in 90% (n = 78) of the 86 NF1 cases including those with septum pellucidum hamartomas.

Discussion

It is known that NF1 is primarily a disease of nerves and astrocytes, and its intracranial manifestations include optic gliomas, astrocytomas and hamartomas. Its incidence is approximately 1 : 2000 - 3000. On the other hand, NF2 is a disease of coverings of the central nervous system, and its intracranial manifestations include schwannomas and meningiomas. Its incidence is approximately 1 : 50,000. The diagnosis of NF1 requires two or more of the following: 1. A first degree relative with NF1 ; 2. Six or more café au lait spots (over 5 mm in diameter) ; 3. Optic glioma ; 4. Two or more pigmented hamartomas of the iris ; 5. Sphenoid dysplasia or cortical thinning of long bone ; 6. Freckling in the axillary or inguinal areas ; and 7. Two or more neurofibromas or plexiform neurofibroma [1-3]. The clinicoradiologic findings of the patients presented in this series met the criteria for NF1. Hamartomas affecting the basal ganglia, globus pallidus in particular, are typical findings in NF1. In this series, we noted globus pallidus hamartomas in 90% of the 86 cases including all the cases with septum pellucidum hamartomas (Figures 1-3).
Associations NF1 with different diseases or syndromes have been reported in the recent literature. These have included tuberous sclerosis [5], Noonan syndrome [6], Watson syndrome [7], Chiari I malformation [8], Alport syndrome [9], and some others [10, 11]. Esl et al. [4], recently described new findings in NF1, and these have included aqueductal web, and asymptomatic enlargement of the septum pellucidum.
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In conclusion, septum pellucidum hamartomas can exist in NF1. These can be picked up on especially FLAIR and proton density weighted images. With respect to proton MR spectroscopy studies, further data is required from future studies. A low Cho level with a normal NAA peak, as noted in our patient, should exclude development of a neoplasm in hamartomas of NF1.

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In our patients, enlargement of the septum pellucidum was apparently due to hamartomas. Their MR imaging characteristics on especially FLAIR and proton density weighted images, were similar to those located in the globi pallidi (figures 1-3), therefore we believe that they can be confidently diagnosed as hamartomas.

Proton MR spectroscopy provides biochemical information about the brain tissue. N-acetyl aspartate (NAA), choline (Cho), creatine (Cr), and myoinositol (mI), and glutamate-glutamine (Glx) are the main metabolites, studied on the spectra. Lactate, amino acids, and lipids are not visible in the normal brain. On MR spectroscopy obtained with any TE value the main metabolites seen are NAA, Cho, and Cr. NAA is exclusively located in neuronal cell bodies and axons, so it is accepted as a neuronal and axonal marker. Cho is a component of phosphoglyceride, and is the main component of the cell membrane. Changes in the Cho peak reflect cell membrane turnover. Cr is an indicator for energy exchange related with high-energy phosphates [12].

In our patient studied by MR spectroscopy an apparently decreased Choline (Cho) peak was noted compared to NAA (N-acetyl aspartate) and Creatine (Cr) peaks. This resulted in a very high NAA/Cho ratio (= 2.91), and a low Cho/Cr ratio (= 0.53) compared to the control group (mean NAA/Cho = 1.86, and Cho/Cr = 0.78). However, previous MR spectroscopy studies on parenchymal hamartomas in NF1 showed either entirely normal findings or increased Cho, reduced Cr, and normal NAA levels [13, 14]. It is known that in disease processes associated with cell membrane breakdown such as tumors, neurodegenerative conditions, and some viral infections the Cho peak tends to increase [12]. In our patient it is not easy to explain Cho decrease, while in the normal NAA peak excludes a neoplasm.

In conclusion, septum pellucidum hamartomas can exist in NF1. These can be picked up on especially FLAIR and proton density weighted images. With respect to proton MR spectroscopy studies, further data is required from future studies. A low Cho level with a normal NAA peak, as noted in our patient, should exclude development of a neoplasm in hamartomas of NF1.