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Disproportionately enlarged subarachnoid-space hydrocephalus (DESH) in normal pressure hydrocephalus misinterpreted as atrophy: autopsy and radiological evidence

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Abstract

Background: Disproportionately enlarged subarachnoid-space hydrocephalus (DESH), a feature of normal pressure hydrocephalus (NPH), is not well known or recognized. It can be misinterpreted as cortical atrophy, suggestive of neurodegenerative disease.

Methods: We report two cases with DESH, the first highlighting autopsy findings and the second the effect of shunting on neuroimaging.

Results: We report a 67-year-old man who presented with clinical features of NPH, but the diagnosis was not considered because radiographic findings were interpreted as cortical atrophy. At autopsy the patient had findings consistent with NPH and no significant neurodegenerative brain disease. The second patient with DESH and NPH underwent shunt surgery. The entrapped

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Author Contributions:

Arthur M. McCarty: drafting of manuscript, acquisition of data

David T. Jones: drafting of manuscript, acquisition of data, analysis and interpretation of data, critical revisions

Dennis W. Dickson: study concept and design, acquisition of data, interpretation of data, critical revisions

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Competing interests:

Arthur M. McCarty and David T. Jones declare no competing interests.

Declarations:

Ethical approval and consent to participate:

Ethical guidelines were followed according to Mayo Clinic policy.

Consent for publication:

Mayo Clinic's policy does not require informed consent for case reports, as general consent is established with the treatment contract. Written consent was received for the autopsy and tissue use for research purposes.

Availability of data and materials:

Individual de-identified participant data will be shared, including neuroradiologic images, gross and microscopic neuropathology images, and redacted medical summaries. The study did not involve a research study protocol or statistical analysis. Data will be made available for a period of not more than 5-years after publication. All reasonable requests for data will be provided upon written request to either Dr. Graff-Radford or Dr. Dickson.

fluid greatly diminished after the surgery, confirming that the cortically entrapped fluid is not atrophy, but due to a CSF dynamic process.

Conclusions: Neurologists should recognize DESH and not misinterpret this as cortical atrophy. Patients with DESH have tight sulci adjacent to the entrapped fluid pockets, distinguishing it from cortical atrophy. 18F-Fluorodeoxyglucose PET can also be used to differentiate DESH from cortical atrophy.

Keywords

Idiopathic normal pressure hydrocephalus; DESH; cerebral atrophy; neuropathology; MRI; FDG PET; Ventriculoperitoneal shunt

Background:

Normal pressure hydrocephalus (NPH) is a late-onset (>65 years) condition characterized by ventricular enlargement disproportionate to the brain volume with normal CSF pressure at lumbar puncture.^{1, 2} Patients have clinical features of gait impairment (slower, wide based and difficulty turning), which then progress to cognitive impairment and/or urinary urgency and then incontinence. Accurate diagnosis is difficult as all the cardinal features have many causes. Given the late-onset of NPH, Alzheimer's disease pathology is a common comorbidity, further complicating NPH diagnosis and treatment.^{3, 4} Recent neuroimaging criteria for diagnosis and management of NPH include disproportionately enlarged subarachnoid-space hydrocephalus (DESH).⁵⁻⁹ Many neurologists involved in diagnosis and care of patients with NPH do not recognize this radiological feature of NPH and interpret the radiological finding as comorbid cortical atrophy. To illustrate this problem, we present two cases, one misdiagnosed and not treated for NPH, who at autopsy had neuropathologic features consistent with NPH without significant degeneration. The second patient was recognized clinically, treated with ventriculoperitoneal shunting and had a good response, including significant improvement of DESH. The purpose of this report is to help clinicians recognize DESH and better manage NPH.

Methods:

The patient in case 1 had written consent provided by family for the autopsy and use of the tissue for research purposes. Informed consent was not required from the patient in case 2 according to Mayo Clinic policy, as general consent for case report presentation is established with the treatment contract.

Results:

Case 1:

This 67-year-old man presented for neurological evaluation 3 years before he died. He sought assistance with gait and balance difficulties that began about 10 years before his death. He had a wide-based gait, which progressively worsened, leaving him wheelchair bound in the end. On initial evaluation, he had difficulty standing, could not perform tandem gait, and looked stiff when he walked. He was unaware of cognitive difficulties but in

retrospect noted “slipping” for a few years. He was alert and oriented but had memory loss, visuospatial difficulties, and no problems with personality or mood. He scored 16/30 on the Montreal Cognitive Assessment, with points lost for trails, clock drawing, language, and memory. During the disease course, he developed urinary incontinence. His past medical history was notable for rheumatoid arthritis affecting feet and spine, and he was treated with methotrexate and Tocacitinib.

MRI revealed ventriculomegaly, with an Evan’s index of 0.35 (Figure 1A). Sulcal dilation was observed on the medial frontal surface and superior parietal lobe (Figure 1A, B), which was interpreted as cortical atrophy. Tight sulci at the convexity of the posterior parietal and occipital lobes were present (Figure 1B). MRI of the spine revealed stenosis at the boundary of L4 and L5, but the spinal cord was unaffected.

At autopsy, gross examination revealed no cortical atrophy, but dilated sulci were notable in the dorsolateral frontal and superior parietal lobule (Figure 2A). The dorsal leptomeninges had patchy dense fibrous thickening, consistent with arachnoid fibrosis (Figure 2A, B). The medial temporal lobe had no significant atrophy (Figure 2B). Coronal sections of the supratentorial structures revealed marked enlargement of the frontal horn of the lateral ventricle and no hippocampal atrophy (Figure 2C).

Microscopic studies revealed features consistent with NPH, including arachnoid fibrosis on trichrome stain (Figure 2D, E) and ependymal denudation with glial overgrowth (Figure 2F, G). There were no Lewy bodies or senile plaques and only a few neurofibrillary tangles consistent with primary age-related tauopathy. There was also mild age-related tau astrogliaopathy. The substantia nigra, locus ceruleus, and hippocampus had normal neuronal populations.

Case 2:

This 76-year-old man with a past medical history of prostate cancer (status post prostatectomy), congenital lumbar stenosis (status post decompressive laminectomies), and glaucoma was seen for a progressive cognitive and gait syndrome. He reported 2 years of gait unsteadiness and began having falls with increasing frequency. Additionally, his family noticed impairment in his memory. All of his activities of daily living were intact. He endorsed urinary urgency without incontinence. There were no reports of acting out dreams or apneic events while sleeping. He denied tremors, delusions, illusions, hallucinations, and changes in personality.

On physical examination he was fully oriented, without evidence of dysarthria or aphasia. He scored 31/38 on the Kokmen short test of mental status, missing 2 points for attention, 2 points for learning, 2 points for construction, and 1 for recall. He was found to have a wide-based gait with impaired tandem walk and difficulty turning. His cranial nerves were intact, and he had normal muscle strength, bulk, and tone throughout. No pathologic reflexes were observed.

Brain MRI revealed confluent periventricular T2 hyperintensities, ventriculomegaly, increased CSF in the subarachnoid space predominantly in the Sylvian fissure and connected

sulci, and mild effacement of the sulci at the vertex consistent with a DESH pattern. The extra-ventricular CSF was interpreted as representing global atrophy (Figure 3A); however, a 18F-fluorodeoxyglucose (FDG) PET scan of the brain revealed normal metabolism throughout the cerebral cortex and a partial volume confound in the Sylvian fissure and connected sulci related to the increased CSF content (Figure 3B). Balance, walking speed, and turning improved after a large volume lumbar puncture (30 ml). Given these clinical and imaging findings, the likelihood of a coexisting neurodegenerative disease was low. Therefore, it was suspected that the clinical syndrome and atrophic appearance of the cerebral cortex would improve with a ventriculoperitoneal shunting procedure. The patient was diagnosed with NPH and underwent shunt surgery. There was a resolution of the gait abnormality and improvement in cognition and in postoperative neuroimaging three months after the procedure (compare Figures 3C and 3D). Specifically the fluid spaces preoperatively decreased substantially.

Discussion:

The first case is a patient who presented with the triad of symptoms and MRI features consistent with NPH; however, due to the extra-ventricular fluid spaces, degenerative dementia was suggested, and he was not further evaluated for NPH. Autopsy findings supported NPH and not degenerative dementia. Distinguishing clinical factors for NPH included the ten year history of gait impairment preceding cognitive difficulty and urinary incontinence. In retrospect, antemortem imaging studies were consistent with DESH. The entrapped fluid leading to tight sulci in other areas was not recognized. Combined with the clinical signs, DESH appears to be an imaging biomarker for NPH and aids in predicting shunt response.⁵⁻⁹

The second case illustrates a patient with NPH and DESH that greatly diminished after ventriculoperitoneal shunting. The presumed “atrophy” (the fluid spaces) is actually related to the CSF dynamics and flow in NPH. The second case also demonstrates the usefulness of FDG-PET in differential diagnosis. The PET study showed artefactual hypometabolism in the Sylvian fissure (enlarged by fluid) secondary to a partial volume effect, while metabolism in the brain was normal, supporting the conclusion that the patient did not have a concomitant degenerative disease. Differentiating DESH-related imaging findings from cortical atrophy with enlarged subarachnoid spaces can be difficult in some cases, and the presence of DESH does not preclude the co-occurrence of a neurodegenerative disease that affects shunt response. In such a setting, FDG-PET may reveal cortical hypometabolism if the atrophic imaging appearance is secondary to a neurodegenerative disease. In contrast, FDG-PET will be normal if it is related only to CSF dynamics. Therefore, as our second case illustrates (Figure 3), normal cortical metabolism in the setting of an MRI appearance of global atrophy within the clinical context of NPH symptoms is good supporting evidence that a co-existing neurodegenerative disease is not present and may indicate a positive surgical outcome.¹⁰

Conclusion:

Despite the strong evidence supporting DESH as a feature of NPH, many neurologists still do not recognize DESH. Our findings substantiate the importance of discerning DESH on neuroimaging and avoiding the erroneous diagnosis of degenerative disease when only DESH is present. Neurologists should recognize DESH and not misinterpret this as cortical atrophy. Patients with DESH have tight sulci adjacent to the entrapped fluid pockets, distinguishing it from cortical atrophy. Furthermore, we demonstrate how 18F-Fluorodeoxyglucose PET can be used to differentiate DESH from cortical atrophy.

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Figure 1.

Case 1: DESH misinterpreted as cortical atrophy. (A) Axial FLAIR MRI demonstrating ventriculomegaly (Evan's index of 0.35) and sulcal dilation. Lines indicate the measurements for Evan's index – the maximum width of the frontal horns of the lateral ventricles divided by the maximum diameter of the inner skull wall at that same level (> 0.30 is considered ventriculomegaly). (B) Post-contrast coronal FLAIR MRI demonstrating ventriculomegaly, sulcal dilation ("atrophy") and tightening in the posterior convexity.

Figure 2.

Case 1: Neuropathological findings consistent with NPH. (A) Macroscopic findings reveal focal arachnoid fibrosis and sulcal dilation, but no gyral atrophy. (B) Medial view shows dilation of parieto-occipital fissure and ventriculomegaly, but no gyral atrophy. (C) Coronal sections at two levels show marked dilation of the frontal horn of the lateral ventricle and no hippocampal atrophy. (D & E) Collagen deposition (blue) in the leptomeninges on a trichrome stain. (F & G) There is loss of ependymal cells and glial overgrowth in the lining of the frontal horn of the lateral ventricle on routine histologic stains (H&E) and with Luxol fast blue with periodic acid Schiff (LFB-PAS) stain.

Figure 3.

Case 2. Radiographic findings consistent with NPH. (A) Orthogonal slices of the baseline T1 MRI demonstrating ventriculomegaly, tight high convexity, increased CSF content in the Sylvian fissures and connected sulci producing a “global atrophy” appearance to the cortex. (B) The baseline FDG-PET image formatted with the CortexID software program (GE Healthcare) demonstrating normal cortical metabolism and partial volume confound from the CSF in the Sylvian fissures and connected sulci producing artefactual hypometabolism in these anatomic regions (red and yellow areas). (C) Pre-surgical coronal head CT co-registered to the (D) post-surgical head CT demonstrating a reduction in the extraventricular CSF content in the Sylvian fissures and connected sulci (orange arrows).