Delayed appearance of wing-beating tremor after liver transplantation in a patient with Wilson disease

Joong-Seok Kim, Su-Young Kim, Jong-Young Choi, Hee-Tae Kim, Yoon-Sang Oh

1. Introduction
Orthotopic liver transplantation (OLT) is the sole etiological treatment for Wilson disease (WD), but the efficacy of transplantation in improving the neurological symptoms of WD is still debated [1]. Several neurological symptoms after OLT have been reported; most are related to immunosuppressive therapy and the remainder are acute neurological symptoms such as dystonia subsequent to surgery [2,3]. Only a few patients have been reported with new extrapyramidal symptoms [3]. We present a 45-year-old WD patient who developed a wing-beating tremor 6 years after OLT.

2. Case report
A 45-year-old woman was referred to our Movement Disorders Clinic for evaluation of a 3 month history of left arm tremor when holding a cup. She was diagnosed with a hepatic form of WD 8 years previously [genetically confirmed recently by ATP7B gene mutations in c.[2200G>T]+[3443T>C] [p.[V734F]+[I1148T]], and she had undergone OLT 6 years prior to this presentation. Her diagnosis at that time was made on the basis of biopsy-proven cirrhosis, low ceruloplasmin level, increased urinary copper excretion and presence of corneal Kayser-Fleischer ring. Prior medical records before OLT revealed no tremor, bradykinesia, dysarthria, or gait disturbance. The patient also underwent removal of a left parotid cancer 5 years ago and, thereafter, a left facial palsy and left hemifacial spasm developed and remained. The patient was on immunosuppressive therapy with cyclosporine; however, the plasma level was undetectable because of her compliance. Her younger brother had died 10 years previously due to acute hepatic failure from WD and her elder sister (patient’s donor) had been treated for 2 years for major depression without a confirmed diagnosis. No resting tremor, bradykinesia, dystonia, or gait disturbance was observed (Supp. Video 1).

Biochemical examination of copper metabolism parameters were performed, showing a low serum ceruloplasmin of 14 mg/dl (laboratory norm, 16–60 mg/dl), normal serum copper of 84.14 μg/dl (laboratory norm, 64.0–134.0 μg/dl), and a mild increase in copper excretion in urine of 76.82 μg/day (laboratory norm, 0–50 μg/day). An ophthalmologic examination revealed persistent Kayser-Fleischer rings bilaterally. A penicillamine (PCN) challenge test was performed after loading with 1500 mg PCN which showed a borderline increase in copper excretion in urine of 414.09 μg/day.

MRI of the brain, including diffusion-weighted images, did not show any definite abnormalities. Additionally, positron emission tomography using 18F-N-(3-fluoropropyl)-2beta-carbon ethoxy-3beta-(4-iodophenyl) nortropine also showed no abnormalities.

A liver biopsy was performed to confirm disease status and was compared with pre-OLT specimens and the donor using hematoxylin and eosin (H&E) and rhodanine staining. The pre-OLT specimen showed cirrhotic changes on H&E staining (Fig. 1A) and a marked positive reaction to copper in the rhodanine-stained specimen (Fig. 1B). In contrast, that of the donor showed mild leukocyte infiltration, which was probably due to surgical stress (Fig. 1C) and a very mild degree of copper reactivity (Fig. 1D). The specimen obtained after the new neurological symptoms appeared showed a very mild cirrhotic change (Fig. 1E) and mild to moderate copper positivity (Fig. 1F).

3. Discussion
This patient’s history was very intriguing. The patient’s donor was her elder sister. Because of the donor’s unconfirmed WD diagnosis and as the patient suffered from a newly developed tremor, we firstly inferred that her symptoms were caused by a recurrence of WD, although the transplanted liver was free of genetic defects responsible for WD [4]. The patient did exhibit persistent Kayser-Fleischer rings, and liver biopsy performed after the patient presented with neurological symptoms showed mild to moderate copper positivity, suggestive of copper accumulation. However, 24-hour urinary copper excretion and PCN challenge test results did not support WD recurrence [5]. Another possibility is that the
development of neurological symptoms in our patient represents a
delayed manifestation, resulting from the initial hepatic disease.

Nearly 100% of patients with neurologic WD are reported to
have Kayser-Fleischer rings [6]. The patient’s relative late age of
onset of symptoms (diagnosed at age 37) may explain why tremor
onset was also so delayed.

Tremor in one or both hands is one of the most common initial
symptoms of WD. One of the characteristic components is
proximal tremor activity with a wing-beating quality [4].

However, several reports have indicated that this type of tremor
is associated with other structural and metabolic lesions [7,8].
Furthermore, the development of mild cirrhotic changes and mild
copper accumulation in the liver can influence these neurological
symptoms. Finally, we should consider other naturally occurring
diseases such as an essential tremor or drug-induced tremors,
including that induced by cyclosporine.

In summary, we report, to our knowledge, the first patient with
delayed appearance of extrapyramidal symptoms after OLT in WD
for which the pathophysiology is still unknown.

Conflicts of Interest/Disclosures

The authors declare that they have no financial or other
conflicts of interest in relation to this research and its publication.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in
the online version, at http://dx.doi.org/10.1016/j.jocn.2013.10.036.

References

in pediatric patients with the hepatic form of Wilson’s disease. J Child Neurol
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Fig. 1. The patient’s pre-orthotopic liver transplantation liver specimen showed marked cirrhotic changes on hematoxylin and eosin staining (A; original magnification × 100) and marked reactivity to copper on rhodamine staining (B; original magnification × 400). That of the donor showed mild leukocyte infiltrations, which were probably due to surgical stress (C; original magnification × 100) and a very mild degree of copper reactivity (D; original magnification × 400). Finally, a specimen obtained from the
patient’s donor liver after the new neurological symptoms appeared showed a mild cirrhotic change (E; original magnification × 100) and mild to moderate copper positivity (F; original magnification × 400).
Ventriculoperitoneal shunt infection following uterine instrumentation for dysfunctional uterine bleeding

Andrew B. Shaw*, Evan S. Marlin, Daniel S. Ikeda, Mario Ammirati

Wexner Medical Center, Department of Neurological Surgery, Ohio State University, 410 W 10th Avenue, 1014 N Doan Hall, Columbus, OH 43210, USA

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ABSTRACT

Shunt infections are most common within the first 6 months following implantation. A shunt infection 19 years after implantation secondary to uterine ablation has not been reported to our knowledge. Office hysteroscopic procedures have become commonplace in gynecologic practice. Infectious complication rates are low, but peritonitis has been described. We present a patient with a ventriculoperitoneal shunt infection following a uterine ablation for dysfunctional uterine bleeding. Three days following the ablation she developed abdominal pain. CT scan of the abdomen 5 months after the procedure revealed a pseudocyst. She then underwent removal of her shunt with intra-operative cultures revealing Streptococcus agalactiae. Definitive treatment consisted of shunt explantation and antibiotic treatment with complete resolution of her pain and pseudocyst. Consideration for prophylactic antibiotics should be made when a patient with a ventriculoperitoneal shunt undergoes any transvaginal procedure.

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1. Introduction

Uterine ablation via hysteroscopy is widely accepted for the treatment of dysfunctional uterine bleeding. Advances in sterilization, technique, and equipment have made ambulatory hysteroscopic procedures safe with rare complications such as uterine perforation and infection [1]. The infectious complication rates are so low that the American College of Obstetricians and Gynecologists do not recommend the use of routine prophylactic antibiotics in hysteroscopic surgery [2].

Yet there are specific groups at higher risk for unusual complications including polymicrobial peritonitis as seen in patients receiving dialysis. Here we report to our knowledge the first Group B Streptococcus agalactiae ventriculoperitoneal shunt infection secondary to a hysteroscopic procedure. Shunt infections carry significant morbidity with potential for meningitis, prolonged hospitalization, and multiple surgeries. Streptococcus agalactiae shunt infections have been documented following caesarean section in colonized mothers and dialysis patients [3,4].

2. Case report

A 35-year-old woman with a history of a ventriculoperitoneal shunt placed as a child for congenital hydrocephalus presented to our hospital with chronic abdominal pain. She had one revision of her shunt system in her lifetime at 16 years of age. At the age of 35 she developed dysfunctional uterine bleeding that resulted in treatment with hysteroscopic uterine ablation. The procedure was uncomplicated. Three days following the procedure she developed right upper and lower quadrant abdominal pain. She was seen several times in the emergency department without a diagnosis. She underwent abdominal imaging that was unremarkable. Her ventricular catheter was challenged and found to be poorly functioning. The intra-operative cultures from pseudocyst fluid. Intra-operatively, the ventricular catheter was suspected. She was then taken to the operating room for removal of her shunt. Intra-operative cultures were taken from the shunt catheters, valve, proximal cerebrospinal fluid, and distal abdominal pseudocyst fluid. Intra-operatively, the ventricular catheter was found to be poorly functioning. The intra-operative cultures from the pseudocyst revealed Group B Streptococcus agalactiae. Ultimately, she was discharged on ertapenem. Given the long history without shunt revision and the possibility of a poorly functioning system, her ventricular catheter was challenged and removed. At follow-up, her abdominal pain and pseudocyst had resolved (Fig. 1C). Clinically and radiographically there were no signs of hydrocephalus without cerebrospinal fluid diversion.

3. Discussion

Typically, shunt infections are detected in the first 6 months following insertion [5]. They can happen remotely in the setting...