Lhermitte-Duclos Disease (Dysplastic Gangliocytoma of the Cerebellum) and Cowden Syndrome: Clinical Experience From a Single Institution with Long-Term Follow-Up

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BACKGROUND: **Adult-onset Lhermitte-Duclos disease (LDD) and Cowden syndrome (CS) are considered a single phakomatosis that belongs to PTEN hamartoma tumor syndrome (PHTS) now. There is still controversy regarding the diagnosis and treatment. The authors describe the clinical features of LDD and CS with long-term follow up.**

METHODS: **From January 2001 to January 2017, 18 patients were admitted to the neurosurgery department of Beijing Tiantan Hospital. The authors analyzed the medical records of each patient and followed every case.**

RESULTS: **Seventeen of 18 patients underwent surgery to remove the tumor. The results of pathologic analysis revealed LDD. There was obvious enhancement on magnetic resonance imaging (MRI) in 2 patients who received gamma knife and radiotherapy before surgery. During surgery, it is difficult to determine the exact margin. Tumors were removed gross totally in 9 patients, partially in 6 patients, and only subtotally in 2 patients. CS was diagnosed in 11 patients. Two patients received DNA analysis, revealing heterozygous mutation of exon 5 in an 11-year-old girl. There was no recurrence of the tumor during follow-up.**

CONCLUSIONS: **LDD has the unique appearance on T2-weighted MRI. The most difficult aspect of surgery is determining the actual margins of the tumor. Total resection is difficult in some patients. There was no tumor recurrence after long-term follow-up in our case series. For pediatric LDD patients, DNA analysis should be performed to rule out CS.**

INTRODUCTION

Lhermitte-Duclos disease (LDD; dysplastic gangliocytoma of the cerebellum) is a rare hamartoma of the cerebellum with a unique "tiger-stripe" appearance on magnetic resonance imaging (MRI).[1,2] Cowden syndrome (CS) is an autosomal dominant, hereditary, multisystem disease involving hamartomatous overgrowth of tissues of all embryonic layers. It mainly affects the breast, thyroid, uterus, and skin. Since 1991, LDD has been considered part of CS.[3] *PTEN* is known as a tumor suppressor gene, and the mutation of this gene has been shown in multiple cancer types. Almost all adult-onset LDD cases were associated with *PTEN* gene mutations.[4,5] Nowadays, LDD and CS are included in PTEN hamartoma tumor syndrome (PHTS).[4-9]

Since its first description by Lhermitte and Duclos in 1920,[10] more than 200 cases have been reported in the literature.[11,12] Because of the rarity of this disease, there is currently controversy regarding LDD and CS diagnosis and management. Therefore, in this study, we discuss the relationship between these two diseases and provide a summary of the patient diagnosis and management.

MATERIALS AND METHODS

This study was approved by the Ethics Committee of Beijing Tiantan Hospital, Capital Medical University. Informed consent was obtained from all participants or their parent or legal

Key words
- Cowden syndrome
- Dysplastic gangliocytoma of the cerebellum
- Lhermitte-Duclos disease
- PTEN Hamartoma Tumor Syndrome
- Rapamycin

Abbreviations and Acronyms
CS: Cowden syndrome
CT: Computed tomography
LDD: Lhermitte-Duclos disease
MRI: Magnetic resonance imaging
PHTS: PTEN hamartoma tumor syndrome

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Citation: World Neurosurg. (2017) 104:398-406.
http://dx.doi.org/10.1016/j.wneu.2017.04.147

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

Table 1. Patient Characteristics

Patient Number	Age (years)	Sex	Location	Neurologic Manifestations	Other Disease	Diagnosis of CS	Resection Degree	Follow-Up (months)
1	26	Female	Right cerebellum	Dizziness, gait disturbance	Facial lesions, acral keratoses, thyroid goiter, hepatic angiomas	Yes	No surgery	180
2	46	Female	Left cerebellum	Gait disturbance	Facial lesions, acral keratoses, thyroid goiter, endometrial cancer, hepatic angiomas	Yes	Subtotal	24
3	47	Female	Right cerebellum	Seizure	Meningioma, arteriovenous fistula, astrocytoma, breast adenoma, uterine fibroids, endometrial cancer, acral keratoses	Yes	GTR	24
4	34	Female	Left cerebellum	Dizziness, headache	Lipoma, fibrocystic disease of the breast	Yes	GTR	117
5	39	Female	Right cerebellum	Headache, gait disturbance	Thyroid goiter, oral papillomatosis, angioma, fibrocystic disease of the breast, gastric polyps, facial cutaneous lesions	Yes	GTR	93
6	2	Female	Right cerebellum	Seizure	None	No	GTR	83
7	40	Female	Right cerebellum	Dizziness, gait disturbance	Facial lesions, acral keratoses, oral papillomatosis, breast fibroma	Yes	Partial	69
8	11	Female	Left cerebellum	Headache, gait disturbance	Facial lesions, acral keratoses, thyroid goiter, ganglioglioma	Yes	Partial	51
9	27	Male	Right cerebellum	Dizziness	None	No	Partial	52
10	52	Female	Right cerebellum	Gait disturbance	Thyroid adenoma; breast fibroma; lipoma	Yes	Total	6
11	50	Male	Left cerebellum	Headache, gait disturbance	None	No	Partial	12
12	44	Female	Right cerebellum	Dizziness	None	No	GTR	18
13	45	Male	Right cerebellum	Headache	Facial lesions, thyroid nodule, lipoma	Yes	GTR	109
14	61	Female	Right cerebellum	Dizziness	Thyroid nodule, breast fibroma, fibroma	Yes	Subtotal	25
15	33	Male	Right cerebellum	Headache	None	No	Partial	22
16	52	Female	Cerebellar tonsil	Headache, dizziness	Thyroid goiter, endometrial cancer	Yes	GTR	20
17	52	Male	Right cerebellum	Headache, dizziness, gait disturbance	None	No	Partial	6
18	56	Male	Cerebellar tonsil	Headache, dizziness	None	No	GTR	52

GTR, gross total resection.

guardian. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. Between January 2001 and January 2017, 18 patients with LDD were admitted to Beijing Tiantan Hospital. Seventeen patients underwent surgery to remove the cerebellar tumor, with the exception of 1 patient who received only a ventriculoperitoneal shunt. Pathologic specimens showed dysplastic gangliocytoma of the cerebellum in all 17 patients. The degree of resection was determined by MRI performed no more than 1 week postoperatively. We followed all the patients and reviewed the medical records, neuroimaging, and other available information. Patients received examinations in local hospitals according to our suggestions, including skin examinations and ultrasonic scanning of the thyroid gland and uterus, among other tests. Gastroscopy was only performed in 1 patient. CS was