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Lhermitte-Duclos disease: Clinical study with long-term follow-up in a single institution

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ABSTRACT

Objective: LDD is a rare lesion, controversy about diagnosis and treatment of LDD and CS still exists. We aimed to clarify clinical and radiological characteristics, the optimal treatment timing and strategies of LDD with long-term follow-up.

Patients and methods: From January 2004 to May 2017, 12 LDD patients were enrolled in our study. The clinical and radiological features, treatment strategies and long-term follow-up data were retrospectively analyzed.

Results: The mean follow-up was 89.1 ± 36.9 months (range, 31–161months). Twelve patients (7 males and 5 females, mean age 28.0 ± 14.8 years, range 3–55 years) were included in this study. The most frequent symptoms were those related to increased intracranial pressure. Mean duration of symptoms was 15.6 ± 9.5 months. Average tumor size was 62 ± 9.3 mm in its maximal diameter (range, 50–84 mm). Tonsillar herniation and preoperative hydrocephalus were observed in 9/12 and 12/12 patients. Four of them confirmed the diagnosis of CS. Gross total resection were achieved in 3 patients, partial in 6 patients and subtotal in 3 patients. All patients experienced improvement of symptoms. Recurrence and progression were identified in only 1/12 patient.

Conclusions: LDD has pathognomonic appearance on T2-weighted MRI. We recommend surgery decision should be based on symptoms appearance or progress in imaging. Total resection is difficult due to the indistinct tumor margin, favorable outcome and rare recurrence were also observed despite of partial or subtotal resection in our series. A long-term screening for Cowden's disease and tumor recurrence is essential for every patient.

1. Introduction

Lhermitte-Duclos disease or dysplastic gangliocytomas of the cerebellum was first documented as a rare cerebellum entity in 1920 [1]. Although LDD has been considered having close association with CS since 1991 [2], and has been included in PTEN hamartoma tumor syndrome (PHTS) now, a spectrum of disorders caused by phosphatase and tensin homolog (PTEN) gene mutations [3], the frequency of CS in LDD patients is still unclear. LDD can frequently get a definitive preoperative diagnosis on MRI [4–6], however, the optimum time of surgical intervention is still a matter of debate.

Complete resection of the lesion is currently considered as the optimum therapeutic procedure, but due to the indistinct tumor boundary, gross total resection is especially difficult to follow, subtotal or partial resection is ordinary in the literature [1,7,8], however, rare reports studied long-term prognosis.

Since Lhermitte-Duclos disease is a rare disorder, most studies are case reports concerning radiological features; rare systematic studies and literature data from single institution focusing on treatment strategy and long-term follow-up were depicted. Therefore, we analyzed clinical and radiological features, associations with CS, management and long-term follow-up of this rare entity.

2. Materials and methods

We retrospectively analyzed 12 cases of Lhermitte-Duclos disease treated from 2004 to 2017. Medical records including clinical and neuroimaging features, diagnosis, treatment and outcome of these patients were obtained. Data including patient age, gender, symptoms and duration of symptoms prior diagnosis were analyzed. All the patients underwent cranial gd-enhanced magnetic resonance imaging (MRI) scan and magnetic resonance spectrophy (MRS). The locations and size of the tumors, presence of hydrocephalus were recorded. The PTEN/MMAC1 mutation was examined in five patients. The extent of

Abbreviations: LDD, Lhermitte-Duclos disease; CS, Cowden Syndrome; PHTS, PTEN hamartoma tumor syndrome; PTEN, Phosphatase and tensin homolog; MRI, Magnetic resonance imaging; MRS, Magnetic resonance spectrophy; KPS, Karnofsky performance score; PTHC, Pseudotumoral hemicerebellitis; CVST, Cerebral venous sinus thrombosis

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Table 1
Summary of clinical characteristics in 12 LDD patients.

Case (No)	Gender	Age (yrs)	Duration (mos)	Symptoms & Signs	PTEN mutation	Other diseases	Diagnosis of CS
1	F	18	2	Dizziness, ataxia	Y	Lipoma, acral keratoses, facial lesions, hepatic angiomas	Y
2	M	18	36	Headache, ataxia, visual disturbance	Y	Facial trichilemmomas, acral keratoses	Y
3	F	16	24	Dizziness, gait and visual disturbance	N	Thyroid nodule, lipomas, fibromas	Y
4	F	40	15	Dizziness, gait disturbance	NA	N	N
5	F	55	5	Bilateral orbital paroxysma	NA	N	N
6	F	3	16	Gait disturbance	N	N	N
7	F	26	6	Headache, vomiting	NA	N	N
8	M	38	24	Headache	NA	N	N
9	F	51	24	Headache, dizziness	N	N	N
10	M	19	3	Headache, vomiting	NA	N	N
11	M	19	15	Headache	NA	N	N
12	M	33	18	Headache, vomiting	NA	Thyroid goiter, fibrocystic disease of the breast, gastrointestinal polyps	Y

M: male, F: Female, Y: yes, N: no, NA: Not received.

operation was based on postsurgical MRI and was defined as follows: gross total resection was defined as 100% macroscopic resection, subtotal resection was defined as < 100% but > 50%, and partial resection was demonstrated as < 50%. The follow-up was performed at 3 months after surgery and once a year thereafter. During the follow-up period, changes in neurological deficits (improved, stable or aggravated), karnofsky performance score (KPS) and MRI were assessed in outpatient center. The residual tumor and tumor recurrence were recorded.

3. Results

3.1. Clinical features

From January 2004 to May 2017, twelve patients suffered from LDD underwent surgical treatment in our department. The clinical features of these patients were summarized in Table 1. There were 7 males and 5 females with mean age of 28 years (ranging from 3 to 55 years old). Symptoms of intracranial hypertension were observed in 7 patients. Other symptoms and signs included cerebellar dysfunction (n = 3), visual disturbance (n = 2), dizziness (n = 4), bilateral orbital paroxysma (n = 1). The duration of symptoms prior diagnosis varied from 1/10 to 36 months (mean duration = 15.4 months). After admission, a screening for Cowden's disease was applied in every patient with important markers such as skin, thyroid, colonic, breast, ovarian and endometrial lesions.

3.2. Radiological features

The radiological findings were listed in Table 2. All the lesions were located in the unilateral cerebellar hemisphere and the size of tumors ranged from 5 to 8.4 cm with a mean size of 6.25 cm. In MRI, the lesions frequently showed hypo- to isointense on T1-weighted images and hyperintense on T2-weighted images with typical ill-defined "parallel linear striations" appearance which was also called tiger stripping sign (Figs. 1, 3–5). After administration of gadolinium, case 6 depicted obvious diffuse enhancement (Fig.2). Every patient in our series experienced preoperative hydrocephalus and tonsillar herniation was observed in 9 patients.

3.3. Surgical management

All the patients underwent surgery via suboccipital approach. Gross total resection was achieved in 3 patients, partial in 6 patients and subtotal in 3 patients. One patient achieved an emergency external ventricular drainage operation due to the acute hydrocephalus.

3.4. Histological analysis

Histopathological examination revealed disarrangement of the normal cerebellar laminar cytoarchitecture and enlargement of cerebellar folia, and the widen layer was composed of abnormally hypertrophic ganglion cells. Furthermore, myelination of abnormal molecular layer was also depicted. No distinct pathological characteristic was found in sporadic LDD or LDD associated with CS.

3.5. Complications and prognosis

After tumor resection, preoperative presenting symptoms improved in all patients. Postoperative complications are rare while cerebellar mutism was founded in a patient who achieved extensive resection. Cerebellar mutism was transient and recovered spontaneously in 3 months. After a mean follow-up of 89.1 ± 36.9 months (range from 2.5 to 13.4 years), one patient experienced tumor recurrence four years after the initial surgery and then an observation therapy was performed until symptoms appearance. 4/12 patients were diagnosed as CS according to the International Cowden Consortium operational criteria [9] in the long-term follow-up. The other patients recovered well and remained recurrence-free.

4. Discussion

In 1920, Lhermitte and Duclos reported the first patient with dysplastic gangliocytoma (Lhermitte-Duclos disease), a rare tumor located in the posterior fossa classified as WHO grade I [1]. Although more than 220 cases have been reported in the English literature [10], due to its rarity, there remains controversy regarding diagnosis and management of LDD and CS. Furthermore, as most of the lesions are case reports, datas focusing on long-term follow-up in a single institution are rare. In our study, we retrospectively analyzed 12 LDD patients in order to emphasize long-term prognosis, optimize the treatment and elaborate the essence of this disease.

4.1. Clinical features

Investigators have described LDD preferentially occurs in young adults, majority in the third or fourth decade, but the onset age ranges from neonatal period to 74 years old, with no gender predilection [7,11]. In our series, there were 7 males and 5 females, with a mean age of 28.0 ± 14.8 years, range 3–55 years, which was consistent with