Palliative Epilepsy Surgery in Dravet Syndrome

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Introduction

Dravet syndrome (DS), also known as severe myoclonic epilepsy of infancy, is a rare syndrome carrying a poor prognosis. DS results from mutations of the neuronal sodium ion channel gene SCN1A. DS presents at around 1 year of age with seizures that are often associated with fevers. As patients age, seizures occur without fevers and multiple seizure types develop. There are few reports and no guidelines regarding surgical treatment for DS. Here, we present our institution's experience with surgical treatment of DS which is the largest published to date.

Methods

We conducted a retrospective review of all patients with genetically confirmed DS who underwent either vagal nerve stimulator (VNS) implantation or corpus callosotomy (CC) from August 1999 to January 2014 at our institution. All inpatient and outpatient relevant documentation was reviewed. Demographic information, SCN1A mutation, operation performed, and preoperative and postoperative seizure frequency were recorded. Inclusion criteria required 1 year postoperative follow up.

Results

Eleven surgeries were performed on eight patients during the study period. Five VNS and three CC were performed in eight patients that met inclusion criteria. At least one year elapsed from presentation to our hospital and surgery for all patients. Average time to surgery was 4.3 years. The mean age of patients undergoing CC was 8.4 years compared to 6.0 years for those undergoing VNS implantation. Seizures were decreased in all patients after each procedure and CC was more effective than VNS for seizure control.

Table 1 - Patient Demographics

Patient Number	Sex	Age at first seizure	SCN1A Mutation	Age at presentation	Age at surgery
1	M	6 months	SCN1A deletion	2 years	7
2	F	10 months	SCN1A 2794 T>C	10 months	4
3	F	9 months	SCN1A 1bp deletion	7 years	9
4	M	unknown	SCN1A 2657 C>T	unavailable	11
5	M	2 years	SCN1A (2 mutations, both shared with a parent)	5 years	6
6	M	3 months	SCN1A 5347 G>A	8 years	14
7	M	4 months	SCN1A 3429 G>A	9 months	7
8	M	2 months	SCN1A 1186 G>T	7 months	4 (VNS), 4 (CC)

Table 2 - Seizure Outcomes

Patient Number	Preop Seizure Frequency	Seizure Type	Procedure	Duration of F/U	Improvement with Surgery
1	weekley to monthly	complex partial with secondary generalization	VNS	17 months	Yes
2	100's of myoclinic seizures per month, monthly tonic seizures	myoclonic jerks, complex partial seizures	VNS	16 months	Minimal
3	monthly nighttime seizures	gen tonic-clonic	VNS	15 years	Minimal
4	unknown	drop attacks, GTC, myocloinc, complx partial, absence	VNS,callosotomy (x2)	lost to followup	Unknown
5	up to 50 per day	drop attacks	callosotomy	7 years	Yes
6	10-12 per day, not every day	GTC and staring spells	VNS,callosotomy	11 months	Yes
7	1 per week	GTC with occasional SE	callosotomy	50 months	Yes
8	100+ day prior to callosotomy	absence, myoclonic, GTC, simple partial	VNS, callosotomy	1 month	Yes

Representative Case

This is a male patient who presented to the neurosurgery service at 5 years of age. He had been having seizures since 2 years of age and at the time of presentation to our clinic was taking keppra, lamictal, and ethosuximide with inadequate seizure control. His seizures consisted of over 50 myoclonic seizures a day as well as drop attacks. He had significant developmental delay and was non-verbal. He underwent complete CC without complications. Two weeks after surgery, at his first neurosurgical follow-up, his myoclonic seizures were markedly diminished and he was experiencing no drop attacks. Six months after surgery, he was able to have his antiepileptics weaned, but not discontinued. One year after surgery, he was still free form drop attacks but had made no further progress with reduction of seizure frequency or weaning of medication. At this time, his family was presented with the option of addition of VNS therapy but did not wish to proceed. At last follow-up, 7 years after his surgery, he is free of drop attacks but still has daily myoclonic seizures. He has not been able to discontinue any of his antiepileptics. He has progressed developmentally but remains non-verbal.

Conclusions

Both VNS and CC in patients with DS can be effective at reducing seizure frequency and improving quality of life. Patients with DS may benefit from earlier and more aggressive surgical intervention. Further studies will help determine the optimal time and type of surgical intervention. Seizure reporting methods should be standardized to provide better assessment of treatments, especially in severe seizure syndromes.

Learning Objectives

- Identify the cause and natural history of Dravet syndrome
- Discuss surgical and non-surgical treatments for Dravet syndrome