

## Improved Neurodevelopmental Outcome in a Patient with Aicardi syndrome after Palliative Surgical Resection

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### Abstract

Aicardi syndrome (AS) is characterized by the triad of agenesis of the corpus callosum, infantile spasms, and chorio-retinal lacunae. AS patients often exhibit multiple seizure types, which are typically pharmacoresistant. We present the case of a 6 year-old girl with likely AS, developmental delays, and medically refractory epilepsy who was found to have diffuse MRI abnormalities characteristic of AS. Video-EEG showed interictal pattern of 'epilepsia partialis continua' from the right cerebral hemisphere. She underwent palliative selective right temporal lobectomy and right frontal lesionectomy aimed at ameliorating seizure burden. The surgery did not significantly improve seizure control, but resulted in notable neurodevelopmental improvements with regard to quality of life (QOL) parameters, social relatedness, and motor functioning. This reiterates the role of palliative epilepsy surgery in patients with intractable seizures when seizure burden, antiepileptic medication burden, cognitive deterioration or QOL issues are weighed in against the risks of epilepsy surgery.

**Key words:** Aicardi syndrome; Infantile spasms; Palliative surgery; Epilepsy

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### Introduction

Aicardi Syndrome (AS), as first described by Jean Aicardi in 1965, is an X-linked dominant disorder, which is characterized by the triad of agenesis of the corpus callosum, infantile spasms (IS), and congenital chorio-retinal lacunae [1,2] Features that support this diagnosis include cortical malformations like polymicrogyria, periventricular and subcortical heterotopias, cysts around the third ventricle or choroid plexus, choroid plexus papillomas, and optic disc or optic nerve colobomas [3] In cases when only 2 of the 3 core features are present, AS may be considered likely when at least two of the supporting features are fulfilled.

Seizures are a common presenting symptom in patients with AS. IS are the most common seizure type. The spasms are often asymmetric and longer in duration compared to idiopathic IS [5]. In addition to IS, patients may also exhibit other seizure types such as complex partial, myoclonic, atonic, tonic, atypical absence, and generalized tonic-clonic. Commonly described electroencephalogram (EEG) abnormalities include asymmetric hypsarrhythmia and bilateral independent bursts of high amplitude sharp and slow waves admixed with low amplitude or burst-suppression pattern [2]

The successful management of seizures in AS can be daunting despite the use of broad-spectrum anti-epileptic drugs (AEDs), adrenocorticotrophic hormone, ketogenic diet, or insertion of a vagal nerve stimulator (VNS) [4,5] Limited literature exists regarding the use of resective surgery for seizure management in AS. Rosser et al presented a series of 77 patients with AS who completed questionnaires about their seizure history and treatment [4] In this series, one subject underwent hemispherectomy and was seizure-free on one AED with post-surgical development improving from a 2-month to a 9-month level. Saito et al described a patient with AS and hypoplasia of the corpus callosum who first underwent corpus callosotomy of a partial corpus callosum with some improvement in seizure severity and then underwent left functional hemispherectomy with seizure freedom [6]. Kasasbeh and colleagues reported a series of 4 patients who underwent palliative epilepsy surgery with either callosotomy and/or VNS implantation with surgical outcomes that varied from complete resolution of seizures to worsening of seizure frequency [7]. The authors proposed that further studies would be required to identify the optimal surgical approach in AS patients.

We present this case with possible AS who underwent partial lobectomy and lesionectomy for palliative treatment of her medically refractory seizures. To our knowledge, this is the first reported case of selective resective epilepsy surgery being used for palliation in AS.

## Case Study

Our patient is a 6-year-old Nepalese girl who was brought to medical attention due to IS and developmental delays. She was born at full-term via normal spontaneous vaginal delivery without prenatal, perinatal, or postnatal complications. At the age of 6 months, she began to experience multiple clusters of spasms and complex partial seizures on a daily basis in addition to exhibiting speech, gross and fine motor delays. Her complex partial seizures were characterized by eye deviation to the left and smirking. Ophthalmological examination did not reveal any chorioretinal lesions. Skeletal survey did not show any costovertebral segmentation anomalies. Non-contrast CT head was remarkable for agenesis of the corpus callosum, nodular heterotopia, and an interhemispheric cyst.

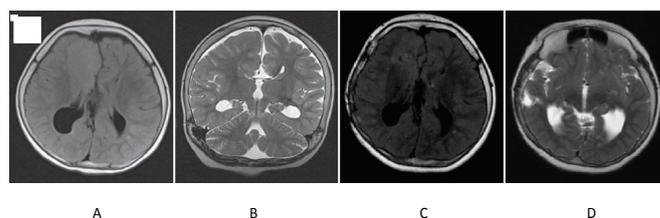
Between the ages of 4 and 6, the patient had trials of high-doses of topiramate and valproic acid, clonazepam, oxcarbazepine, and levetiracetam in different combinations in an outside hospital without improvements in her seizure frequency or severity. Neuropsychological assessment revealed that she functioned at the developmental level expected of a 6 month old at the age of 6 years, based on the Denver II Developmental Assessment test [8]. Genetic testing was negative for Fragile X, Rett's syndrome and Angelman's syndrome. MRI brain demonstrated multiple abnormalities including agenesis of the corpus callosum with mild enlargement of the third and lateral ventricles without acute hydrocephalus. There was medial right frontal and parietal polymicrogyria, and a cyst in the mesial right parietal lobe (Figure 1). Smaller foci of grey matter heterotopia were seen along the left lateral ventricle and right occipital horn. Routine EEG revealed diffuse bilateral cerebral dysfunction with paroxysmal bursts of high-voltage slow waves and multifocal epileptiform discharges, right more than left. Video EEG showed moderate generalized slowing with superimposed focal right hemispheric slowing and nearly continuous high-amplitude slow spikes-and-slow wave complexes maximal in the right frontal and frontocentral regions (Figure 2). Given the correlation of the abnormalities on imaging and electrographic pattern of nonconvulsive epilepsy partialis continua in the right hemisphere, the decision was made to do a 2-stage palliative resective surgery of the epileptogenic zone.

Intracranial monitoring was performed for ten days with two grids placed over the right fronto-temporal and parietal regions, one strip placed over the mid-posterior temporal region, and one depth electrode placed in the anterior mesial frontal region. The study showed abundant, moderate to high voltage, synchronous 1-2 Hz epileptiform spike-and-slow waves with seizures onset over numerous fronto-temporal grid and depth electrodes. Nearly continuous epileptiform spike-and-wave discharges were seen over one electrode in the frontal area, occurring up to a rate of 2-3Hz. Several habitual partial seizures, which had ictal onset over the right hemisphere, were captured. Given identification of the

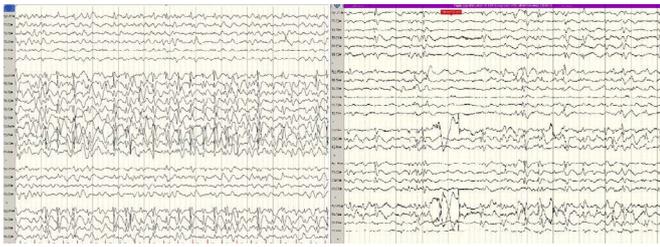
right anterior temporal and right frontal depth electrodes as the most active epileptiform foci, our patient underwent a palliative right temporal resection and a right frontal partial lesionectomy (Figure 1). She tolerated the procedure well without post-operative complications. Histopathological examination of the right frontal lesion revealed aberrant tangential neocortical dyslamination with foci of immature neurons consistent with focal cortical dysplasia (FCD) Type Ib as defined by the International League Against Epilepsy [9]. After the surgery, our patient showed marked improvement in her overall daily functioning within 3 months. Her parents reported improved interactions and responses to interpersonal cues. She would smile and babble more often. She started humming and swaying to a song with her parents. About 6 months after the surgery, she was able to stand with minimal assistance and walk for short distances with support. Her seizure severity and frequency did not show improvement. Follow-up video EEG monitoring demonstrated epilepsy partialis continua in the right hemisphere and generalized paroxysmal fast activity (GPFA). Clinical seizures, characterized by either head drops or head deviation to the left, generally correlated with diffuse attenuation of the EEG background for a few seconds (Figure 2).

## Discussion

This is the first documented report of a patient with the likely diagnosis of AS who underwent selective surgical resection of seizure foci with the goal of palliation. Our patient showed Engel Class IV outcome with regard to seizure control [10]. However, she exhibited a notable advancement of her developmental milestones and her family endorsed an improvement in their



**Figure 1** A. Pre-surgical MRI T2-weighted FLAIR axial image shows a large area of cortical dysplasia (polymicrogyria) in the medial right frontal lobe that is associated with architectural distortion and relative paucity of white matter signal in the right frontal lobe. B. Pre-surgical MRI T2-weighted coronal image demonstrated agenesis of the corpus callosum and mildly enlarged lateral ventricles. C. Post-surgical MRI T2-weighted FLAIR axial image shows parenchymal loss in the high right frontal lobe extending from the cortex through to the deep white matter laterally, consistent with a surgical resection cavity. At the deepest margin of the cavity there remains thickened irregular cortex consistent with cortical dysplasia. D. Post-surgical MRI T2-weighted axial image shows parenchymal loss at the most inferior lateral right temporal lobe corresponding roughly to the middle and inferior gyrus extending from the cortex to the underlying white matter, consistent with a surgical resection cavity.



**Figure 2** A: Pre-surgical interictal EEG during light sleep showing almost continuous spike and slow wave activity in the right hemisphere consistent with *epilepsia partialis continua*.  
B: Post-operative Video EEG clip showing the ictal onset with diffuse attenuation of the EEG background for two seconds (marked by black arrow). There are admixed F4 electrode artifacts.

perceived quality of life (QOL) within 3 months of undergoing epilepsy surgery.

Epilepsy surgery has already proven to be useful in the management of many subsets of intractable pediatric epilepsy syndromes like West Syndrome, Tuberous Sclerosis, and Landau-Kleffner Syndrome [11]. Although seizure control is the most commonly reported outcome when evaluating the efficacy of epilepsy surgery, additional parameters like neurodevelopmental

improvements and improved QOL are noted to be additional benefits with surgical intervention [12]. To that extent, surgical management should be pursued in candidates with medically refractory seizures for either cure or palliation.

Our case suggests that epilepsy surgery may be a valuable consideration in the management of medically refractory seizures in AS, especially if there is concern for significant developmental stagnation or deterioration. Future clinical studies that evaluate the efficacy of surgery in AS in improving long-term outcomes, including seizure control and neurodevelopmental level, will help to better delineate the value of adding this option in the repertoire of potential therapeutic interventions for the management of AS.

## Conclusion

The improvement of developmental level seen after right temporal partial lobectomy and frontal lesionectomy in our patient raises the possibility of using palliative epilepsy surgery in the management of AS. Further studies are required to further assess outcomes with the use of this intervention in patients with both epilepsy and Aicardi syndrome.

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