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Cognition, health-related quality of life, and mood in children and young adults diagnosed with a glioneuronal tumor in childhood

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ABSTRACT

Aims: The aim of this study was to investigate long-term cognitive outcome, health-related quality of life (HRQoL), and psychiatric symptoms in children and young adults diagnosed with a glioneuronal tumor in childhood.

Methods: Twenty-eight children and adolescents (0–17.99 years) with a minimum postoperative follow-up time of five years were eligible for the study; four persons declined participation. A cross-sectional long-term follow-up evaluation was performed using the following study measures: Wechsler Intelligence Scale for Children (WISC-IV) or Wechsler Adult Intelligence Scale (WAIS-IV), Reys Complex Figure Test (RCFT), Short Form 36 version 2 (SF-36v2), Short Form 10 (SF-10), Quality of Life in Epilepsy 31 (QOLIE-31), Hospital Anxiety Depression Scale (HADS) or Beck Youth Inventory Scales (BYI), and Rosenberg Self-Esteem Scale. Historical WISC-III and RCFT data were used to compare cognitive longitudinal data.

Results: Mean follow-up time after surgery was 12.1 years. Sixty-three percent (15/24) were seizure-free. Despite a successive postoperative gain in cognitive function, a significant reduction relative to norms was seen in the seizure-free group with respect to perceptual reasoning index (PRI), working memory index (WMI), and full-scale intelligence quotient (FSIQ). Seizure freedom resulted in acceptable HRQoL. Thirty-two percent and 16% exceeded the threshold level of possible anxiety and depression, respectively, despite seizure freedom.

Conclusion: Although lower than in corresponding reference groups, cognitive outcome and HRQoL are good provided that seizure freedom or at least a low seizure severity can be achieved. There is a risk of elevated levels of psychiatric symptoms. Long-term clinical follow-up is advisable.

1. Introduction

Glioneuronal tumors, ganglioglioma (GG), and dysembryoplastic neuroepithelial tumors (DNETs) are common low-grade central nervous system (CNS) tumors of childhood. In a recent study, they represented 13% of the CNS tumors in children below the age of 18 years [1]. Survival rates are excellent, but these tumors often cause epilepsy that seldom resolves with antiepileptic drugs (AEDs) [2–5]. Consequently, GGs and DNETs might cause problems, such as cognitive decline, lowered quality of life, and psychiatric comorbidity, and they might also have a negative psychosocial impact.

Treatment outcomes in previous studies mainly relate to seizure outcome, and lesionectomy has been proven a safe and effective method to alleviate or reduce seizures, especially if gross total resection (GTR) is achieved [4,6–8]. In Sweden, all patients operated on for epilepsy are followed up at six and 24 months after surgery with a physical and neurological assessment, an electroencephalogram, and neuropsychological tests. Prolonged clinical review beyond this point is subject to individual judgments by the physician, and patients may be considered cured and no longer included in subsequent follow-ups. If the tumor has been gross totally resected and the patient is seizure-free after AED withdrawal, there is a high risk that further follow-ups will be limited to structured telephone interviews five, 10, and 15 years postoperatively, according to the Swedish National Epilepsy Surgery Register [9].

Long-term outcome studies addressing cognition and quality of life in pediatric epilepsy surgery patients are published, but the etiologies behind the epilepsy are often mixed [10,11]. Concerning glioneuronal tumors, there is a scarcity of long-term studies although some studies stress the risk of cognitive problems and psychosocial impact [5,7,12,13]. The aim of this population-based study was to investigate the long-term cognitive outcome and quality of life of a cohort of children with glioneuronal tumors. Furthermore, we wanted to screen for psychiatric symptoms: depression, anxiety, and low self-esteem. We also

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wanted to investigate if tumor location and seizure outcome, i.e., seizure freedom or remaining epilepsy, had an impact on outcome.

2. Material and methods

This single-center study was performed at Uppsala University Children's Hospital, Sweden, a tertiary referral center for children with CNS tumors and medically refractory epilepsies. The referral center serves six counties in mid-Sweden with a population of 1.7 million inhabitants. Patient data were retrieved from the local registry, the National Brain Tumor Registry, and the National Epilepsy Surgery Registry. A total of 30 patients with a neuropathological confirmed diagnosis of a glioneuronal tumor (age: 0–17.99 years) and a minimum postoperative follow-up time of five years were diagnosed during a fifteen-year period (1995–2009) [5]. Two patients diagnosed with a glioneuronal tumor before two years of age were excluded: one with severe cerebral palsy with gross motor function classification system (GMFCS) level IV [14] and one patient with a progressive glioneuronal tumor in the medulla oblongata/pons, who died despite intensive chemotherapy. Thus, 28 patients were eligible for participation in the study.

A total of 24 patients (86%) came for the follow-up: 19 adults (range 18–34 years), 3 adolescents (15–18 years), and 2 children (<15 years). The male–female (M:F) ratio was 1.2:1. Pathologic anatomic diagnosis consisted of 20 GGs, three DNETs, and one desmoplastic infantile GG.

Table 1
Characteristics of the 28 eligible patients (patients 25–28 declined participation). Age (so = seizure onset). Seizure type: A = focal seizures with impairment of awareness, B = focal seizures with and without impairment of awareness, C = focal seizures with impairment of awareness and generalized tonic–clonic seizures, D = generalized tonic–clonic seizures. Surgical indication: E = epilepsy, T = tumor. Extent of surgery: GTR = gross total resection, STR = subtotal resection. PAD = pathological anatomical diagnosis, GG = ganglioglioma, DNET = dysembryoplastic neuroepithelial tumor, DIG = desmoplastic infantile ganglioglioma, AED = antiepileptic drug, CBZ = carbamazepine, OXC = oxcarbazepine, VPA = valproic acid, LTG = lamotrigine, VGB = vigabatrin, CZM = clonazepam, LEV = levetiracetam, TPM = topiramate, NTZ = nitrazepam, PBT = phenobarbital, GBP = gabapentin.

	Age (so)	Seizure type	Seizure frequency (T1)	AED (tried preop)	Age (T1)	Surgical indication	Extent of surgery	Tumor location	PAD	Age (T3)	Seizure frequency (T3)	AED (T3)	Comorbidity
Pat 1	14	C	Single/sporadic	CBZ	14	E + T	STR	Extratemporal	GG	33	Seizure-free	None	None
Pat 2	1	B	>1/week	CBZ, VPA, LTG, VGB	12	E	GTR	Right temporal	GG	29	Seizure-free >2 years	OXC	Learn. dis., dyslexia, ank. spond.
Pat 3	6	A	>1/year	CBZ, OXC, LTG	12	E + T	GTR	Extratemporal	DNET	23	Seizure-free	None	ADHD
Pat 4	8	A	Daily	None	8	E + T	GTR	Right temporal	GG	23	Seizure-free >2 years	CBZ	None
Pat 5	1	B	>1/year	VPA, LTG	18	E	GTR	Right temporal	GG	30	Seizure-free	None	None
Pat 6	6	A	>1/year	VPA, LTG, CBZ	17	E	GTR	Left temporal	GG	29	Seizure-free	None	None
Pat 7	11	A	>1/year	VPA, CZM	13	E	GTR	Right temporal	GG	24	Seizure-free	None	None
Pat 8	5	A	Daily	OXC	12	E + T	GTR	Left temporal	GG	17	Seizure-free >2 years	OXC	None
Pat 9	16	A	>1/week	VPA, CBZ	18	E	GTR	Right temporal	GG	23	Seizure-free	None	Pachyonychia congenita
Pat 10	4	A	>1/month	VPA, CBZ	8	E + T	STR	Right temporal	GG	15	>1/year	CBZ	None
Pat 11	13	A	>1/month	OXC, VPA, LEV, LTG	13	E + T	Biopsy	Left temporal	GG	23	Daily	LTG, GBP	Depression
Pat 12	5	A	Daily	OXC, LTG	7	E + T	STR	Extratemporal	DNET	12	Seizure-free	None	None
Pat 13	3	B	Daily	CBZ, VPA, TPM, LTG, VGB	8	E	Biopsy + STR	Extratemporal	GG	21	>1/week	LEV, CBZ	None
Pat 14	12	A	Daily	CBZ	14	E + T	STR	Left temporal	GG	32	Daily	LTG, LEV	None
Pat 15	11	A	Single/sporadic	LTG	14	E + T	GTR	Left temporal	GG	25	>1/year	LTG	None
Pat 16	7	A	Single/sporadic	OXC	18	T	GTR	Left temporal	GG	30	Seizure-free	None	Learn. dis., dyslexia
Pat 17	9	A	>1/week	CBZ	15	E	GTR	Right temporal	GG	33	>1/week	LEV, CBZ	None
Pat 18	1	A	Single/sporadic	CBZ	1	T	GTR	Right temporal	GG	19	Seizure-free	None	None
Pat 19	1	A	>1/week	VPA, CBZ, TPM, LTG, VGB, NTZ	11	E	GTR	Left temporal	GG	28	Seizure-free	None	None
Pat 20	1	No epilepsy	No seizures	None	1	T	STR	Extratemporal	DIG	17	>1/year	LTG	Asperger
Pat 21	16	C	Single/sporadic	CBZ	20	E	GTR	Extratemporal	DNET	31	Seizure-free	None	Depression
Pat 22	5	A	Daily	CBZ	6	E + T	STR	Left temporal	GG	18	Daily	VPA, LTG	None
Pat 23	17	D	Single/sporadic	None	17	T	GTR	Extratemporal	GG	26	Seizure-free	None	None
Pat 24	0	A	>1/year	PBT, OXC, CBZ, LTG	2	E + T	Biopsy + STR	Left temporal	GG	9	>1/year	OXC	None
Pat 25	4	B	>1/week	CBZ	14	E + T	GTR	Extratemporal	DNET	32	Seizure-free	None	None
Pat 26	12	No epilepsy	No seizures	None	13	T	GTR	Right temporal	GG	33	>1/year	VPA	None
Pat 27	7	A	>1/week	CBZ, OXC, LTG, VPA, VGB	12	E	GTR	Left temporal	GG	28	Unknown	Unknown	Unknown
Pat 28	15	A	>1/year	LTG, VPA	16	E + T	GTR	Extratemporal	GG	26	Seizure-free >2 years	LTG	Unknown