Published in final edited form as:

Childs Nerv Syst. 2016 August ; 32(8): 1359–1362. doi:10.1007/s00381-016-3145-8.

Psychiatric manifestations as initial presentation for pediatric CNS germ cell tumors, a case series

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Abstract

Background—CNS germ cell tumors account for 3% of all pediatric brain tumors in the US. Presenting symptoms are typically location based with pineal tumors presenting with obstructive hydrocephalus and suprasellar tumors with hypothalamic/pituitary dysfunction and ophthalmologic abnormalities. Psychiatric manifestations such as psychosis and behavioral changes are atypical presentations of CNS germ cell tumors, with only 11 previously reported cases.

Methods—This is a retrospective case series describing patients with CNS germ cell tumors with an atypical presentation including psychiatric manifestations. Information regarding clinical presentation, treatment course and outcome were obtained.

Results—We report 7 patients who presented with psychiatric symptoms consisting of psychomotor delay as well as behavioral and mood changes. Six of the seven patients were diagnosed ≥ 6 months after onset of psychiatric symptoms. All 7 are alive but 5 continue to have neurologic and psychiatric issues post treatment.

Conflict of Interest Disclosure
The authors have no conflicts of interest to disclose.

Conclusions—Atypical presentations of CNS germ cell tumors can delay diagnosis and treatment and may be secondary to atypical locations as well as endocrine dysfunction manifesting as psychiatric symptoms. Delayed diagnosis did not appear to affect survival but earlier diagnosis may potentially be associated with better neurologic and psychiatric outcome. Patients who present with these symptoms and atypical neuroimaging should have a thorough evaluation for CNS germ cell tumors including serum and CSF markers. Clinicians should be aware of these less common presentations to aid in prompt diagnosis and treatment.

Keywords

CNS germ cell tumors; psychiatric; endocrine dysfunction

Introduction

CNS germ cell tumors represent 3% of all pediatric brain tumors in the US.[1] Typical clinical presentation relates primarily to tumor location, which frequently involves the pineal and suprasellar (SS) regions. Pineal tumors usually cause obstructive hydrocephalus presenting with signs of increased intracranial pressure including headaches, vomiting, lethargy and Parinaud's syndrome. The most common initial symptom of SS tumors, diabetes insipidus (DI), relates to hypothalamic/pituitary dyfunction; delayed or precocious puberty, growth hormone deficiency, hypothyroidism, and adrenal insufficiency are also seen.[3] Atypical locations or endocrinologic dysfunction may cause a variety of protracted behavioral and psychiatric syndromes, often delaying the medical diagnostic team from suspecting the presence of a primary intracranial tumor such as a germ cell tumor.

We report seven patients with atypical symptoms such as psychomotor delay, behavioral changes, and psychosis. All of these patients had either endocrinologic disturbances or atypical imaging features. To the best of our knowledge, there have only been 11 previously reported atypical psychiatric presentations in seven case reports and one retrospective review article.[1,4-10] It is important to recognize that patients with CNS germ cell tumors may present with psychiatric symptoms, which may be secondary to atypical imaging characteristics, metabolic disturbances or a combination of both. Identification of the uncommon presentation is warranted to reduce the risk of delayed diagnosis.

Methods

We performed a retrospective chart review evaluating patients that presented from 2004 to 2014 with atypical presentations including psychiatric symptoms and were found to have CNS germ cell tumors. Data collected consisted of clinical presentation, treatment and outcome. The results are descriptive. This retrospective study was approved by Memorial Sloan Kettering Cancer Center and Montefiore Medical Center/Albert Einstein's Institutional Review Boards and Privacy Boards.

Results

Refer to table 1 for details of case series.

Discussion

Our case series describes seven patients who presented with psychomotor delay, behavioral changes, psychosis and other psychiatric symptoms with or without endocrine abnormalities (Table 1). To the best of our knowledge, there have only been eleven cases reported describing psychiatric manifestations associated with CNS germ cell tumors. In reviewing our cases and the previous literature, the commonality between the cases is atypical location with infiltrative nature. Along with atypical location, our patients also had endocrinologic disturbances that were protracted. Psychiatric manifestations can be seen with endrocrine dysfunction and may explain the atypical presentation. This has not been emphasized previously and is very important to highlight for clinicians who may encounter these patients, to avoid delay in diagnosis. All of our patients in this series are alive and only two had progression of disease, one at 1.5 years and the other at 4 years post initial diagnosis. Delayed diagnosis did not appear to affect survival but earlier diagnosis may be associated with better neurologic and psychiatric outcome.

Previously reported case reports highlighted patients who presented with psychiatric symptoms and were all found to have atypical imaging characteristics with deep gray matter involvement and infiltrating nature[4-8]. Crawford et al published a report on presentation of CNS germ cell tumors with relation to location, as well.[1] In this article, the most common presenting symptom was headache in 70% of patients with pineal region tumors. Patients with delayed diagnosis, which they defined as greater than 6 months, included 4 patients with suprasellar lesions, 3 with basal ganglia lesions, 1 with suprasellar/pineal lesion and 1 with a pineal lesion. Common symptoms that were present in this group included enuresis, psychosis, movement disorders and anorexia. Of the 9 patients with delayed diagnosis, 3 presented with psychiatric symptoms only. Two patients were diagnosed with anorexia nervosa and were both found to have suprasellar lesions, the third presented with poor school performance, change in behavior and psychosis. With further review of their patient population, 4 of 30 patients had abrupt change in school performance. One patient had tics, obsessive compulsive disorder (OCD), dyskinesia and progressive school decline and was found to have a lesion involving the basal ganglia, corpus callosum, cerebellum, periventricular white matter, and mesial temporal lobe. Four patients had psychomotor slowing and were all found to have lesions involving deep gray structures including basal ganglia and thalamus. The delay in diagnosis was attributed to less common symptoms, atypical MRI findings and subtle endocrinologic dysfunction.

Endocrine deficiencies can manifest as psychiatric symptoms.[11] Examples of this include hypercortisolism presenting with depression, cognitive impairment, delirium, psychosis. Hypocortisolism can also present with depression, cognitive impairment as well as delirium. Hyperthyroidism is associated with nervousness, emotional lability and hyperkinesia. Diabetes insipidus and hypernatremia have also presented with psychiatric symptoms such as psychosis. It is plausible that patients with CNS germ cell tumors who have pituitary/hypothalamic dysfunction can present with psychiatric symptoms secondary to endocrine deficiencies. This can also cause a delay in diagnosis. In our case series, patients 5 and7 had endrocrine deficiencies only, without atypical/infiltrative imaging findings. Patient 1, 2 and 6

had both atypical locations with infiltrative features as well as prolonged endocrine abnormalities.

CNS germ cell tumors can present with symptoms such as OCD, cognitive decline, psychomotor delay, psychosis, hemiparesis, dyskinesias, tics, enuresis and anorexia and can have nonspecific MRI findings or endocrine dysfunction. Patients who present with endocrine disturbances, especially prolonged or medically refractory, and atypical neuroimaging should have a thorough evaluation for CNS germ cell tumors including serum and CSF markers. We should be aware of these less common presentations as manifestations of CNS germ cell tumors to aid in prompt diagnosis and treatment to potentially prevent poor neurologic and psychiatric outcomes.

References

1. Crawford JR, Santi MR, Vezina G, et al. CNS germ cell tumor of childhood (CNSGCT) presentation and delayed diagnosis. Neurology. 2007; 68:1668–1673. [PubMed: 17502547]
2. Echevarria ME, Fangusaro J, Goldman S. Pediatric central nervous system germ cell tumors: a review. The Oncologist. 2008; 13:690–699. [PubMed: 18586924]
3. http://www.uptodate.com/contents/pediatric-intracranial-germ-cell-tumors?source=search_result&search=pediatric+germ+cell+tumors&selectedTitle=2%7E128
4. Winston AP, Barnard D, D'Souza G, et al. Pineal germinoma presenting as anorexia nervosa: case report and review of the literature. Int J Eat Disord. 2006; 39:606–608. [PubMed: 17041920]
5. Undurraga J, Baeza I, Valenti M, et al. Case report: Brain germinoma presenting as a first psychotic episode in an adolescent male. Eur Child and Adolescent Psychiatry. 2010; 19:741–742.
6. Sartori S, Laverda AM, Calderone M, et al. Germinoma with synchronous involvement of midline and off midline structures associated with progressive hemiparesis and hemiatrophy in a young adult. Childs Nerv Syst. 2007; 23:1341–1345. [PubMed: 17609967]
7. Mittal VA, Karlsgodt K, Zinberg J, et al. Identification and treatment of a pineal region tumor in an adolescent with prodromal psychotic symptoms. Am J Psychiatry. 2010; 167:1033–1037. [PubMed: 20826854]
8. Heathcote AC, Wormald JC, Stocks R. An unusual suspect causing behavioral problems and pituitary failure in a child. BMJ Case Rep. Dec 14.2012 2012.
9. Etzioni A, Luboshitzky R, Tiosano D, et al. Melatonin replacement corrects sleep disturbances in a child with pineal tumor. Neurology. 1996; 46:261–263. [PubMed: 8559393]
10. Winston AP, Barnard DD, D'souza G, et al. Pineal germinoma presenting as anorexia nervosa: Case report and review of the literature. Int J Eat Disord. 2006; 39:606–8. [PubMed: 17041920]
11. Popkin, MK.; Mackenzie, TB. Somatopsychic disorders. Spectrum publications; New York: 1980. Psychiatric presentations of medical illness.. Print

#	Age	Sex	Symptoms	Location	Time to Dx	Tumor Markers	Pathology	Endocrine deficiencies	Treatment	Outcome
1	8	M	Precocious puberty and behavioral problems 4 months after treatment-right hemiparesis worsening behavior, decline in speech/ cognition	infundibular stalk At recurrence: periventricular white matter and frontal/subfrontal region involvement	2 yrs to initial diagnosis Recurred 4 months post treatment	Serum: β-hCG 78 mIU/ml, AFP 4.6 ng/ml CSF: β-hCG 508 mIU/ml, AFP <2 ng/ml Recurrence: CSF β-hCG 53 mIU/ml	N/A	DI, secondary hypothyroidism, secondary adrenal insufficiency, growth hormone deficiency, pseudo-precocious puberty	chemotherapy-remission At recurrence: high dose chemotherapy (HDCT) with autologous stem cell rescue (ASCR) and radiation (RT)	attending a special education/job training program no more behavioral issues, but continued issues with speech
2	6	M	Polyuria/ polydipsia, weight gain, depression, abnormal thyroid function tests (TFTs) 4 years after: refractory DI , difficulties in school, worsening right hemiparesis, bizarre behavior, uttering inappropriate remarks, perseverating on phrases	contrast enhancing mass in the suprasellar region enveloped optic chiasm and nerves Recurrence: left thalamic region/ internal capsule/ corona radiata	2.5 yrs to initial diagnosis Recurred 4 years later	Negative	Germinoma	Pituitary/hypothalamic dysfunction	Biopsy, chemotherapy and RT At recurrence: Biopsy, HDCT with ASCR	obsessive compulsive disorder (OCD), significant cognitive and speech delay. Wheelch air bound, special education with some regular education classes
3	8	M	Personality changes, depression, cognitive decline and right hemiparesis	left deep white matter from the temporal lobe to the corona radiata with a nodular component in the left corona radiata Spine MRI-central streaks of T2 abnormality of unknown significance	6 months	Initial Serum: β-hCG 14 mIU/ml, AFP <2 ng/ml CSF: β-hCG 29 mIU/ml Repeat few weeks later: CSF β-hCG 36 mIU/ml	N/A	Precocious puberty	Chemotherapy and RT with craniospinal irradiation for infiltrative tumor and spinal cord abnormalities	intractable epilepsy (underwent L frontal disconnection surgery but continues to have seizures) requires three anti-epileptic drugs, continues to receive PT/OT/ST and is in special education
4	8	M	Psychosis (auditory hallucinations), hyperactivity, obsessive compulsive disorder, incoordination,	deep gray nuclei and internal capsules bilaterally, L>R, left basal ganglia, signal intensity in the gray matter and deep structures	~9 years	(prior to diagnosis): CSF: β-hCG 41.9 mIU/ml, AFP 0.5 ng/ml Serum: β-hCG 33.9 mIU/ml, AFP 5.6 ng/ml	Germinoma	Polydipsia	Biopsy, chemotherapy and RT	Nonverbal, nonambulatory, unable to sit/roll.

#	Age	Sex	Symptoms	Location	Time to Dx	Tumor Markers	Pathology	Endocrine deficiencies	Treatment	Outcome
			right hemiparesis, psychomotor delay, progressive cognitive decline and speech delay	(extensive neurologic and metabolic work up done with initially nonspecific findings, thought to be inborn errors of metabolism, repeat imaging with mass effect)						
5	22	M	mood disorder, aggressive behavior, cognitive impairment, hallucinations, enuresis, hypernatremia	Large suprasellar mass involving optic chiasm and bilateral anterior portions of optic nerves	3 months	None sent	Germinoma	Hypernatremia	Partial resection, chemotherapy and RT	Pan-hypopituitary, epilepsy, legally blind, intellectually disabled, mood disorder, hallucinates
6	16	M	Decreased appetite, vomiting (concerning for eating d/o), depression, psychomotor retardation for 9 months Headache for 2-3 months Seizure right prior to diagnosis	Heterogeneously enhancing, partially fatty lesion involving superior midbrain, extending into the thalamus, obstructive hydrocephalus	9 months	Serum: β-hCG 102.7 mIU/ml AFP QNS CSF: β-hCG 165.2 mIU/ml, AFP < 0.3 ng/ml	Insufficient	Polydipsia, polyuria	Endoscopic third ventriculostomy, biopsy, chemotherapy, second look surgery with partial resection, HDCT with ASCR, and RT	In college doing well, treated for DI and is on an anti-epileptic medication, seizure free for years, behavioral issues and depression resolved
7	18	F	Loss of appetite, burning sensation (extensive GI work up negative) weight loss, restrictive eating (concerning for eating d/o), depression cold intolerance-hypothyroid secondary amenorrhea and new onset esophoria right prior to diagnosis	Large sellar/ suprasellar mass measuring up to 5 cm in craniocaudal dimension	9 months	Initially: Serum β-hCG <1 mIU/ml, AFP 2.8 ng/ml CSF: β-hCG 18 mIU/ml, AFP <1 ng/ml Repeat 12 days later: Serum: β-hCG 245 mIU/ml, AFP 6.6 ng/ml	Insufficient	Hypothyroid, secondary amenorrhea, DI	External ventricular drain for increased intracranial pressure (after diagnosis) Chemotherapy, second look surgery, RT	No longer having any issues with appetite, depression, weight loss. Doing well overall, working a regular job, very independent