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Religious singing as an unusual sign of craniopharyngioma. Case report and literature review

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Summary

Craniopharyngiomas are rare and benign intracranial tumours arising in the sellar region. Typically, patients with craniopharyngioma present with headaches, visual disturbances and endocrine deficits due to compression of adjacent proximal structures. Primary psychiatric clinical presentation has been rarely reported. We present the case of a 59-year-old female with craniopharyngioma with suprasellar extension into the third ventricle and a clinical picture dominated by behavioural changes. Due to mental disturbances, the patient was diagnosed and underwent initial surgical treatment in another medical facility. She was admitted to our Department due to a mental disorder relapse attributed to tumour regrowth. On admission, she was singing religious songs spontaneously or in response to questions, and neuropsychological examination revealed disturbances of memory, attention, executive functioning and decreased drive. The patient was scheduled for reoperation. Following subtotal resection, she was discharged home without psychiatric symptoms. Two years later, after initial improvement, the patient was readmitted with the same mental disorder and tumour regrowth. She underwent a second reoperation and was discharged with improved mental status. After a 2-month follow-up period, the patient's family reported a complete resolution of behavioural disturbances. Based on the literature review and our observation, we assume that the psychiatric manifestation of craniopharyngioma might be associated with dysfunction of suprasellar structures, namely the hypothalamus, and in such cases, resection should be carried out to the maximum safe extent.

Key words: craniopharyngioma, skull base, organic mental disorder

Introduction

Craniopharyngiomas (CP) are rare, benign, and slow-growing intracranial tumours that originate from residual epithelial cells of Rathke's pouch and typically arise in the sellar-suprasellar region [1]. Common clinical presentations of CP include headaches, visual defects, hydrocephalus, and pituitary-hypothalamic endocrine disturbances [2]. Primary psychiatric manifestations have been very rarely reported in the literature and may involve mood swings, personality changes, behavioural disorders, or psychosis [3-8]. Surgical treatment with the goal of gross total resection is usually performed through a classic open or endoscopic endonasal transsphenoidal approach [9].

We present a case of recurrent craniopharyngioma with an unusual primary psychiatric manifestation. We also include a systematic literature review. This case report has been written in accordance with the Surgical Case Report (SCARE) guideline [10].

Case report

In April 2021, a 59-year-old woman was diagnosed with a suprasellar tumour involving the third ventricle, with imaging characteristics of CP. The diagnostic process was initiated due to mental disturbances which, according to the patient's family, began several months prior to the diagnosis, initially manifesting mainly as mild memory deficits. In the subsequent weeks, her symptoms progressed rapidly, with a decrease in responsiveness and cooperation. Her mood appeared depressed, and she exhibited behavioural changes, including singing songs of a religious nature in inappropriate situations. In another medical facility, she underwent a right-sided frontotemporal craniotomy with partial tumour resection complicated by an intraoperative right internal carotid artery (ICA) injury. In December 2021, the patient was referred to the Department of Neurosurgery at the Medical University of Warsaw with progression of mental deterioration, multihormonal pituitary insufficiency, diabetes insipidus, and left-sided hemiparesis attributed to tumour progression, mainly within the third ventricle.

Upon admission, the patient appeared cognitively slowed and was singing songs spontaneously or in response to questions, with a religious context. Neurological examination revealed left-sided hemiparesis and absence of the pupillary light reflex in the right eye. Magnetic resonance imaging (MRI) confirmed the progression of suprasellar mass measuring 3.85 x 4.8 x 3.6 cm, with extension into the third ventricle. During the neuropsychological assessment, generalized disturbances of cognitive functioning were found, especially deficits in memory, attention, and executive functioning, as well as decreased drive. The patient was scheduled for resection through a left-sided frontotemporal craniotomy, with a translamina terminalis approach to the third ventricle. Due to troublesome dissection, a part of the tumour near the apex of the basilar artery was left behind. The surgery was completed without intraoperative incidents. Postsurgical neuropathological testing confirmed adamantinomatous craniopharyngioma. During the early postoperative period, the patient was initially conscious but unresponsive, non-cooperative, and opened her eyes in response to stimulation, occasionally sing-

ing. In the following days, the patient remained conscious, became responsive, did not exhibit new neurologic deficits, and was no longer singing. In a state of neurologic and psychiatric improvement, she was ultimately discharged.

During the 2-year follow-up period, the patient experienced weight loss and remained in a stable mental state without psychotropic treatment. She was not singing inappropriately, maintained cooperation with family members, and demonstrated psychomotor slowness and memory deficits no worse than in the pre-surgical state. After 2-years, the patient started exhibiting significant mood swings, shortly followed by a recurrence of reduced responsiveness and singing religious songs. In November 2023, the patient was readmitted to the Neurosurgery Department due to tumour regrowth. On admission, the patient exhibited psychomotor retardation, speech interruptions with songs (religious), melodic repetition of the physician's sentences, impaired finger counting, non-cooperation in performing tasks, and again a decrease in the efficiency of cognitive functioning. The patient was scheduled for reoperation through an endoscopic endonasal transsphenoidal approach. Subtotal resection was performed, with small remnants on the left anterior cerebral artery and right ICA left behind. In the early postoperative period, the patient remained conscious, without significant deficits and with the same psychiatric symptoms as before the surgery.

Psychiatric evaluation revealed apathy, low mood, and excluded the presence of acute positive symptoms. When asked about the nature of her singing, the patient stated that it alleviates the pain and protects her from being taken to the grave. In the opinion of the patient's family, she was moderately religious, comparable to the average person. The songs she sang varied in character and included both mournful and cheerful melodies. Moreover, the songs usually deviated from the original versions – she would often use incorrect words or mix multiple songs. Her singing occurred spontaneously or in response to questions, but neither the medical team nor the family could identify any clear external triggers for this behaviour. The patient appeared unaware of the inappropriateness of her actions. She was discharged home in a conscious state, without neurological deficits, and with improved cooperation. The melodic repetition of questions was no longer present, although spontaneous singing of religious songs persisted. During the 2-month follow-up period, the patient's family reported overall improvement and absence of previous psychiatric symptoms. At the follow-up when asked about the singing, she believed that it served as a form of protection against evil and death and still did not appear to recognize its inappropriateness.

Discussion

Craniopharyngiomas represent about 5% of all sellar region masses, and the clinical picture at the time of diagnosis is often dominated by manifestations of increased intracranial pressure (resulting in headaches or nausea) and compression of the optic chiasm complex and pituitary (resulting in visual impairment and endocrine deficits) [11]. Presentation dominated by psychiatric disturbances is not frequently reported in the literature. We report a case of rare, adult-onset craniopharyngioma presenting as a recurrent behavioural disorder secondary to central nervous system damage in the

form of musical verbigerations and perseverations, along with a systematic literature review of CP case reports with significant mental disorders at the time of admission. Ultimately, we identified 6 articles describing 6 adult patients with craniopharyngioma presenting primarily with psychiatric symptoms (Table 1). Males accounted for 66.7% of all patients, and the overall mean age at the time of admission was 55.5 years (range, 24-55 years). The most frequent symptoms and signs included increased irritability, social disinhibition, delusions, hallucinations, increased aggressiveness, apathy, demotivation, loss of interest, impaired concentration, and anxiety (for details, see Table 1). All included cases were treated either solely surgically (4 cases) or pharmacologically (with antipsychotics and antidepressants) with subsequent surgery (2 cases), and most (5 cases) reported significant improvement during follow-up.

To our knowledge, our case within the existing literature is the first ever reported with such manifestation. The patient was suffering from panhypopituitarism and diabetes insipidus caused by tumour mass effect and the initial surgical intervention. Taking into account the often extensive scope of neurosurgical procedures, appropriate substitution of pituitary tropic hormones and correction of water and electrolyte disorders in the course of diabetes insipidus have a significant impact on the patient's mental state, and failure to do so can contribute to mental disorder exacerbation and treatment resistance [12]. However, despite proper endocrinologic care, adequate hormonal supplementation, and balanced water and electrolytes, her mental status did not improve. We associate the emergence of psychiatric signs with CP suprasellar intraventricular expansion, as the symptoms subsided following initial resection, were the primary manifestation of tumour regrowth, and resolved after reoperation. Our observation and existing evidence suggest that the most probable cause of symptom relapse and resistance was the tumour's mass effect on the hypothalamus. From a neurobiological and anatomical point of view, the hypothalamus, situated in proximity to the third ventricle and functioning as the focal point of various neural pathways linking different brain areas, plays a central role in the pathogenesis of mental alterations [13].

Anatomic distortions of the hypothalamus caused by invasive suprasellar lesions can lead to disturbances in hypothalamic afferent and efferent projections, resulting in behavioural, cognitive, and emotional changes. A study conducted by Pascual et al. [14] documented a statistically significant correlation between both the degree and the mechanism of hypothalamic distortion by a suprasellar tumour and presence of specific psychiatric disturbances in CP patients. The study revealed that psychiatric symptoms occur predominantly in tumours developing primarily in the infundibulotuberal region or within the third ventricle, and the most common documented hypothalamic distortion mechanism was displacement of the floor of the third ventricle and compression of the third ventricle walls from the inside, inflicting damage to hypothalamic structures such as the paraventricular, supraoptic, suprachiasmatic, dorsomedial, and ventromedial nuclei, as well as the columns of the fornix, leading to functional disturbances in hypothalamic networks. This observation is consistent with our patient's case, as the tumour had a substantial mass effect on the third ventricle and adjacent structures, including the hypothalamus, followed by symptom resolution once the lesion was resected.

However, in the aforementioned study, the CP cohort with psychiatric manifestations displayed mainly symptoms characterized by increased irritability, apathy, mood swings, memory deficits, and psychotic features. None exhibited a behavioural disorder similar to that observed in our patient's case. The presence of mood disturbances and cognitive impairment, also observed in our patient, might be associated with compression and dysfunction of limbic system structures such as the amygdala, mammillary bodies, and hippocampi. A conceivable explanation for our patient's behavioural manifestation could lie in injury to the medial forebrain bundle, a neural pathway passing through the lateral hypothalamus and the basal forebrain, containing fibres from the basal olfactory regions, the amygdaloid regions, septal nuclei, as well as brainstem regions [15]. The medial forebrain bundle is an important structure in the functioning of the reward and motivation system and has been shown to have a significant influence on the development of compulsive-obsessive disorder and perseverative behaviours [16, 17]. Tumour compression of this tract disrupts connectivity between key brain areas, such as the ventral striatum, the medial subthalamic nucleus, the inferior thalamic peduncle, and the nucleus accumbens, potentially leading to symptoms similar to those observed in our patient.

Another potential explanation involves compression of the septal nuclei, which are located in the lower posterior region of the medial surface of the frontal lobe, adjacent to the septum pellucidum. The septal nuclei receive input from various structures, including the olfactory bulb, hippocampus, amygdala, hypothalamus, midbrain, habenula, cingulate gyrus, and thalamus. They are believed to play a key role in the motivation and reward system, and their dysfunction may contribute to the development of compulsive and stereotypic behaviours.

In conclusion, CP clinical presentation dominated by psychiatric alterations is unusual and might be associated with local compression of neighbouring structures. Compulsive or stereotypic behaviour may correlate with injury to far lateral portions of the hypothalamus, such as the medial forebrain bundle, or to structures anterior to the third ventricle, such as the septal nuclei, particularly in the later stages of the disease. In such instances, maximal resection should be pursued whenever feasible. In some instances, psychiatric symptoms may persist despite the removal of the compressive lesion. This highlights the need for further investigation into the pathogenesis of psychiatric manifestations in tumours of the third ventricle.

Table 1. **Literature review of craniopharyngioma cases with a clinical picture dominated by psychiatric symptoms**

Author and Year	Patient sex/age	Lesion measurements [cm]	Main psychiatric disturbances	Treatment	Outcome
Shekhar et al. 2023 [6]	Female/55	3.7 x 2.7 x 2.1	Visual hallucinations – seeing lady on a lion	Initially pharmacological – risperidone; next – surgical	Notable improvement after pharmacological treatment; no information regarding post-surgical status
Huang et al. 2021 [5]	Male/51	4.1 x 3.9 x 4.4	Decreased attention, increased irritability and aggressiveness, pressure of speech, delusions	Surgical	Significant improvement after 3-month follow-up
Bowers et al. 2021 [3]	Male/50	4.7 x 4.7 x 3.1	Increased irritability, hostility, aggressiveness, quick to temper, social disinhibition, short memory impairment, delusions about his brother tracking his phone, hoarding behaviour	Surgical	Initially increased anxiety, restlessness, aggressive behaviour towards medical staff; 11 days after the surgery euthymic, reflective, not exhibiting any overt psychiatric pathology, without cognitive abnormalities
Das et al. 2018 [4]	Male/51	4.5 x 3.4 x 4.8	Rapidly progressive dementia – recent memory impairment, decreased motivation, decreased attention, inability to perform complex mathematics	Surgical	Significant improvement after 2-month follow-up
Sinai et al. 2003 [7]	Male/24	4.7 x 3.6 x 3	Loss of interest in usual activities, decreased appetite, decreased energy and concentration, sleep disturbances, increased aggressiveness, demanding and child-like behaviour, intrusiveness (attempts to touch and kiss strangers), mannerisms, increased suspiciousness	Surgical	Not specified
Spence et al. 1995 [8]	Female/51	No data	Decreased mood, anhedonia, decreased concentration, social withdrawal, reduced rate of speech, agitation, increased aggressiveness, sexual disinhibition	Initially pharmacological – lofepramine; next – surgical	Euthymic 9 months after surgical treatment with certain degree of cognitive impairment

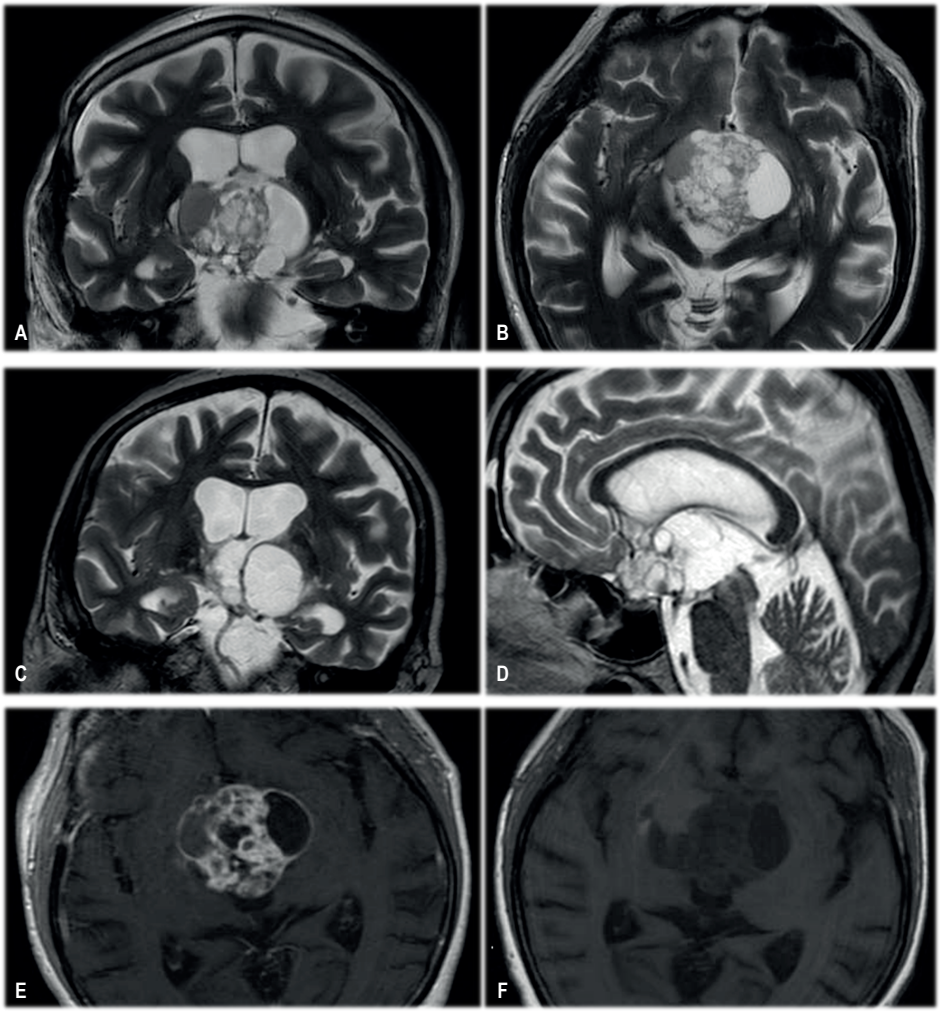

Figure 1. **Images of a large sellar-suprasellar tumour with third ventricle compression: before the first reoperation (A-B, E-F) T2-weighted MRI – coronal (A) and axial (B), T1-weighted axial with contrast enhancement (E) and without contrast enhancement (F); and before the second reoperation - (C-D) T2-weighted MRI – coronal (C) and sagittal (D)**

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