CASE REPORT

Peduncular psychosis

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SUMMARY

Psychotic symptoms are rarely documented in association with cortex-sparing central nervous system (CNS) lesions limited to the midbrain. We present the case of a 15-year-old boy with hereditary and environmental risk factors for psychiatric illness, as well as a history of midbrain pilocytic astrocytoma treated with chemotherapy and focused radiation, who presented with non-epileptic seizures, hyper-religiosity and frank psychosis. The space-occupying midbrain lesion has been radiographically stable while the patient has decompensated psychiatrically. Differential aetiology for the patient's psychiatric decompensation is discussed, including psychosis secondary to a lesion of the midbrain. Literature linking midbrain lesions to psychotic features, such as in peduncular hallucinosis, is briefly reviewed. This case suggests that a midbrain lesion in a susceptible patient may contribute to psychosis.

BACKGROUND

The atypical presentation of a rare condition presents a diagnostic conundrum regarding how much a clinical picture may deviate from prior reports and still be grouped with that syndrome. Peduncular hallucinosis is a syndrome of visual or auditory hallucinations in the context of midbrain, pontine and thalamic lesions, first described by Lhermitte in 1922.^{1–5} Hallucinations associated with this syndrome have been described as complex and difficult to distinguish from reality.^{2–3} Hallucinations are also one of the key features that define psychotic disorders. While the signature feature of peduncular hallucinosis is hallucination, delusions and cognitive deficits have been documented.² Frank psychosis with hyper-religiosity and disorganised thought has not previously been reported as part of the clinical picture accompanying midbrain lesions.

CASE PRESENTATION

In September 2015, a 15-year-old boy with a history of midbrain tumour, status-postchemotherapy, radiation therapy and ommaya reservoir placement presented to the emergency department (ED) following several 1 min episodes described as seizures in school. The episodes involved rigidity, drooling and unresponsiveness. The patient's guardian had noted a history of increasingly frequent anger outbursts by the patient since 2011, with a concomitant rise in obsessive organising behaviours. In early 2013, the patient began exhibiting religious preoccupation and claiming to hear the voice of God instructing him to fulfil his destiny. The patient had previously described visual hallucinations of 'shadowy figures'

that reportedly increased during chemotherapy in 2013 and have been intermittently been reported since that time. Over the year leading up to his September 2015 admission, the patient's outpatient psychiatrist reported increasing psychotic features.

In the ED, the patient was disorganised and responding to internal stimuli. Medical staff witnessed an episode of apnoea with clonic extension of extremities and emesis, all lasting <5 min. A similar convulsive spell occurred during video EEG, which revealed no EEG evidence of seizure activity despite an outward appearance of convulsions. In the ED, the patient remarked that he was afraid to leave the hospital because of 'so many voices'.

The patient's medical history is significant for a pilocytic astrocytoma diagnosed in 2009. At age 8, he presented to an outside hospital with right-sided weakness, headache, mental status changes and seizures. MRI revealed an intra-axial mass lesion with extension into the left midbrain, thalamus and hypothalamus. Pathology was consistent with a pilocytic astrocytoma. He was treated with a chemotherapy regimen of carboplatin, vincristine and temozolomide, completing therapy in April 2011. In November 2012, the patient underwent focused radiation therapy for tumour progression, receiving 50.4 Gy focally to his tumour. He began another round of chemotherapy using vinblastine in January 2013, which was discontinued later that year when an October 2013 MRI showed cystic expansion. The cystic region was drained and has since been monitored by MRI. An ommaya reservoir was placed in December 2014 for persistent cyst reaccumulation.

The patient has a history of mood dysregulation predating the 2009 tumour discovery and has carried diagnoses of anxiety, obsessive-compulsive disorder (OCD), bipolar disorder and attention-deficit/hyperactivity disorder (ADHD). The patient has had multiple trials of antipsychotics, including aripiprazole and risperidone, which failed secondary to non-compliance. Social history is notable for psychosocial stress associated with early childhood trauma, unstable home life and periodic homelessness. Family history includes bipolar disorder in the mother and maternal aunt and schizophrenia in the maternal uncle. The patient's outpatient medications at the time of presentation were valproate 500 mg to be taken every 12 hours, perphenazine 4 mg two times a day and olanzapine 5 mg to be taken daily.

In the ED, his temperature was 37.4°C, blood pressure 116/65 mm Hg, pulse 84 bpm, respiratory rate 14 breaths/min, with 100% oxygen saturation on room air. Physical examination revealed mild,

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right-sided weakness without other focal neurological deficits. Mental status examination revealed that the patient was disorganised with a flat affect. He exhibited loose associations, thought blocking and impaired attention. He stated that he had been admitted for a 'panic attack' and explained that his life was a parallel of biblical figures. The patient endorsed auditory, but not visual hallucinations. He denied suicidality and homicidality.

The patient was admitted to psychiatry with a diagnosis of unspecified convulsions and psychosis, made by the ED medical staff with regard to the periods of apnoea with clonic extension of extremities in the context of disorganised thought and reaction to internal stimuli.

INVESTIGATIONS

Quick-brain MRI showed a 36×21 mm cystic mass centred in the left midbrain and cerebral peduncle, unchanged from imaging 1 month previously, without evidence of hydrocephalus (figure 1). As noted, EEG showed no abnormalities, despite capturing an episode of witnessed convulsions on video monitoring. All available EEG data in the electronic medical record have been read as normal without evidence of epileptogenic activity. Recent neuropsychological testing, including Wechsler Intelligence Scale for Children fifth edition (WISC-V), revealed an IQ of 67 (first centile), with severe deficits in processing speeds, but relatively spared visual-spatial reasoning indices. Similar testing from 2009, at the onset of the patient's chemotherapy, included fourth edition of WISC (WISC-IV) showing a second centile IQ and comparably severe deficits in processing speeds and other measures.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis discussed here includes three aetiologies: psychosis as primary psychiatric pathology, psychosis secondary to tumour treatment and psychosis secondary to a midbrain lesion.

TREATMENT

On admission, the patient's perphenazine was discontinued and he was resumed on valproate 500 mg to be taken every 12 hours and olanzapine 5 mg to be taken nightly. He spent 7 days as an inpatient for stabilisation and monitoring of the drug regimen.

OUTCOME AND FOLLOW-UP

The patient gradually showed less disorganisation and exhibited a broader range of affect, though hyper-religiosity continued. Following a week of improving psychotic symptoms, he was discharged with a primary diagnosis of unspecified psychotic disorder. This diagnosis was judged to be the most objective at the

time, considering the uncertainty surrounding specific aetiology, as well as least likely to lead future treatment teams in the wrong direction. The patient has since had several admissions with similar courses.

DISCUSSION

We report the case of a 15-year-old boy developing psychosis in the years following diagnosis and treatment of a midbrain tumour. The differential diagnosis discussed here includes psychosis as primary psychiatric pathology, psychosis secondary to tumour treatment and psychosis secondary to a midbrain lesion.

Psychosis could be the primary pathology, independent of his space-occupying brain lesion. The patient is young, but not an outlier with regard to onset of a psychotic syndrome on the schizophrenia spectrum.⁶ A mood disorder with psychotic features could also underlie the symptomatology. Of note, features of his presentation are consistent with catatonia, but an in-depth discussion of catatonia is beyond the scope of this report. The patient has hereditary and environmental risk factors for psychiatric disease. His maternal family history includes bipolar disorder in his mother and aunt and schizophrenia in his uncle. Paternal family history is unknown. Relatively stable IQ in the low range and persistent cognitive deficits over a 6-year period prior to documented psychotic symptoms suggests that these metrics may represent baseline characteristics of the patient. The presence of documented intellectual disability from a young age is relevant because mental illness, including psychotic disorders, has been reported to have a higher prevalence in intellectually disabled populations.^{7 8}

The patient has experienced psychological stress associated with an unstable home life, including periodic homelessness from a young age. The presentation discussed here occurred during the second week of school following a summer break. This acute stressor may have contributed to the patient's illness, precipitating either a psychotic break or psychosis associated with an underlying mood disorder. Psychiatric notes, however, describe the school's stabilising influence, where the patient gets medication as scheduled and has an individualised education plan. In contrast, during summers there is well-documented medication non-compliance. It is relevant here to mention that the patient's family is engaged in services of the government agency charged with attending to the needs of at-risk youth. This agency has decision-making authority regarding the safety of the homes and guardians of minors, and department officials make regular visits to evaluate the safety in the patient's home life. While this does not preclude neglect or abuse as contributing factors to the patient's mental illness, no evidence of acute changes in the patient's home life and guardianship has been noted by medical or departmental personnel.

Figure 1 (A) Sagittal and (B) axial slices of T2-weighted MRI from August 2015 compared with (C) an axial slice of the September 2015 admission MRI showing lack of significant change in size.

The patient's seizure-like episodes without an EEG correlate are worthy of comment. The confluence of psychiatric features and lack of EEG correlate suggest psychogenic non-epileptic seizures.⁹ However, a seizure was the original impetus for imaging in 2009 that revealed his brain tumour. Psychogenic non-epileptic seizures may coexist with epileptic seizures,¹⁰ but the lack of EEG abnormalities in the presence of an obvious anatomical candidate for an epileptic focus is curious. This may either exemplify the limits of EEG sensitivity or suggest a more complicated relationship between the patient's acquired brain injury and his psychiatric symptomatology.

One of the diagnostic criteria for primary psychotic disorders of the schizophrenia spectrum in DSM-5 is that the psychiatric disturbance not be attributable to another medical condition. Criteria for, psychotic disorder due to another medical condition however, stipulate that there be evidence that psychosis is the direct pathophysiological consequence of another medical condition.⁶ The patient then is somewhere in between, where it is difficult to dismiss his space-occupying CNS lesion or confidently to assign causality.

The course of the illness may also point to chronic morbidity associated with treatment of the tumour. The patient's hyper-religiosity reportedly crystallised over the year following his radiation therapy. Radiotherapy for intracranial tumours has indeed been associated with cognitive dysfunction.^{11 12} Late onset psychosis arising after treatment of childhood CNS malignancy has also been reported, but has been accompanied by either cortical tumour involvement or evidence of diffuse radiation damage from whole brain radiation.¹² The patient, however, has neither cortical tumour extension and nor did he receive whole brain radiation. Moreover, imaging shows no evidence of radiation injury. While neuropsychological testing was notable for low IQ and processing speeds in the extremely low range, these results were relatively consistent with testing at the start of the patient's chemotherapy in 2009. In the light of this, chemotherapy and radiation are insufficient to explain the patient's current presentation. Of note, no neuropsychological testing is available prior to discovery of the patient's brain tumour, so the impact of the neoplastic brain injury on his neuropsychological profile is unknown.

Psychosis is an atypical manifestation for cortex-sparing lesions, particularly those confined predominantly to the midbrain. However, there are reports associating such lesions with psychotic symptoms. Documented cases of psychosis secondary to cortex-sparing brain tumours have involved the hydrocephalus and germinomas of the pineal gland and basal ganglia.¹³ There are also reports of midbrain lesions leading to emotional lability and executive function deficits, with at least one report of psychotic features emerging after traumatic injury to the midbrain.^{14 15}

Dopaminergic and serotonergic systems are pharmacological targets of antipsychotic medications. Notably, the midbrain is the seat of dopaminergic nuclei for the entire human brain, as well as the serotonergic dorsal and medial raphe and nucleus linearus. Imaging studies suggest that patients with psychotic disorders have differences in connectivity between the midbrain and prefrontal cortex and others report differences in morphology of the midbrain compared to persons without psychotic disorders.^{16 17} Such studies lend credence to the possibility of a midbrain lesion contributing to psychiatric illness.

Peduncular hallucinosis is a rare, heterogeneous syndrome of visual and auditory hallucinations associated with midbrain lesions.¹⁻³ While the patient of this report clearly has symptomatology extending beyond hallucinations, it should be noted that

peduncular hallucinosis has been looked at through a broader lens encompassing some features overlapping with this case. Peduncular hallucinosis was described by Benke in 2006 as a 'syndrome of impaired reality monitoring'² with regard to delusional misidentification, anosognosia and confabulation. In the present case, the patient's failure to recognise his mother while talking to her in the ED echoes the misidentification observed in cases of peduncular hallucinosis.² While the patient showed clear signs of auditory hallucinations, remarking on 'so many voices', visual hallucinations were not a prominent feature of the presentation. The patient's history of visual hallucinations in the context of chemotherapy is remote and most likely of limited significance to the current presentation. Continued reports of hallucination are complicated by cultural and family beliefs, as the family endorses a cultural belief in spirits, with a history of seeing spirits in the maternal family. This limits the relevance of these reported hallucinations to the current diagnosis. However, the patient's guardian does remark that the patient's visions affect him negatively, which she suggests is atypical for her cultural belief system.

When combined with the hyper-religiosity and delusions of grandeur observed in this case, the impaired reality interaction is an aspect of peduncular hallucinosis that the patient's clinical picture fits well. The case reported here involves a midbrain lesion and disrupted reality monitoring, not inconsistent with peduncular hallucinosis. However, the patient's disorganised thought and the constellation of psychotic symptoms might be more aptly described as peduncular psychosis.

Learning points

- Non-psychiatric aetiology should be sought out when patients present with psychotic symptoms.
- Peduncular hallucinosis is a rare syndrome of hallucinations associated with lesions of the midbrain.
- This case suggests that midbrain lesions in a susceptible host may contribute to psychosis.

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