CASE REPORT

Locus coeruleus syndrome as a complication of tectal surgery

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SUMMARY

We describe a case of a 48-year-old woman who underwent a resection of a tectal pilocytic astrocytoma complicated by a sequence of fluctuating consciousness, psychosis with complex hallucinations and lasting sleeping disturbances in which she vividly acts out her dreams. Based on the clinical and anatomical evidence of this case, we propose the term locus coeruleus syndrome to describe this association of iatrogenic symptoms. Along with those of the locus coeruleus, lesions of the dorsal raphe nucleus, ventral tegmentum, substantia nigra pars compacta, the superior colliculus and other peduncular lesions (such as peduncular hallucinosis) are involved in the regulation of sleep-wake/arousal, behaviour, sleeping disorders and rapid eye movement atonia. However, iatrogenic lesion of the locus coeruleus could explain the complications on all levels in our patient.

BACKGROUND

Tectal tumours are well-circumscribed, indolent lesions that follow a benign course and simply warrant radiological follow-up.¹ Neurosurgical intervention is, however, needed when these tumours induce progressive local deficits, obstructive hydrocephalus or are suspected of anaplastic transformation based on imaging. Cerebrospinal fluid-circulation shunting, third ventriculostomy or microsurgical resection then become indicated.

Tumour surgery in the tectal region remains challenging. Complications depend on the local vascular and neurological anatomy of this region, and notably comprise homonymous hemianopia, hydrocephalus, extraocular palsies, Parinaud's syndrome, extrapyramidal disorders and even coma.²⁻³

The locus coeruleus is a noradrenergic (NA) system that modulates behavioural and forebrain activity, and state-dependent cognitive processes, and is located in the direct vicinity of the tectum.⁴ Damage to this nucleus can result in cognitive dysfunction, psychiatric conditions and sleep and arousal disorders.⁵⁻⁶ This report illustrates a novel, severe, albeit in this case to a large extent reversible, complication of tectal surgery.

CASE PRESENTATION

A 48-year-old patient with no relevant history presented with recurrent syncope, vertigo, intermittent diplopia, walking disturbances and diminished vision of the right eye for several weeks; papilloedema was objectified. MRI showed a non-enhancing 2.1 by 1.6 cm tectal cystic lesion and an obstructive hydrocephalus. Symptoms were

relieved by placement of a ventriculoperitoneal shunt. For 7 years, the tumour did not progress clinically or radiologically. However, even though clinically asymptomatic, the tumour began to enhance with contrast on MRI. Neurosurgical intervention was indicated for fear of anaplastic transformation ([figure 1](#)).

TREATMENT

Standard left occipital transtentorial craniotomy²⁻³ was performed allowing a complete resection of the tumour. Histological examination showed a pilocytic astrocytoma.

OUTCOME AND FOLLOW-UP

Postoperatively, the patient awoke slowly in the intensive care unit with bilateral gaze paresis. She followed simple orders, but would neither speak nor follow finger movements with the eyes. On day 1, the patient became even less alert. Classical complications such as hydrocephalus, ischaemia, haemorrhage, infection and metabolic disorders were ruled out by CT and laboratory tests. EEG on the other hand demonstrated diffuse encephalopathy, without any signs of epilepsy. She was considered to suffer from a pure sleep-arousal disturbance. After 4 days she began to speak again and the arousal symptoms completely recovered within 11 days. The patient, however, developed an extensive unilateral pneumonia for which antibiotic therapy (ceftriaxone) was started. Despite rapid resolution of this infection, the patient remained disorientated, with mild anterograde amnesia, attention deficits, a pupil-sparing third and a fourth cranial nerve palsy and mild right-sided paresis. Brain MRI revealed a small amount of bleeding in the quadrigeminal plate, oedematous changes of the tectum down to the level of the locus coeruleus and complete removal of the contrast-enhancing tumour ([figure 2](#) left-plane). The symptoms resolved slowly, and the patient was discharged to a rehabilitation facility.

Forty-eight days after the surgery, the patient had to be readmitted to our ward due to increased memory loss, disorientation and the development of anxiety, auditory hallucinations and religious delusions. Neuroimaging showed complete resolution of the postoperative changes; EEG and laboratory tests were unremarkable. Drug-induced psychosis was ruled out and antipsychotic drugs (quetiapine and benzodiazepine) were started. The patient's symptoms almost completely disappeared within 3 weeks and the drugs were discontinued. The patient, however, began to complain of vivid

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Figure 1 Preoperative gadolinium-enhanced T1-weighted MRI showing the tectal tumour and its contrast enhancement.

dreams, where the normal inhibition of movements and tonus did not occur. Her husband confirmed these symptoms, notably mentioning that the patient regularly hit him during her sleep when she dreamed of playing tennis.

At 18-month follow-up, the motor, equilibrium and cranial nerve deficit had completely recovered except for a light paresis of the right fourth cranial nerve, and the patient did not suffer any residual psychotic symptoms. She did, however, still complain of vivid dreams.

DISCUSSION

In this case report, we described a sequence of unusual complications that followed the surgical resection of a tectal tumour.

First, 24 h postoperatively, our patient suffered from a *dysregulation of the sleep-wake/arousal state*, which fully recovered after 11 days. Multiple areas of the brain stem and basal forebrain neural systems—for instance, the perimesencephalic nucleus of the reticular activating system—are located relatively close to the tectum and regulate the arousal state through the serotonin (5-HT), dopamine DA, cholinergic, histaminergic and NA (table 1).^{4 8 9} Among these, the locus coeruleus-NA system is paramount^{4 5} and is located in the direct vicinity of postoperative MRI changes observed in our patient (figure 2 right plane). This small pontine brainstem nucleus provides, through its projections to the hippocampus, thalamus and neocortex, most of the norepinephrine (NE) in the central nervous system,

except the basal ganglia.⁵ Through activation of central NA receptors, the locus coeruleus provides an alert waking state: even moderate activity of the locus coeruleus-NA system is incompatible with the state of sleep and generally lesions of these nuclei do not cause somnolence. Conversely, blockage of these receptors or suppression of NE release causes a sedative state with slow-wave activity on EEG,⁴ reminiscent of the diffuse encephalopathy EEG signs of our patient. In animal experiments, lesions of the locus coeruleus also provoke a transient period of inactivity and a sedative state, before compensation develops within the NE-system, within 5–14 days,⁵ a sequence that correlates well with the time course of the disrupted sleep-wake/arousal state in our patient.

Later, the patient suffered a *psychosis*, consisting of auditory hallucinations and religious delusions inducing a great amount of fear. NE has been shown to influence the collection and processing of sensory information, attention and memory processes and dysregulation of the locus coeruleus can cause cognitive and/or psychiatric disorders.^{4–6} Alternatively, this psychosis might have resulted from a postoperative tectal dysfunction, where the superior colliculus has been shown to participate to the inhibition of fear both in animal and pharmacological studies,¹¹ or from other peduncular lesions, as seen in the so-called peduncular hallucinosis (table 1).^{10 12}

Finally, our patient experienced vivid dreams, in which, for example, she performed tennis movements when dreaming

Figure 2 Postoperative changes and anatomy of the locus coeruleus. Left plane: 12-day postoperative sagittal gadolinium-enhanced T1-weighted MRI illustrating the resection cavity with a small haemorrhage in the tectal plate and local oedema. Right plane: A transversal histological section of an unrelated cadaver midbrain illustrates the area of the locus coeruleus (LC) and its proximity to the inferior colliculus (IC) and the fourth ventricle (IVth).

Table 1 Brainstem structures and syndromes that may cause disturbances of the sleep-arousal cycle, behavioural disorders or psychosis and/or RBD when altered, and located in the vicinity of the tectum

Disorder	Nucleus involved	Other explanatory related nuclei or syndromes	
Sleep-awake/arousal disturbances	Locus coeruleus ^{3–5 7}	Dorsal raphe nucleus ^{8 9} <i>Peduncular hallucinosis</i> ^{2 10}	Ventral tegmentum area/substantia nigra pars compacta (DA) ^{7 11}
Behavioural disorder/psychosis	Locus coeruleus ^{4 12}	<i>Peduncular hallucinosis</i> ¹⁰	Superior colliculus ¹³
REM-sleep behaviour disorder (RBD)	Locus coeruleus ^{5 14}		

DA, dopamine; RBD, rapid eye movement behaviour disorder; REM, rapid eye movement.

about playing this sport. This *sleeping disorder* is named a rapid eye movement (REM) behaviour disorder (RBD) or REM sleep without atonia.¹³ A number of brainstem regions (eg, the pons and the disinhibition of mesencephalic motor pattern generators) and neurotransmitters contribute in the atonia of REM sleep.^{9 13} In humans, indeed, acute RBD is usually induced by medications (such as tricyclic antidepressants, monoamine oxidase inhibitors, serotonin-specific reuptake inhibitors, etc) and chronic causes are found in neurodegenerative disorders such as Parkinson disease.¹³ In animal studies, however, RBD also ensues following bilateral lesions of the locus coeruleus in cats, rats and rabbits,^{9 15} and we believe that iatrogenic damage to this nucleus may have been responsible for the RBD symptoms of our patient.

Learning points

- Surgery of the tectal area remains challenging.
- Structures involved in the regulation of sleep-wake/arousal, behaviour, sleeping disorders and rapid eye movement atonia are located in or close to the tectum.
- Severe complications due to iatrogenic tectal lesions may be reversible.

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