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THE CUSHING RESPONSE EVOKED BY A FOURTH VENTRICULAR BRAINSTEM MASS

We report a case of a patient with a mass lesion of the pontomedullary junction with paroxysmal episodes of autonomic and other homeostatic dysfunction that echo the classic Cushing response to intracranial hypertension.¹

Case report. A 32-year-old man presented with episodes of (1) involuntary eye, eyelid, and facial movements; (2) conjunctival injection; (3) blurry vision; (4) diaphoresis and sometimes pruritus and mild rashes; (5) hypertension; (6) bradycardia and feeling faint; (7) hoarse or deepened voice; (8) dyspnea; and (9) gastrointestinal distress. Other symptoms were chronic: difficulty sleeping, excessive daytime sleepiness, and depression. The episodes, although sometimes spontaneous, were reliably triggered by state change (arising or falling asleep), abrupt startles or emotive triggers, orgasm, or Valsalva-inducing triggers. Episodes were at their worst at onset with ~12 hours gradual improvement.

The patient had first presented at 6 months of age when frequent gagging or emesis occurred during feedings; short stature was linked to gastrointestinal symptoms. By age 4 years, he had onset of daily episodes of eyelid fluttering. A notation of a “possible right Horner” was mentioned during examination. Two findings from extensive endocrinologic and neurologic evaluations stood out: although brain/brainstem MRIs were not all available for our review, one report noted a “right enlarged cerebellar tonsil.” Arterial blood gases measured during an overnight evaluation disclosed hypercapnic hypoxemia.

During admission to our epilepsy unit, the patient’s interictal examination results were normal. The patient had 2 episodes: the first triggered by a bowel movement, the second by an abrupt startle. Initial symptoms included oscillatory nystagmus, blepharospasm, flushed appearance, and pruritus, with normal attention and cognition. Video-EEG/multimodal polygraphy demonstrated eye movements, normal wakefulness, irregular breathing, and oxygen desaturation. Both episodes featured hypercapnic hypoxemia, bradycardia, and hypertension similar to the classic Cushing response (figure).

Brain/brainstem MRI revealed a 0.9×1.4 cm nonenhancing mass projecting into the roof of the fourth ventricle (figure). A noncontrast MRI from 2004 from another institution revealed the same finding, not commented upon in the report.

Polysomnography demonstrated a central apnea-hypopnea index of 111/hour with O₂ saturation nadir of 80%. Outpatient wrist actigraphy showed mixed features of an irregular, non-24 rest-activity pattern and a free-running, poorly entrained pattern with a daily delay of ~1.5 hours/day. Brainstem auditory and median nerve somatosensory evoked potentials were normal. Blood glucoses/chemistries, morning cortisol, and 24-hour collections of catecholamines, 5-hydroxyindoleacetic acid, and vanillylmandelic acid were normal.

Discussion. The patient’s episodes comprise the triad of the Cushing response: hypertension, bradycardia, and hypoventilation. An acute supratentorial mass lesion that causes intracranial hypotension evokes the classic response, which most investigators believe to be a physiologic attempt to maintain cerebral perfusion.¹ In contrast, sensory stimuli, made potent by a chronic mass located in the fourth ventricle, trigger the events of the current patient.

The case makes associations among the patient’s symptoms, his brainstem mass, and symptoms similar to the Cushing response. Animal models, either with supratentorial mass lesions or fourth ventricular electrical or pharmacologic stimulations, demonstrate localization of the Cushing response at the level of the baroreceptor complex at the fourth ventricle along bilateral paramedian strips.² The current case most resembles that of an occult pontine astrocytoma masquerading as pheochromocytoma³; the main differences are in that the earlier case, attacks of hypertension were accompanied by tachycardia rather than the bradycardia of the classic triad, respiratory changes were not documented, and plasma catecholamines were elevated between attacks.

To our knowledge, this case uniquely demonstrates the salient features of the Cushing response not elicited by intracranial hypertension or by physical manipulation of the brainstem. In contrast to the current case, most other reports of brainstem mass lesions with autonomic consequences—tumors of primary or metastatic

(A) Results of arterial blood gas collections and cardiac monitoring demonstrated the acute onset of a Cushing response of the triad of hypoventilation (acidosis, hypoxia, and hypercapnea), hypertension, and bradycardia that improved gradually over 8-12 hours. (B-I) Magnetization-prepared rapid gradient echo sequence MRI demonstrated a $0.9 \times 0.9 \times 1.4$ cm exophytic smooth, homogeneous lobulated mass arising from the right posterolateral medulla/inferior cerebellar peduncle that projected into the inferior aspect of the fourth ventricle, the foramen of Magendie, and the right foramen of Luschka. (B-G) Axial cuts through the pontomedullary brainstem. (H) Locator sagittal and (I) detail sagittal cuts through the mass. T2 and contrast sequences were also obtained (not shown). The mass followed normal white matter signal except for a small focus of increased T2 signal at the lateral edge of the mass. There was no evidence of acute or chronic infarct, hemosiderin deposits, intracranial hematoma, or extra-axial fluid collection. There was no abnormal contrast enhancement. The brain and other regions of the brainstem were normal. Interpretation included dysplasia, hamartoma, or low-grade exophytic medullary glioma.

source—focus on syncope or presyncope arising from orthostatic hypotension.^{1,4–7} These cases involve alteration of baroreceptor input into cardioregulatory centers with motor or sensory “neighborhood signs.”^{4–7} In contrast, the current case, probably because of the indolent nature of the mass, forms a dysmodulatory network rather than an interruptive lesion, an opinion reinforced by the absence of any fixed deficits and by normal evoked potentials.

Autonomic dysfunction beyond that of the Cushing response was present. Oscillatory nystagmus and circadian dysfunction probably represent the closest analogue to en passant dysfunction demonstrated in the patient.

We report a man with a syndrome of a static pontomedullary mass who has episodes of inappropriate, triggered dysautonomia—a reflexic Cushing response. Further follow-up and serial neuroimaging will be required to provide a clear diagnosis of the mass. Brainstem masses may present solely with transient physiologic abnormalities.

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