Rhombencephalitis in cocaine-induced nasal septal perforation and skull base erosion

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ABSTRACT

Rhombencephalitis is a rare and potentially fatal condition involving the brainstem, with infectious, autoimmune, and paraneoplastic etiologies. We present a patient presenting with left-extremity weakness and dysphonia who had brainstem imaging findings suggestive of rhombencephalitis. We suspect that the case was due to inoculation of the brainstem from nasopharyngeal adenoviral infection. Due to heavy cocaine use, extensive basiocciput erosion led to direct contact between the brainstem and the nasopharyngeal mucosa. The patient's milder clinical course might have been due to some degree of pre-existing immunity against adenovirus. Additionally, clinicians need to be aware of the proximity of the brainstem to the nasopharynx when there is basiocciput erosion, due to the potential risk of injury during instrumentation.

KEYWORDS Cocaine abuse; direct spread; rhombencephalitis; skull base erosion

Rhombencephalitis is a potentially fatal inflammation involving the components of the brainstem (midbrain, pons, and medulla) as well as the cerebellum. There are several causes of rhombencephalitis, including neoplastic, autoimmune, and infectious processes secondary to either bacterial or viral agents.^{1–5} We encountered a patient with symptoms of left-extremity weakness and dysphonia. Imaging revealed extensive basiocciput erosion from prior cocaine abuse and findings suggestive of rhombencephalitis.

CASE PRESENTATION

A 38-year-old man with no significant past medical history presented to our outpatient imaging center for evaluation of fever, persistent throat and neck pain, left arm and leg weakness, and progressive dysphonia. He also had a recent episode of upper respiratory tract infection. He was not taking any medicines. He had been a heavy cocaine user. Computed tomography (CT) of the cervical spine demonstrated a lack of the C2 dens, anterior arch of C1, and partial absence of the clivus. The nasal septum, nasal turbinates,

and medial walls of the maxillary sinuses were absent (*Figure 1*).

Magnetic resonance imaging (MRI) performed at the time of presentation (*Figure 2*) demonstrated extensive signal abnormalities in the inferior pons and medulla, including T2/fluid attenuation inversion recovery (FLAIR) sequence hyperintensity in the same area, with no significant contrast enhancement. Diffusion-weighted images did not demonstrate evidence of restricted diffusion to suggest infarction. The brainstem was found to be intimately contacting the nasopharyngeal mucosa. A subsequent nasal swab was positive for adenovirus. A nasal septal and nasopharynx biopsy performed at an outside institution reported only inflammatory changes, without evidence of infection or granulomatous changes. Rheumatologic workup demonstrated negative anti-nuclear antibody screen and a rheumatoid factor of 10 IU/mL. The patient was treated with antibiotics and later experienced a resolution of symptoms. Unfortunately, a lumbar puncture was not performed, because the patient declined any invasive procedure. A follow-up brain MRI after 2 months demonstrated complete resolution of the brainstem signal abnormalities (*Figure 3*).

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Figure 1. CT of the sinus obtained prior to the patient's current presentation. **(a)** Coronal view at the level of the basiocciput shows an absence of the odontoid with irregular, sclerotic margins. **(b)** A midline sagittal image demonstrates a markedly eroded clivus with increased distance between the clivus and remnant of the dens (blue double arrow). The basion-dens interval is measured at 3.8 cm (not shown; normal is <8.5 mm on CT). **(c)** A more anteriorly located coronal view showing the extent of the erosion.

Figure 2. Brain MRI obtained without and with intravenous contrast. **(a)** Sagittal T1-weighted image at midline demonstrates the nasopharyngeal mucosa directly contacting the medulla (thick blue arrow), without intervening cerebrospinal fluid. **(b, c)** Contiguous axial T2 FLAIR images show marked hyperintensity of the brainstem (red arrow). **(d)** Diffusion-weighted image and **(e)** apparent diffusion coefficient show increased signal on both sequences (yellow circle), indicating T2 shine through without restricted diffusion. **(f)** A similar T1-weighted postcontrast image at a same level does not show any abnormal enhancement.

DISCUSSION

The most common causative agents of rhombencephalitis include *Listeria monocytogenes*, enterovirus 71, and herpes simplex virus. Adenovirus is a rare cause, and adenovirus-associated rhombencephalitis usually presents with cerebellar

Figure 3. A repeat brain and cervical spine MRI obtained 2 months after resolution of the symptoms. **(a)** T1-weighted image extension and **(b)** flexion images of the cervical spine again demonstrate intimate association of the nasopharyngeal mucosa to the inferior pons and medulla. The nasopharyngeal mucosa appears to be adherent to the medulla. **(c, d)** Abnormal T2/fluid attenuation inversion recovery hyperintensity of the medulla in the previously involved region demonstrates resolution of abnormal signal (yellow circle).

ataxia. Because this virus is so common and immunocompetent adults are almost always immunized, observations of sequelae in this population are highly unlikely.⁶ In immunocompromised populations, the most common pathogenesis is hematological spread of the virus to the brain. Our patient, although immunocompetent, had no other suspected obvious source of infection. Therefore, we attribute the occurrence of this condition to direct anatomic contact and subsequent viral inoculation from nasopharyngeal mucosa to the affected region of the brainstem. Resolution of symptoms with antibiotics and negative immunological workup excluded other etiologies as well.

Imaging is used to support clinical and laboratory investigations. CT is of limited utility in diagnosis of encephalitis. MRI is the preferred method of evaluation of encephalitis due to its superior sensitivity and specificity compared to CT. T2-weighted MRI typically shows nonspecific elevated signal hyperintensity in areas of edema. FLAIR may offer increased sensitivity in early infection and aid in the detection of more subtle patterns of injury. Diffusion-weighted images can be used to distinguish edema from infarction versus inflammation/infection causes.^{7–9} These imaging sequences may provide the necessary information to yield a diagnosis when combined with laboratory testing and clinical exam.

Diagnosis of rhombencephalitis is established by cerebrospinal fluid analysis, which demonstrates increased lymphocytes, proteins and intracranial pressure.^{3,6,10} It is crucial to determine the cause of the rhombencephalitis for optimal

management. Because *Listeria* and herpes simplex virus are the two most common treatable causes of rhombencephalitis, treatment directed at these two pathogens should be initiated empirically with ampicillin and acyclovir.¹¹ Imaging, such as brain MRI, can be performed after treatment is initiated but should not delay initiation of treatment.⁴ If atypical organisms are suspected, doxycycline should be added empirically.¹¹

Though cocaine use was the most likely cause of skull base erosion in this patient, other causes may lead to a similar appearance. Other reported etiologies include crowned dens syndrome, tubercular infection, invasive aspergillosis, malignancy such as nasopharyngeal carcinoma, and expansion of local tumors such as craniopharyngioma or prolactinoma.^{12–17} Of these cases, none were reported to be associated with rhombencephalitis. Extensive review of the literature revealed only two reported cases of clival destruction and rhombencephalitis associated with cocaine use. Both case reports described culture-positive multi drug-resistant *Staphylococcus aureus* rhombencephalitis in patients with skull base lesions secondary to chronic cocaine abuse.^{18,19} Unfortunately, because our patient declined invasive testing, isolation of organisms could not be performed, but the most likely culprit was secondary to adenovirus infection from the adjacent nasopharyngeal mucosa.

We present this case to emphasize the importance of detailed radiological workup prior to any surgical planning to anticipate difficulties or complications in patients presenting with cocaine abuse, where destruction of the clivus and nasal septum can be seen. The treating clinician should be aware of anatomic considerations in such patients, because any nasopharyngeal procedure can be potentially challenging due to additional risk of injury and infection.

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- Campos LG, Trindade RAR, Faistauer Â, Pérez JA, Vedolin LM, Duarte JÁ. Rhombencephalitis: pictorial essay. *Radiol Bras*. 2016; 49(5):329–336.
- Noel N, Hutié M, Wechsler B. Pseudotumoural presentation of neuro-Behcet's disease: case series and review of literature. *Rheumatology*. 2012;51(7):1216–1225. doi:10.1093/rheumatology/ker449.
- Moragas M, Martínez-Yélamos S, Majós C, Fernández-Viladrich P, Rubio F, Arbizu T. Rhombencephalitis: A series of 97 patients. *Medicine (Baltimore)*. 2011;90(4):256–261. doi:10.1097/MD.0b013e318224b5af.
- Jubelt B, Mihai C, Li TM, Veerapaneni P. Rhombencephalitis/brainstem encephalitis. *Curr Neurol Neurosci Rep*. 2011;11(6):543–552. doi:10.1007/s11910-011-0228-5.
- Kumar Y, Drumsta D, Mangla M, et al. Toxins in brain! Magnetic resonance (MR) imaging of toxic leukoencephalopathy—a pictorial essay. *Pol J Radiol*. 2017;82:311–319. doi:10.12659/PJR.901791.
- Zagardo MT, Shanholtz CB, Zoarski GH, Rothman MI. Rhombencephalitis caused by adenovirus: MR imaging appearance. *AJNR Am J Neuroradiol*. 1998;19(10):1901–1903.
- Steiner I, Budka H, Chaudhuri A, et al. Viral encephalitis: A review of diagnostic methods and guidelines for management. *Eur J Neurol*. 2005;12(5):331–343. doi:10.1111/j.1468-1331.2005.01126.
- Kumar G, Kalita J, Misra UK. Raised intracranial pressure in acute viral encephalitis. *Clin Neurol Neurosurg*. 2009;111(5):399–406. doi:10.1016/j.clineuro.2009.03.004.
- Bhatt N, Gupta N, Soni N, Hooda K, Sapire JM, Kumar Y. Role of diffusion-weighted imaging in head and neck lesions: pictorial review. *Neuroradiol J*. 2017;30(4):356–369. doi:10.1177/1971400917708582.
- Michael LM, Mazumder SA, Gelfand MS. Differential diagnosis of a patient with rhombencephalitis: case study. *Infect Dis Clin Pract*. 2011;19(2):134–136. doi:10.1097/IPC.0b013e3181f47394.
- Tunkel AR, Glaser CA, Bloch KC, et al. The management of encephalitis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis*. 2008;47(3):303–327. doi:10.1086/589747.
- Ali S, Hoch M, Dadhania V, Khurana JS. CPPD crowned dens syndrome with clivus destruction: a case report. *J Radiol Case Rep*. 2011; 5(8):30–37. doi:10.3941/jrcr.v5i8.802.
- Hoshino C, Narita M. Craniovertebral junction tuberculosis: A case report and review of the literature. *J Infect Chemother*. 2010;16(4): 288–291. doi:10.1007/s10156-010-0052-x.
- Fang FM, Leung SW, Wang CJ, et al. Computed tomography findings of bony regeneration after radiotherapy for nasopharyngeal carcinoma with skull base destruction: Implications for local control. *Int J Radiat Oncol Biol Phys*. 1999;44(2):305–309.
- Lee Y, Kim S, Lim D, Park J, Chung Y, Kim Y. Isolated petroclival craniopharyngioma with aggressive skull base destruction. *Yonsei Med J*. 2009;50(5):729–731. doi:10.3349/ymj.2009.50.5.729.
- Narese D, Virzi V, Virzi G, et al. Ectopic prolactinoma in the clivus: a case report. *Clin Ter*. 2015;166(4):176–178.
- Wenzel S, Sagowski C, Kehrl W, Metternich FU. Course and therapy of an invasive aspergilloma of the skull base in a non-immunocompromised patient. *HNO*. 2004;52(8):724–728.
- Dubow JS, Singer S, Segal AZ. Rhombencephalitis due to cocaine-induced bony erosion of skull base. *Neurology* 2011;77(13):1313 doi: 10.1212/WNL.0b013e318230209a.
- Molteni M, Saibene AM, Luciano K, Maccari A. Snorting the clivus away: an extreme case of cocaine-induced midline destructive lesion. *BMJ Case Rep*. 2016;2016. pii: bcr2016216393. doi: 10.1136/bcr-2016-216393.