Open Access Original Research Article

MedPeer Publisher
Abbreviated Key Title: MedPeer
ISSN : 3066-2737
homepage: https://www.medpeerpublishers.com

From Subtle Insular Changes to Cerebral Circulatory Arrest: Serial CT Evolution of Fulminant Herpes Simplex Virus Type 1 Encephalitis

DOI: 10.70780/medpeer.000QGVY

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ABSTRACT

Herpes simplex virus type 1 (HSV-1) encephalitis is a major cause of sporadic viral encephalitis in adults and may initially present with subtle or nonspecific findings on computed tomography (CT). We report the case of a 69-year-old man presenting with a seizure and persistent impairment of consciousness, without fever or other overt clinical features suggesting infection. Initial non-contrast CT demonstrated subtle isolated loss of the left insular ribbon, raising the possibility of early ischemia but remaining nonspecific in this clinical setting. HSV-1 encephalitis was subsequently confirmed by cerebrospinal fluid analysis, and antiviral therapy was initiated. Despite treatment, the patient remained unconscious, and serial CT demonstrated rapid progression to extensive bilateral, left-predominant encephalitic involvement with severe cerebral edema, intracranial hypertension, and mass effect, ultimately followed by cerebral circulatory arrest. This case highlights the diagnostic challenge of early HSV-1 encephalitis, as an isolated subtle insular abnormality may overlap with ischemic or peri-ictal abnormalities. HSV encephalitis should therefore remain in the differential diagnosis in patients presenting with seizures and persistent impairment of consciousness, even in the absence of fever or other overt infectious features and before the characteristic temporo-limbic imaging pattern becomes apparent.

KEYWORDS

Herpes Simplex Encephalitis, HSV-1, Intracranial Hypertension, Cerebral Circulatory Arrest, Encephalitis

MAIN ARTICLE

INTRODUCTION

Herpes simplex virus type 1 (HSV-1) is a major cause of sporadic encephalitis in adults and remains associated with substantial neurological morbidity and mortality despite the availability of effective antiviral therapy [1,2]. Early administration of intravenous acyclovir is a major determinant of outcome, making prompt recognition particularly important [2,3].

Neuroimaging plays an important role in the diagnostic evaluation of suspected HSV encephalitis. Magnetic resonance imaging (MRI) is substantially more sensitive than computed tomography (CT), particularly during the early phase of disease, and typically demonstrates asymmetric abnormalities involving the mesial temporal lobes, insulae, and other components of the limbic system [1,4]. Initial CT findings, however, may be absent, subtle, or nonspecific. Classic CT series described unilateral low-attenuation abnormalities involving the medial temporal lobe and/or insular cortex early in the disease course [6]. These findings can overlap with other acute neurological conditions, particularly in patients presenting with seizures, as peri-ictal imaging abnormalities may themselves mimic acute ischemia or encephalitis [5].

In severe cases, HSV encephalitis may progress beyond the typical temporo-limbic distribution and lead to extensive cerebral edema, intracranial hypertension, and hemorrhagic necrosis [8-10]. We report the serial CT evolution of fulminant HSV-1 encephalitis initially presenting with an isolated subtle insular abnormality in an afebrile patient with a seizure and persistent impairment of consciousness, and subsequently progressing to extensive bilateral encephalitic involvement, severe cerebral edema, intracranial hypertension, and cerebral circulatory arrest. This case highlights the importance of considering HSV encephalitis in this clinical setting even when early CT findings are nonspecific and overt infectious features are absent.

CASE PRESENTATION

A 69-year-old man was admitted following a seizure with persistent impairment of consciousness. He was afebrile at presentation, with no other overt clinical features suggesting an infectious process.

Initial non-contrast CT of the brain demonstrated loss of the left insular ribbon (Figure 1). Given the acute presentation, an early ischemic abnormality was considered; however, the finding remained nonspecific in the setting of a recent seizure.

As the impairment of consciousness persisted, encephalitis was considered in the differential diagnosis and a lumbar puncture was performed. A second non-contrast CT obtained approximately 24 hours later because of the absence of clinical improvement showed no significant interval progression of the previously identified insular abnormality.

Cerebrospinal fluid analysis demonstrated an elevated protein concentration of 0.71 g/L, and polymerase chain reaction (PCR) testing was positive for HSV-1, establishing the diagnosis of HSV-1 encephalitis. Intravenous acyclovir therapy was initiated 48 hours after symptom onset.

Despite treatment, the patient remained unconscious. A third non-contrast CT obtained on day five demonstrated marked progression, with extensive bilateral cortico-subcortical hypodensity, markedly predominant in the left cerebral hemisphere. The abnormalities involved both temporal lobes and insulae, the cingulate gyri, frontal lobes, and parahippocampal gyri, with additional involvement of the basal ganglia and left thalamus (Figure 2).

Extensive associated cerebral edema had developed, particularly within the left frontal region, resulting in diffuse sulcal effacement, greater on the left, compression of the left lateral ventricle, and approximately 4 mm of rightward midline shift. There was associated effacement of the ambient cisterns. Additional findings included prominence of the Meckel caves and tortuosity of the optic nerves (Figure 3).

New swelling and hypodensity of the midbrain and pons were also present. In the context of severe intracranial hypertension and extensive cerebral edema, these abnormalities were considered to reflect severe brainstem involvement and/or secondary brainstem injury (Figure 4).

Within hours of this examination, the patient developed bilateral fixed, nonreactive mydriasis, raising clinical suspicion of death by neurologic criteria. Given this rapid neurological deterioration, decompressive surgery was not pursued. CT angiography was

subsequently performed to assess cerebral circulation and demonstrated bilateral absence of opacification of the M4 cortical branches of the middle cerebral arteries and the internal cerebral veins, consistent with cerebral circulatory arrest (Figure 5).

DISCUSSION

HSV encephalitis remains a neurological emergency despite the availability of effective antiviral therapy. Contemporary series continue to report substantial mortality and long-term neurological disability, and delayed initiation of acyclovir is consistently associated with unfavorable outcome [1-3]. The present case is notable both for the diagnostic challenge of its early presentation and for its fulminant radiological and clinical progression, beginning with an isolated subtle insular abnormality and culminating in extensive bilateral encephalitic involvement, severe cerebral edema with intracranial hypertension, and cerebral circulatory arrest within less than one week of symptom onset.

The clinical presentation itself illustrates an important diagnostic consideration. Our patient presented with a seizure followed by persistent impairment of consciousness but was afebrile and had no other overt clinical features suggesting infection. Although fever is common in HSV encephalitis, its absence does not exclude the diagnosis. In a recent prospective population-based cohort of adults with HSV-1 encephalitis, only 62% of patients were febrile at admission, while altered consciousness was present in the majority [4]. Seizures are also a recognized manifestation of HSV central nervous system infection [1,4]. Persistent unexplained impairment of consciousness following a seizure should therefore raise the possibility of encephalitis even in the absence of fever or other overt infectious features. In our patient, the persistence of impaired consciousness prompted consideration of encephalitis and cerebrospinal fluid analysis, which established the diagnosis of HSV-1 encephalitis.

The initial CT further illustrates the diagnostic difficulty of early HSV encephalitis. Loss of the insular ribbon, reflecting reduced gray-white matter differentiation at the insular cortex, is a well-recognized early sign of cerebral ischemia, while peri-ictal abnormalities may similarly produce focal cortical hypoattenuation and swelling [5]. The insula, however, is also a characteristic site of HSV encephalitis involvement. In a classic CT series, the most characteristic initial abnormality was a unilateral low-density lesion involving the medial temporal lobe and/or insular cortex, identified on the initial examination in 10 of 13 patients [6]. More recently, MRI literature has emphasized the diagnostic relevance of insular

involvement through the “insular knife-cut” sign, defined as a sharp boundary between FLAIR hyperintensity of the insular cortex and the basal ganglia. In a 2025 cohort, this sign was present on initial MRI in 52.3% of patients with HSV encephalitis and had a specificity of 99.3% [7]. This MRI sign should not, however, be directly extrapolated to CT. Although insular involvement is therefore well established in HSV encephalitis, a subtle isolated insular ribbon abnormality on early CT is not an established specific sign of the disease. In the present case, the isolated left insular abnormality initially raised a differential diagnosis including early ischemia, a peri-ictal abnormality, and early encephalitic involvement. Its subsequent evolution into a characteristic temporolimbic pattern emphasizes that HSV encephalitis should remain in the differential diagnosis when an unexplained insular cortical abnormality accompanies persistent impairment of consciousness after a seizure, even before temporal-lobe abnormalities become apparent.

The early radiological evolution is also noteworthy. The second CT showed no significant progression of the isolated insular abnormality despite persistent impairment of consciousness. This initial imaging stability did not predict the subsequent clinical or radiological course. By day five, the abnormalities had progressed dramatically and acquired a distribution much more characteristic of HSV encephalitis. HSV-1 has a marked predilection for the temporal and limbic regions. In a recent clinical series, temporal lobe abnormalities were identified in more than 90% of patients, with frequent involvement of the insula and frontal lobes [2]. The combination of temporal, insular, parahippocampal, and cingulate involvement subsequently observed in our patient therefore followed the characteristic anatomical distribution of the disease. Bilateral involvement is well recognized but is often asymmetric, as was strikingly demonstrated in this case, with substantially greater abnormalities in the left hemisphere [1,2].

The progression also extended beyond the classical temporolimbic regions to the frontal lobes, basal ganglia, thalamus, and brainstem. Involvement of three or more lobes was significantly more frequent among patients with severe neurological outcomes in a recent clinical series [2]. The absence of substantial progression on the early repeat CT should therefore not provide false reassurance when neurological impairment persists. Likewise, persistent or worsening neurological impairment after diagnosis and initiation of treatment should prompt consideration of repeat neuroimaging to evaluate for disease progression and its complications.

Deep gray nuclear and brainstem abnormalities are less characteristic than temporal and insular involvement. Although HSV encephalitis can extend beyond the limbic system in severe disease, the ponto-mesencephalic abnormalities observed in our patient should be interpreted cautiously. Their development occurred concurrently with extensive cerebral edema and severe intracranial hypertension. Direct extension of the encephalitic process cannot be excluded on CT alone; however, secondary brainstem edema and injury related to severe intracranial hypertension may also have contributed. MRI could have provided additional characterization of these abnormalities; however, no MRI examination was performed.

The most severe complication in this case was the development of severe cerebral edema. Although uncommon, fulminant HSV encephalitis can produce extensive cytotoxic and vasogenic edema, hemorrhagic necrosis, and refractory intracranial hypertension [8-10]. Importantly, neurological and radiological deterioration may continue after antiviral therapy has been initiated. In our patient, antiviral therapy was initiated approximately two days after symptom onset, following microbiological confirmation. Despite treatment, neurological and radiological deterioration continued, illustrating the potential for rapid progression of HSV encephalitis even after antiviral therapy has been initiated. Recent reports continue to describe severe or fatal progression despite appropriate acyclovir administration [8].

Several reports have described decompressive craniectomy as rescue treatment in patients with HSV encephalitis complicated by refractory intracranial hypertension and severe mass effect [9,10]. Favorable outcomes have been reported in selected patients, although the evidence remains limited to individual cases and small series, and no standardized criteria exist for surgical decompression in this setting. In our patient, however, neurological deterioration was exceptionally rapid, with bilateral fixed, nonreactive mydriasis developing within hours of the CT demonstrating severe cerebral edema and intracranial hypertension. Given the resulting clinical suspicion of death by neurologic criteria, decompressive surgery was not pursued.

In our patient, diffuse sulcal and cisternal effacement, ventricular compression, midline shift, prominence of the Meckel caves, and optic nerve tortuosity were imaging findings occurring in the setting of severe intracranial hypertension. The subsequent demonstration of bilateral absence of opacification of the M4 cortical branches of the middle cerebral arteries and internal cerebral veins on CT angiography was consistent with cerebral circulatory arrest

according to the four-point CT angiography scoring system [11]. Progressive elevation of intracranial pressure reduces cerebral perfusion pressure and, when intracranial pressure approaches or exceeds mean arterial pressure, may ultimately result in cessation of cerebral blood flow and cerebral circulatory arrest [12].

This case demonstrates the particular value of serial imaging in fulminant HSV encephalitis. The striking progression from a subtle, nonspecific initial abnormality to extensive bilateral encephalitic involvement with severe cerebral edema and intracranial hypertension within less than one week emphasizes the importance of continued imaging reassessment when neurological impairment persists or worsens.

CONCLUSION

HSV-1 encephalitis may initially present with subtle and nonspecific CT abnormalities that overlap with early ischemic and peri-ictal changes. Although the insula is a recognized site of HSV involvement, a subtle isolated insular abnormality on early CT is not specific. In patients presenting with seizures and persistent impairment of consciousness, HSV encephalitis should remain in the differential diagnosis even in the absence of fever or other overt infectious features and before the characteristic temporo-limbic imaging pattern becomes apparent. Early radiological stability does not exclude subsequent rapid progression. Persistent neurological impairment should prompt continued clinical and imaging reassessment, as fulminant HSV encephalitis may progress despite antiviral therapy to extensive cerebral edema, severe intracranial hypertension, and ultimately cerebral circulatory arrest.

FIGURES:

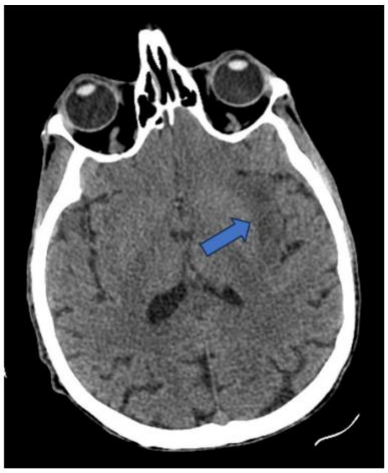

Figure 1: Initial non-contrast CT showing isolated left insular involvement.
Axial non-contrast computed tomography (CT) image obtained at initial presentation demonstrates loss of gray-white matter differentiation involving the left insular cortex (arrow), corresponding to loss of the left insular ribbon.

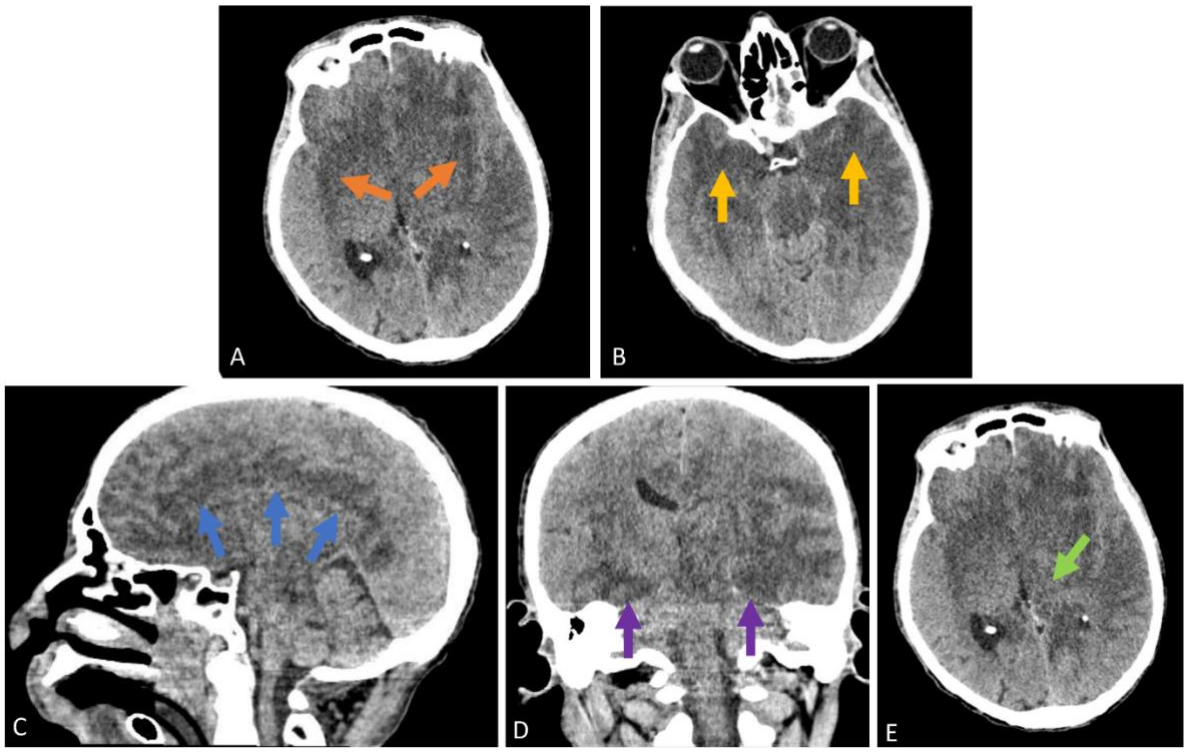

Figure 2: Extensive progression of HSV-1 encephalitis on day five.
Axial (A, B), sagittal (C) and coronal (D) non-contrast CT images obtained on day five demonstrate extensive bilateral, markedly left-predominant cortico-subcortical hypodensity involving the temporal lobes (yellow arrows) and insulae (orange arrows), with extension to the cingulate (blue arrows) and parahippocampal (purple arrows) gyri, and left thalamus (green arrow).

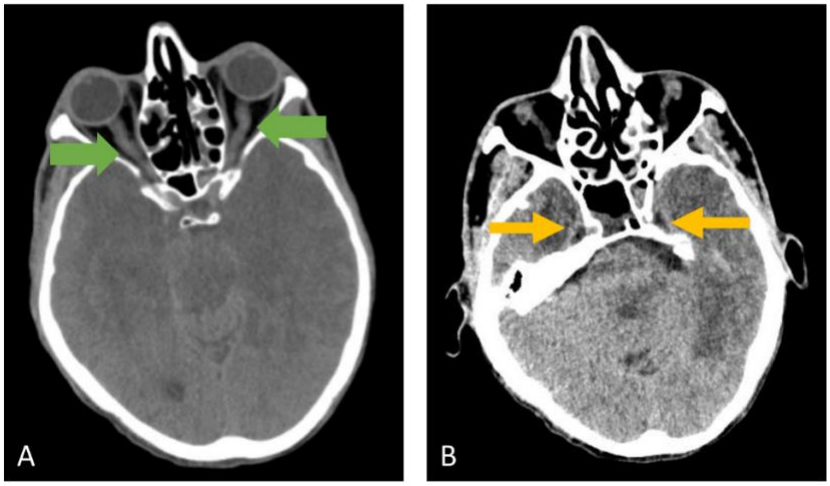

Figure 3: Imaging findings associated with severe intracranial hypertension.
Axial non-contrast CT images demonstrate tortuosity of the optic nerves (green arrows) and prominence of the Meckel caves (yellow arrows) in the setting of extensive cerebral edema and severe intracranial hypertension.

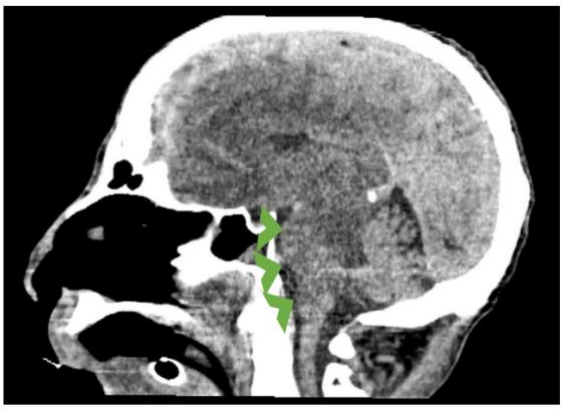

Figure 4: Ponto-mesencephalic abnormalities during fulminant disease progression.
Sagittal non-contrast CT image demonstrates swelling and hypodensity involving the midbrain and pons (arrowheads).

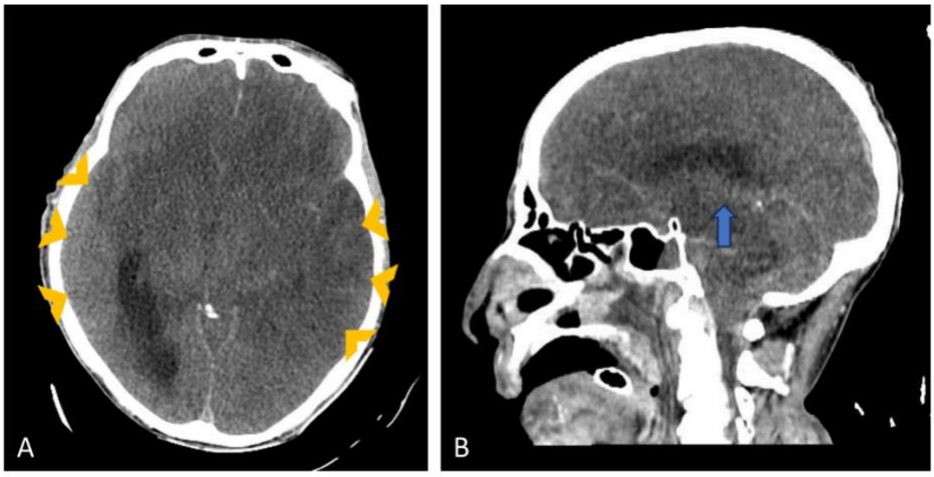

Figure 5: CT angiographic findings of cerebral circulatory arrest.
CT angiography demonstrates bilateral absence of opacification of the M4 cortical branches of the middle cerebral arteries (yellow arrowheads) and of the internal cerebral veins (blue arrow), fulfilling the four-point CT angiography criteria for cerebral circulatory arrest.

ACKNOWLEDGEMENTS

The authors have no acknowledgements to declare and report no conflicts of interest.

REFERENCES

1. Grzonka P, Mosimann T, Berger S, et al.: Unveiling the clinical spectrum of herpes simplex virus CNS infections in adults: a systematic review. Syst Rev. 2025, 14:55. 10.1186/s13643-025-02797-0
https://doi.org/10.1186/s13643-025-02797-0

2. Ngan TTD, Tuyet NT, Hung DT, Cap NT, Nguyen DM, Dat VQ: Clinical characteristics and outcomes of patients with herpes simplex encephalitis in Vietnam: a retrospective study. BMC Infect Dis. 2024, 24:556. 10.1186/s12879-024-09453-3
https://doi.org/10.1186/s12879-024-09453-3

3. Poussier L, Mailles A, Tattevin P, Stahl JP, Fillâtre P: Characteristics, management and outcome of herpes simplex and varicella-zoster virus encephalitis: a multicentre prospective cohort study. Clin Microbiol Infect. 2024, 30:917-923. 10.1016/j.cmi.2024.03.017

4. Duerlund LS, Larsen L, Storgaard M, et al.: Herpes simplex virus type 1 encephalitis: a prospective population-based cohort study. Clin Infect Dis. 2026, 82:e1384-e1392. 10.1093/cid/ciag136
https://doi.org/10.1093/cid/ciag136

5. Tosto F, Lobianco C, Magro G, Pascarella A: Stroke or seizure? Diagnostic role of neuroimaging in acute neurologic mimics. NeuroSci. 2026, 7:71. 10.3390/neurosci7030071
https://doi.org/10.3390/neurosci7030071

6. Enzmann DR, Ranson B, Norman D, Talberth E: Computed tomography of herpes simplex encephalitis. Radiology. 1978, 129:419-425. 10.1148/129.2.419
https://doi.org/10.1148/129.2.419

7. Marini S, Usai ML, Falso S, et al.: Diagnostic value of the "insular knife-cut" sign in patients with suspected herpes simplex virus encephalitis. Eur J Neurol. 2025, 32:e70152. 10.1111/ene.70152
https://doi.org/10.1111/ene.70152

8. Zhong XL, Yang CL, Yu XL, Wang L: Limited efficacy of adjunctive therapy in a case of severe herpes simplex virus encephalitis: a case report and literature review. IDCases. 2025, 41:e02307. 10.1016/j.idcr.2025.e02307
https://doi.org/10.1016/j.idcr.2025.e02307

9. Byun YH, Ha EJ, Ko SB, Kim KH: Decompressive craniectomy for herpes simplex encephalitis complicated by frank intracerebral hemorrhage: a case report and review of the literature. BMC Neurol. 2018, 18:176. 10.1186/s12883-018-1181-6
https://doi.org/10.1186/s12883-018-1181-6

10. Kusulja M, Santini M: Decompressive craniectomy as salvage treatment in herpes simplex encephalitis: two case reports. Int J Infect Dis. 2018, 73:49-51. 10.1016/j.ijid.2018.05.016
https://doi.org/10.1016/j.ijid.2018.05.016

11. Frampas E, Videcoq M, de Kerviler E, et al.: CT angiography for brain death diagnosis. AJNR Am J Neuroradiol. 2009, 30:1566-1570. 10.3174/ajnr.A1614
https://doi.org/10.3174/ajnr.A1614

12. Roth C, Ferbert A, Matthaei J, Kaestner S, Engel H, Gehling M: Progress of intracranial pressure and cerebral perfusion pressure in patients during the development of brain death. J Neurol Sci. 2019, 398:171-175. 10.1016/j.jns.2019.01.048
https://doi.org/10.1016/j.jns.2019.01.048