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Case Report

“Bloomy rind sign” in varicella-zoster virus brainstem meningoencephalitis ☆

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ABSTRACT

The bloomy rind sign, characterized by band-like abnormalities along the surface of the brainstem on magnetic resonance imaging without contrast enhancement, has been considered a specific imaging marker for leptomeningeal metastasis from lung adenocarcinoma. In this study, we describe the case of an 85-year-old male with a 3-week history of headache, fever, and progressive cognitive impairment. The patient was diagnosed with varicella-zoster virus brainstem meningoencephalitis and magnetic resonance imaging revealed hyperintensities along the brainstem surface on fluid-attenuated inversion recovery and diffusion-weighted imaging that mimicked a bloomy rind sign. However, the patient showed no signs of lung cancer or meningeal carcinomatosis. This case suggests that the bloomy rind sign is not exclusive to leptomeningeal metastasis but can also be observed in other conditions, such as central nervous system infections.

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Introduction

The varicella-zoster virus (VZV) is a human alphaherpes virus that causes chickenpox and shingles. More than 90% of adults have been infected with the VZV and are at risk for herpes zoster [1]. Although herpes zoster is characterized by a vesicular rash with a unilateral and dermatomal distribution with pain, 44% of VZV infections associated with central ner-

vous system (CNS) complications have no cutaneous lesions [2]. The virus can affect the CNS and manifests as meningitis, meningoencephalitis, or vasculopathy [3–5]. Major imaging findings include hyperintense areas on T2-weighted imaging, meningeal enhancement, and hemorrhage [3,5,6]. Early diagnosis is critical to prevent serious complications. However, the sensitivity of imaging for detecting VZV meningitis and meningoencephalitis is low: Yan et al. reported that abnormal magnetic resonance imaging (MRI) findings were detected in

Abbreviations: CNS, central nervous system; CSF, cerebrospinal fluid; DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging; VZV, varicella-zoster virus.

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only 3 of 43 (7.0%) patients with VZV meningitis and or meningoencephalitis [3].

The bloomy rind sign presents as band-like abnormal hyperintensities along the brainstem surface on fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) without contrast enhancement. Although rare, this sign is a characteristic imaging marker of leptomeningeal metastasis from lung adenocarcinoma. In this report, we describe the case of an 85-year-old male with VZV brainstem meningoencephalitis who presented with a bloomy rind sign.

Case report

An 85-year-old male was referred to our hospital with a 3-week history of headache, fever, and progressive cognitive impairment. He had a history of lingual cancer in his fifties. No cutaneous lesions were observed on physical examination. Neurological evaluation revealed signs of dysarthria and positive bilateral Babinski signs. Laboratory findings included elevated serum C-reactive protein (19.2 mg/dL; normal range: 0.00–0.14 mg/dL), pleocytosis of the cerebrospinal fluid (CSF; 120 cells/ μ L; normal range: 0–5 cells/ μ L), and elevated CSF protein levels (385.6 mg/dL; normal range: 8–43 mg/dL). Cytological analysis of the CSF and imaging studies, including chest and abdominal computed tomography, revealed no evidence of malignancy.

On MRI, FLAIR imaging revealed abnormal hyperintensity in the left middle cerebellar peduncle, indicative of brainstem

encephalitis. Additionally, band-like hyperintensity along the brainstem surface was noted. DWI also displayed restricted diffusion on the brainstem surface, the so-called bloomy rind sign. No ischemic or hemorrhagic changes were observed. A multiplex polymerase PCR test of the CSF was positive for VZV. CSF examination also revealed elevated anti-VZV IgG antibody levels (enzyme immunoassay, 569 IU/mL; normal range: 0.0–0.2 IU/mL) and an elevated VZV-IgG index (11.0; normal range: 0.0–2.0). Repeated CSF cytology showed no evidence of malignancy. Based on these results, the patient was diagnosed with VZV meningoencephalitis and administered antiviral treatment and steroid therapy. Seven days later, follow-up MRI demonstrated a more pronounced FLAIR hyperintensity along the brainstem (Figs. 1A–D), and DWI and an apparent diffusion coefficient map also displayed restricted diffusion on the brainstem surface (Figs. 1E and F). However, gadolinium contrast-enhanced T1-weighted imaging revealed no leptomeningeal enhancement (Fig. 1G). DWI hyperintensity on the left side of the pons and hypointensity on T2*-weighted imaging in the brainstem (Fig. 1H) were suggestive of brainstem infarction and hemorrhage, consistent with VZV vasculopathy.

Despite undergoing 1 month of antiviral treatment and 2 courses of steroid pulse therapy, the patient did not fully recover and his clinical symptoms remained. During this period, chest computed tomography showed complications of aspiration pneumonia but no signs of lung cancer. Two months later, the follow-up MRI examination showed persistent FLAIR hyperintensity and restricted diffusion along the surface of the brainstem (Figs. 2A–C), although the FLAIR

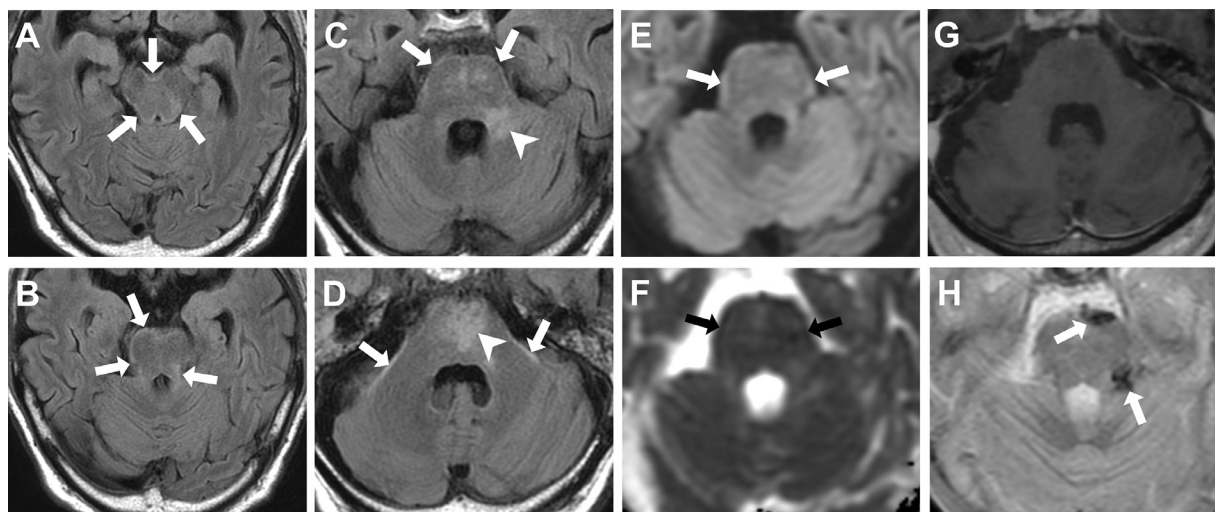


Fig. 1 – Magnetic resonance imaging shows band-like hyperintensity along the surface of the brainstem on fluid attenuated inversion recovery (FLAIR). (A) and (B) show FLAIR hyperintensity on the anterior and ventrolateral surfaces of the midbrain (arrows). (C) and (D) show FLAIR hyperintensity on the anterior surface of the pons and along the anterolateral cerebellar peduncle (arrows). FLAIR imaging also shows hyperintensity in the pons and left middle cerebellar peduncle indicating a complication of varicella-zoster virus vasculopathy (arrowheads). (E) shows diffusion-weighted imaging hyperintensity on the anterior surface of the pons and (F) shows the low apparent diffusion coefficient map of the pontine surface (arrows); the images in (E) and (F) were captured at the same level as that in (C). (G) No contrast enhancement is present on gadolinium contrast-enhanced T1-weighted imaging; the image in (G) was captured at the same level as that in (D). (H) T2*-weighted imaging shows hypointensity on the anterior surface of the pons and left cisterna ambiens indicating a complication of varicella-zoster virus vasculopathy (arrows).

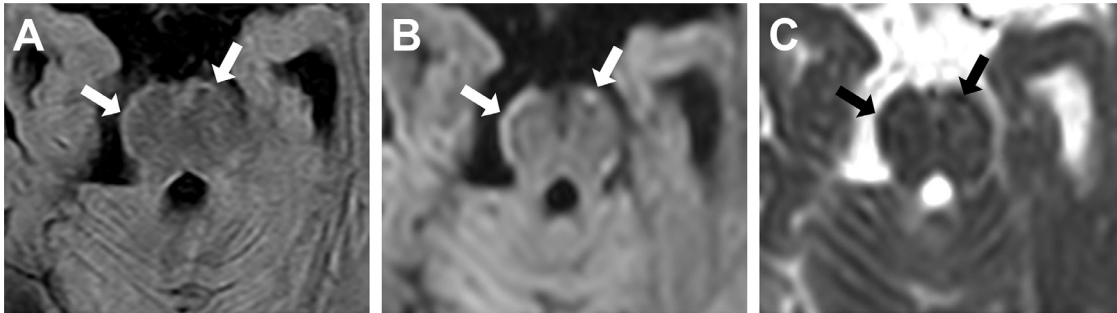


Fig. 2 – Two-month follow-up magnetic resonance imaging findings. The continued presence of the band-like hyperintensity along the surface of the brainstem is shown on fluid attenuated inversion recovery (A, arrows), diffusion-weighted imaging (B, arrows), and low apparent diffusion coefficient map (C, arrows). However, the fluid attenuated inversion recovery hyperintensity in the pons and left cerebellar peduncle has disappeared, indicating improvement of the encephalitis.

hyperintensity in the pons and left cerebellar peduncle had disappeared. These changes indicated improvement of the encephalitis.

Discussion

We present a case of VZV meningoencephalitis characterized by hyperintensity on FLAIR imaging and DWI along the brainstem surface without contrast enhancement. Mitsuya *et al.* first reported this feature, which they observed in 11 of 142 (7.7%) patients with leptomeningeal metastasis, predominantly in those with lung adenocarcinoma with EGFR mutations [7]. To the best of our knowledge, all relevant previously reported cases described this sign as being associated with meningeal metastasis from lung adenocarcinoma [8,9].

The pathophysiological mechanism underlying the bloomy rind sign remains unclear. The distribution of the lesion did not follow the typical blood supply of the brainstem; therefore, explaining the lesion as an infarction is difficult. It is postulated to result from tumor invasion along the brain surface or microinfarction secondary to vascular injury caused by tumor infiltration [10]. Although the underlying mechanism leading to the bloomy rind sign in the current case of CNS VZV infection remains unclear, we propose 2 reasons. First, it may be due to inflammatory cell infiltration within the subarachnoid and subpial spaces of the brainstem. However, it is difficult to explain the lack of contrast enhancement. Second, VZV infection may cause microinfarction of the brainstem and consequent vessel regression, leading to reduced contrast enhancement. VZV can occasionally cause CNS vasculitis or vasculopathy, affecting both large and small blood vessels [4,5]. Hence, the involvement of small vessels, such as the pial arteries of the brainstem, may cause these MRI abnormalities.

Conclusion

This case report describes a patient with VZV brainstem meningoencephalitis in which the bloomy rind sign was de-

tected, mimicking leptomeningeal metastasis from lung adenocarcinoma. This case suggests that the bloomy rind sign is not exclusive to leptomeningeal metastasis but can also be observed in other conditions, such as central nervous system infections.

Patient consent

Written and informed consent was obtained from the patient.

REFERENCES

- [1] Lal H, Cunningham AL, Godeaux O, Chlibek R, Diez-Domingo J, Hwang SJ, *et al.* Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. *N Engl J Med* 2015;372:2087–96. doi:10.1056/nejmoa1501184.
- [2] Koskiniemi M, Piiparinen H, Rantalaiho T, Eränkö P, Färkkilä M, Rähkä K, *et al.* Acute central nervous system complications in varicella zoster virus infections. *J Clin Virol* 2002;25:293–301. doi:10.1016/s1386-6532(02)00020-3.
- [3] Yan Y, Yuan Y, Wang J, Zhang Y, Liu H, Zhang Z. Meningitis/meningoencephalitis caused by varicella-zoster virus reactivation: a retrospective single-center case series study. *Am J Transl Res* 2022;14:491–500.
- [4] Patil A, Goldust M, Wollina U. Herpes zoster: a review of clinical manifestations and management. *Viruses* 2022;14:192. doi:10.3390/v14020192.
- [5] Nagel MA, Cohrs RJ, Mahalingam R, Wellish MC, Forghani B, Schiller A, *et al.* The varicella-zoster virus vasculopathies: Clinical, CSF, imaging, and virologic features. *Neurology* 2008;70:853–60. doi:10.1212/01.wnl.0000304747.38502.e8.
- [6] Alvarez JC, Alvarez J, Tinoco J, Mellado P, Miranda H, Ferrés M, *et al.* Varicella-zoster virus meningitis and encephalitis: an understated cause of central nervous system infections. *Cureus* 2020;12:e11583. doi:10.7759/cureus.11583.
- [7] Mitsuya K, Nakasu Y, Deguchi S, Shirata K, Asakura K, Nakashima K, *et al.* FLAIR hyperintensity along the brainstem surface in leptomeningeal metastases: a case series and literature review. *Cancer Imaging* 2020;20:84. doi:10.1186/s40644-020-00361-8.

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- [8] Liu X, Tan C, Zhu Y, Li S, Lai H, Deng F, et al. Teaching NeuroImage: bloomy rind sign of leptomeningeal carcinomatosis. *Neurology* 2023;101:e99–100. doi:[10.1212/WNL.0000000000207124](https://doi.org/10.1212/WNL.0000000000207124).
- [9] Huang Y, Xu Q. Bloomy rind sign: a marker of meningeal metastasis of lung adenocarcinoma. *Neurol India* 2023;71:1339–40. doi:[10.4103/0028-3886.391374](https://doi.org/10.4103/0028-3886.391374).
- [10] Yokota H, Mukai H, Hattori S, Ohira K, Higuchi A, Umeda K, et al. Band-like hyperintensity along the ventral surface of the brain stem on FLAIR and DWI in leptomeningeal carcinomatosis of lung adenocarcinoma. *Radiol Case Rep* 2022;17:544–8. doi:[10.1016/j.radcr.2021.11.054](https://doi.org/10.1016/j.radcr.2021.11.054).