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Febrile neutropenia induced by adjuvant radiotherapy for a patient with breast cancer accompanied with reversible splenial lesion syndrome (RESLES, Typel): a case report

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Abstract

Background Reversible splenial lesion syndrome (RESLES) is known as a neuro-imaging syndrome with recurrent but reversible lesion of the corpus callosum, characterized by nonspecific but usually mild encephalopathies and specific imaging manifestations.There are few published reports in the field of oncology.

Case presentation A 33-year-old female with right breast cancer and with no particular family history was admitted to hospital with high fever and severe headache, after receiving adjuvant radiotherapy. Blood routine test upon admission suggested neutropenia, considering myelosuppression associated with radiotherapy. There were no definite findings of common pathogenic microorganism, and no imaging indication of certain infectious sites other than a likely reversible corpus callosum syndrome suggested by brain MRI, which was relieved after systemic antibiotic therapy and granulocyte colony-stimulating factor injection.

Conclusions Reversible splenial lesion syndrome is a kind of clinical-imaging syndrome with multiple clinical manifestations and etiologies. This breast cancer patient after postoperative adjuvant radiotherapy develops a complication of RESLES that rings an alarm bell to the oncologists not to easily recognize the corpus callosum lesion as infarction or metastasis. Meanwhile, the potential pathogenic mechanisms need to be explored further.

Keywords Febrile neutropenia, Reversible corpus callosum syndrome, Breast cancer, Radiotherapy, Infection

Introduction

Reversible splenial lesion syndrome (RESLES) is known as a neuro-imaging syndrome with recurrent but reversible lesion of the corpus callosum, characterized by nonspecific but usually mild encephalopathies and specific imaging manifestations [1]. It usually occurs in children, with adult cases rarely reported [2]. RESLES was initially reported to be associated with anti-seizure medication (ASM) withdrawal [3], and infection was later reported to be a common precipitating factor, as well as encephalitis, epileptic seizures and certain metabolic disorders, such as hypoglycemia and hypernatremia [4]. The gold

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standard for the diagnosis of reversible splenial lesion syndrome is brain MRI which usually shows high signal in diffusion-weighted imaging (DWI) and T2-weighted imaging(T2WI) sequence and low signal in apparent diffusion coefficient (ADC), which is caused by cytotoxic edema formation, with the mechanism of which not yet well understood, maybe due to the myelin cytotoxic edema, water-electrolyte imbalance, and transient inflammatory response [5]. There has been a gradual increase in the number of case reports on the occurrence of RESLES, which enriched the awareness of the disease [6]. However, there are few published reports in the field of oncology. By conducting this case report, we aim to draw attention to cancer patients accompanied with reversible corpus callosum syndrome to possibly avoid misdiagnosis and excessive medical care. This case is reported according to CARE guidelines.

Case presentation

The patient is a 33-year-old female who underwent a breast-conserving surgery and pathological diagnosis indicated invasive carcinoma, non-specific type, histological grade 2 with negative surgical margins. Immunohistochemistry: ER (3+), PR focal (+), HER-2(3+), Ki67 positive index 50%, Metastatic cancer was seen in 1 lymph node of the total 11 right axillary lymph nodes(1/11). Considering the diagnosis of right breast cancer, T2N1M0, stage IIB, the postoperative treatment plan was formulated as AC-TH regimen: chemotherapy (4 cycles of doxorubicin liposome+cyclophosphamide every 3 weeks, 4 cycles of paclitaxel combined with anti-HER2-targeted therapy every 3 weeks, and 1 year of anti-HER2-targeted maintenance therapy) with sequential radiotherapy and endocrine therapy. After radiotherapy, the patient suffered from high fever with a maximum temperature of 40℃, without obvious sore throat and runny nose, cough and sputum, chest tightness and chest pain, abdominal pain and diarrhea, urinary frequency or pain, or other infectious manifestations, but accompanied by a heavy headache, without dizziness, blurred vision. She was finally admitted to hospital 1 week after finishing the radiotherapy(Fig. 1). Physical examination showed no obvious positive signs, especially though the patient has fever and severe headache, the patient's showed no abnormalities in neurological examination and exhibited no signs of meningeal irritation.

Laboratory examinations(Table 1): blood routine test revealed a neutropenia of 2.5×10^9/L, with rapid c-reactive protein(31.05 mg/L) and calcitoninogen(0.13 ng/mL) slightly elevated, liver and kidney function, blood

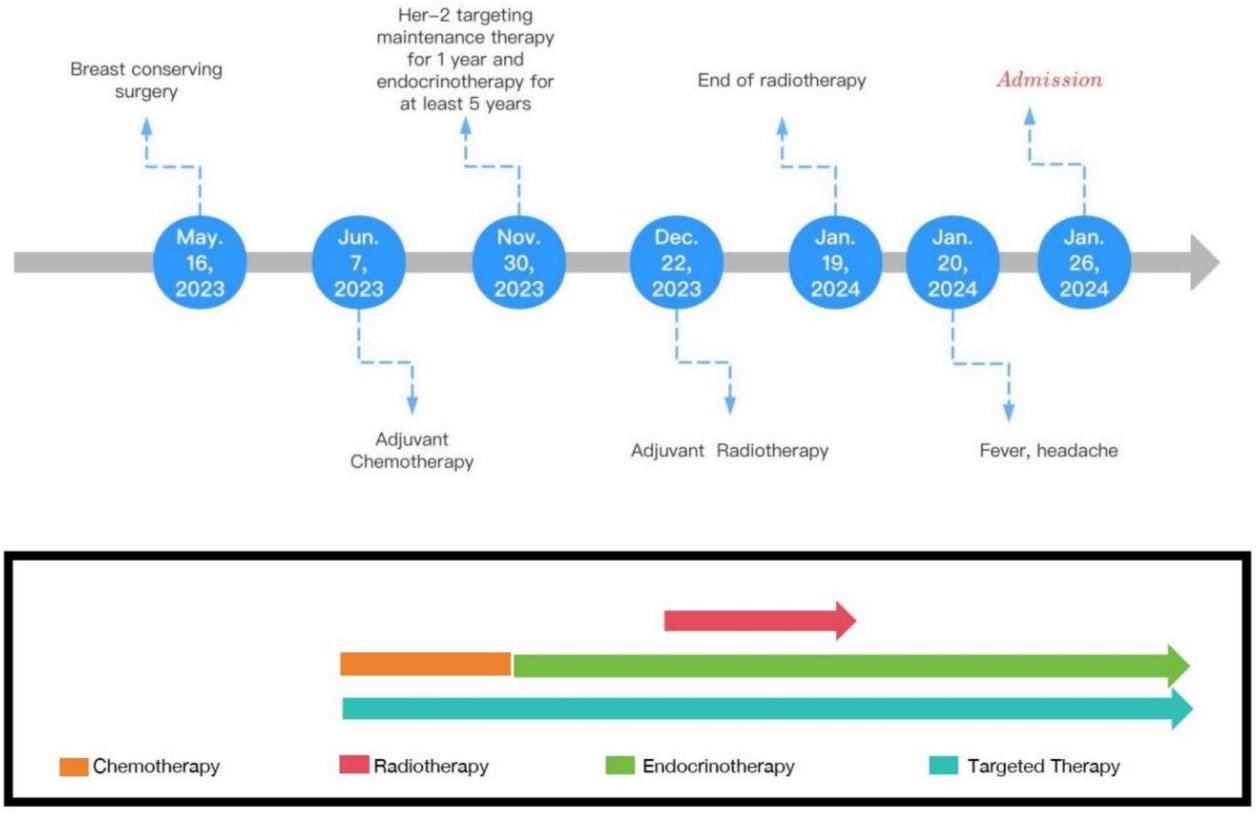

Fig. 1 Timeline of antitumor therapy

Table 1 Indicators of laboratory tests

Peripheral blood analysis	Initials	Index	Normal range
White blood cell count (/L)	WBC	2.50×10^9	3.5–9.5×10^9
Red blood cell count (/L)	RBC	3.79×10^12	3.8–5.1×10^12
Platelet (/L)	PLT	120×10^9	125–350×10^9
C-reactive protein (mg/L)	CRP	31.05	0–10
Procalcitonin (ng/mL)	PCT	0.13	< 0.05
Creatine kinase (U/L)	CK	36	40–200
Creatine kinase isoenzyme (ng/mL)	CKMB	0.8	< 5
Aspartate aminotransferase (U/L)	AST	24.5	13–35
Alanine aminotransferase (U/L)	ALT	31.8	7–40
Serum creatinine (μmol/L)	SCR	51	41–73
Blood urea nitrogen (mmol/L)	BUN	2	2.6–7.5
Uric acid(μmol/L)	UA	129	142–340
Blood sodium (mmol/L)	Na+	138.1	137–147
Blood chlorine(mmol/L)	CI-	103	99–110
Blood calcium(mmol/L)	Ca2+	2.17	2.11–2.52
Tumor markers			
Carcino-embryonic antigen	CEA	(-)	(-)
Cancer antigen 15 – 3	CA15-3	(-)	(-)
Cancer antigen 125	CA125	(-)	(-)
Thyroid antibodies			
Thyroid globulin antibodies	TG	(-)	(-)
Thyroid peroxidase antibodies	TPO	(-)	(-)
Microbiological exams			
Bacteria (blood culture)		(-)	(-)
Influenza a virus	Inf A-RNA	(-)	(-)
Influenza b virus	Inf B-RNA	(-)	(-)
Respiratory syncytial virus	RSV-RNA	(-)	(-)
Adenovirus	ADV-DNA		
Human rhinovirus	HRV-RNA	(-)	(-)
Mycoplasma pneumoniae	MP-DNA	(-)	(-)
Cerebrospinal fluid test			
Pressure		130	80-180mmH_2O
Color		colourless	colourless
Clarity		transparent	transparent
Protein	PRO	(-)	(-)
Total cells	TC	(-)	(-)

sodium, blood chloride and other electrolyte levels are normal. Respiratory pathogens: Influenza A virus RNA, Influenza B virus RNA, respiratory syncytial virus RNA, adenovirus DNA, human rhinovirus RNA, Mycoplasma pneumoniae DNA, and COVID-19 RNA were all negative. Blood culture of aerobic and anaerobic bacteria was also negative; 1,3-beta-D Glucan and GalactoMannan tests were negative. Especially there was no obvious abnormity in intracranial pressure and cerebrospinal fluid test. Abdominopelvic CT scan: no significant abnormality. brain MRI: a patchy corpus callosum lesion with high signal in diffusion-weighted imaging (DWI) and low signal in apparent diffusion coefficient (ADC)(Fig. 2A1-E1).

The patient suffered from febrile neutropenia accompanied by infectious indicators of hsCRP and PCT elevation, although no definite pathogens were detected, hyperpyrexia, poor response to antipyretic drug and freshly underwent radiotherapy were all risk factors of infection. Granulocyte-stimulating factor (G-CSF) 200 ug subcutaneous injection for 3 days and Biapenem 0.3 g intravenous infusion every 12 h(cephalosporins skin test is positive) were given. At the same time, non-steroidal anti-inflammatory drug Loxoprofen was given to relieve fever and analgesia, and the patient's temperature did not recur with headache relieved simultaneously and the lesion in the corpus callosum disappeared on brain MRI examination(Fig. 2A2-E2).

Discussion

Evolution of the concept: Kim and colleagues first reported in 1999 that discrete and focal lesions of the corpus callosumon on magnetic resonance images in patients with epilepsy might be related to Anti-seizure medication(ASM), as the foci disappeared on follow-up after discontinuation of the drugs, indicating the possible mechanism being reversible demyelination associated with ASM toxicity [7]. The concept of mild encephalopathy/ encephalitis with reversible splenial lesion of the corpus callosum(MERS) was defined by Tada et al. in 2004 [8].This referred to a clinical imaging syndrome presenting with mild encephalopathic symptoms and imaging-defined lesions in the corpus callosum that were reversible on both clinical and imaging changes. Garcia - Monco et al. gave the name of Reversible splenial lesion syndrome (RESLES) in 2011 [1].The concept of Cytotoxic Lesions of the Corpus Callosum (CLCC or CLOCCs) was introduced in 2017 by Starkey J, indicating secondary lesions caused by infections or other underlying etiologies, as opposed to primary callosal lesions such as callosal ischemia or lymphoma [9]. RESLES is categorized into type I (involving the splenium of the corpus callosum, SCC, only) and type II [extending to the white matter areas on both sides of the brain and/or involving the entire corpus callosum] according to imaging, with type II being a very rare type [9].In this patient, only SCC was involved, considering to be RESLES Type I.

Pathogenesis: The etiology of RESLES has not yet been clarified, though often be regarded as cytotoxic edema.

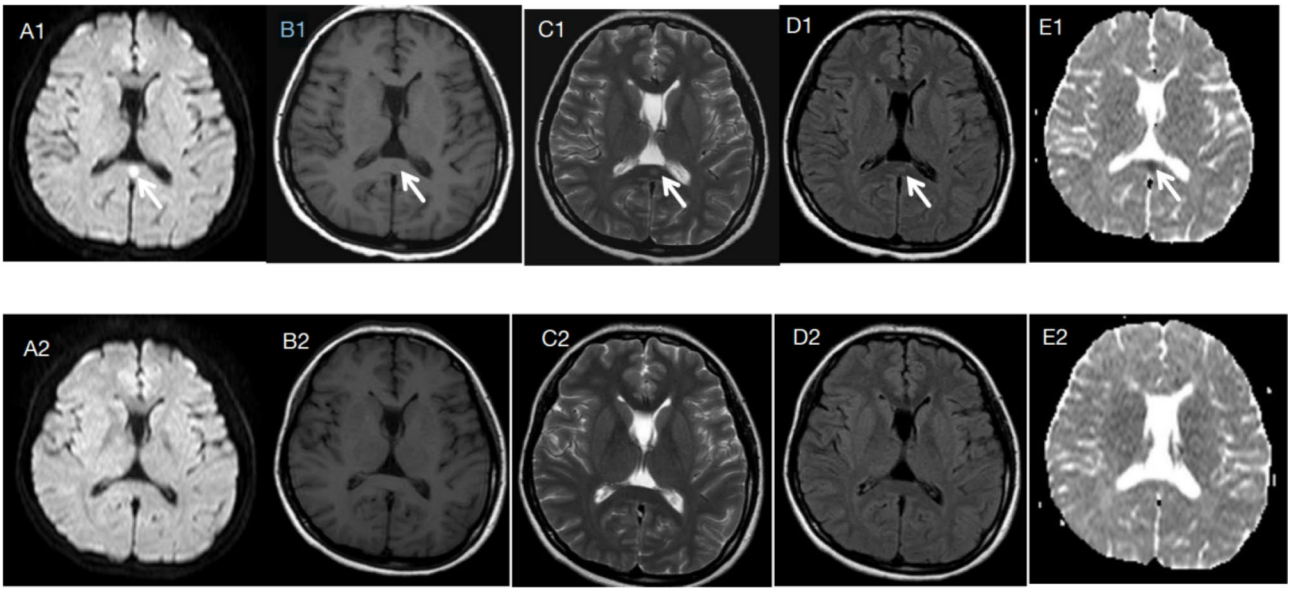

Fig. 2 Brain MRI manifestation of RESLES: High signal in DWI sequence(A1);Slightly low signal in T1WI sequence(B1); High signal in T2WI sequence(C1-D1); Low signal in ADC(E1); The lesion in the corpus callosum disappeared on brain MRI examination after recovery(A2-E2). (A: DWI B: T1WI C: T2WI D: T2WI-FLAIR E: ADC)

With the deepening of related research, a variety of factors have been revealed, mainly including infections [10], metabolic disorders [11], seizures [12] and the use of antiepileptic drugs [13] and chemotherapy [14]. RESLES caused by infection is often characterized by acute or subacute encephalitis or encephalopathy, which is common in children and adolescents, with viruses and bacteria being the main source of infection, not limited to Influenza viruses [10], Hantaviruses [15], Cytomegaloviruses [16],Rhinoviruses [17],Respiratory syncytial virus [18],Mycoplasma pneumoniae [19], Human Herpesvirus 6 [20], COVID–19 [21], Staphylococcus aureus [22], Streptococcus pneumoniae [23], Legionellae [24], Typhus [25]. The exact pathophysiologic mechanism of infection secondary to RESLES is unknown, and some studies have suggested that the likely mechanism is that acute infection activates the immune system, and the releasing antigen has a specific affinity for SCC neuronal axonal receptors, SCC can be easily induced reversible cytotoxic edema [26], for The corpus callosum itself has a variety of receptors including cytokine receptors, toxin receptors, glutamate receptors, and drug receptors. In particular, the density of receptors in SCC is more aggregated, making it more susceptible to cytotoxicity [27] [28]. Non-infectious factors such as metabolic disorder factors like hypoglycemia, hyponatremia or hypernatremia, seizures and use of antiepileptic drugs, especially abrupt withdrawal of antiepileptic drugs represented by carbamazepine and oxcarbazepine, could also induce RESLES. Carbamazepine and oxcarbazepine can act on cation channels in the cytosol membrane, and enhance the effect of antidiuretic hormone, thus causing osmotic pressure changes and finally lead to drug-induced cerebral edema [29]. Besides, several other mechanisms have been proposed for the pathogenesis of RESLES, including oxidative stress [30], neuroaxonal damage [31] and autoimmune processes. Cases of concomitant autoimmune Bickerstaff Brainstem Encephalitis(BBE) and autoimmune gliogenic fibrillary acidic protein (GFAP) astrocytosis have been reported [32–34], It is suggested that immune-related factors may also be potential causative factors. There have also been new developments at the molecular genetic level, with Kurahashi suggesting that the myelin regulatory factor (MYRF) gene may be associated with the development of RESLES [34]. Co-occurrence of RESLES and anti-N-methyl-D-aspartate receptor(anti-NMDAR) encephalitis was described in patients with or without teratoma [35, 36] Next-generation sequencing of a pair of 4-year-old twin sisters with RESLES reveals different CD36 shifted-code mutations that may be associated with pathogenesis [37]. Cases with a family history of RESLES have also been reported in Japan, The patient who was diagnosed with RESLES at the age of 8 had a recurrence at 26 years old, while the patient's younger brother had also experienced recurrent episodes of RESLES between the age of 9 and 16, making genetic factors a potential etiologic factor that should not be ignored [38].

Diagnosis, treatment and prognosis: The clinical manifestations of RESLES varies with fever, headache, seizures, mental abnormalities and vomiting. Viral infections may present with fever, cough, diarrhea, and headache, depending on the pathogen, while bacterial infections are more likely to present with impaired

consciousness and seizures with a longer disease duration. In recent years, there have also been case reports of transient blindness [39], elevated antithyroid antibodies [40], neurodeafness [41], language disorder [42],and transient ischemic attack(TIA)-like symptoms [43]as the only or main manifestations. Significant remission or disappearance of the corpus callosum lesion is necessary for diagnosis. In this case, the patient had bone marrow suppression after radiotherapy, neutropenia with fever, combining with the results of the patient's blood routine and infection indexes, we considered her as of high infection risk. The complete remission after treatment verified our hypothesis. In addition, this patient suffered from a malignant tumor, the tumor microenvironment is considerably complex, she received a variety of anti-tumor treatments, such as surgery, chemotherapy, targeted therapy, radiotherapy and hormone therapy, since there have been few reports of RESLES accompanied with malignant tumors or specific diseases which need to receive chemotherapy [14].Maissa Thabet et al. have reported a case of RESLES due to the application of rituximab to treat IgG4-related disease [44]. Akiko Aoki et al. reported a case of methotrexate-treated elderly rheumatoid patient with diffuse large B-cell lymphoma of the paranasal sinuses who developed a transient corpus callosum lesion after 6 cycles of chemotherapy, which was initially diagnosed as RESLES, but a subsequent follow up showed enlargement of the corpus callosum lesion and new lesions emerged, which led to the final diagnosis of secondary central nervous system lymphoma. Therefore, secondary neoplastic lesions of the corpus callosum should also be excluded in diagnosing RESLES [45]. In this case, in addition to radiotherapy, the patient is still receiving uninterrupted anti-Her2-targeted maintenance therapy and endocrine therapy, which cannot be completely ruled out of the etiology, and the patient still needs to be vigilant for recurrent attacks of RESLES in the course of subsequent drug therapy.The treatment of RESLES is still based on etiological treatment, providing that SCC ischemic cerebral infarction, acute encephalomyelitis, multiple sclerosis, reversible posterior encephalopathy syndrome and the secondary neoplastic lesions mentioned above are excluded. Usually RESLES has a good prognosis, but it can recur. In this case, the lesion in the corpus callosum has completely disappeared.

Conclusions

RESLES is a unique clinical imaging syndrome, characterized by reversible brain MRI findings, good prognosis and a variety of infectious and non-infectious etiologies. Till now, the diagnosis is mainly based on MRI combined with clinical manifestations, lacking of standards for treatment strategy. In the last few years, several cases related to different disciplines but oncology have been reported. By conducting this case report, we aim to draw attention to cancer patients accompanied with reversible corpus callosum syndrome to possibly avoid misdiagnosis and excessive medical care. This breast cancer patient after postoperative adjuvant radiotherapy develops a complication of RESLES, with a prior consideration of radiotherapy-induced myelosuppression to cause the disease, so as to ring an alarm bell to the oncologists not to easily recognize the corpus callosum lesion as infarction or metastasis. Meanwhile, the reported incidence of RESLES in tumor patients, especially in patients receiving multiple antitumor therapies, is relatively low, although should not be ignored, and other potential pathogenic mechanisms need to be explored further.

Abbreviations

RESLES	Reversible splenial lesion syndrome
ASM	Anti-seizure medication
DWI	Diffusion-weighted imaging
ADC	Apparent diffusion coefficient
G- CSF	Granulocyte-stimulating factor
MERS	Mild encephalitis with a reversible lesion in the splenium
CLCC or CLOCCs	Cytotoxic Lesions of the Corpus Callosum
SCC	Splenium of the corpus callosum
BBE	Bickerstaff Brainstem Encephalitis
GFAP	Gliogenic fibrillary acidic protein
MYRF	Myelin regulatory factor
NMDAR	N-methyl-D-aspartate receptor
TIA	Transient ischemic attack

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Author contributions

Xiao Qi wrote the main manuscript text, Dandan Zou prepared the table. Huaqing Wang and Miao Zhang reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study. All data relevant to the study are included in the article.

Declarations

Ethics approval and consent to participate

Written and signed consent to publish the information was obtained from the patient.

Consent for publication

Written and signed consent for publicaiton was obtained from all authors and the patient.

Competing interests

The authors declare no competing interests.

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References

1. Garcia-Monco JC, Cortina IE, Ferreira E, Martínez A, Ruiz L, Cabrera A, Beldarrain MG. Reversible splenial lesion syndrome (RESLES): what's in a name? J Neuroimaging. 2011;21(2):e1–14.
2. Xue J, Duan C, Xu G, Zhang Y, Song Z, Yi Z, Yang C, Li F, Liu K, Zhao H, Liu X. Clinical study of recurrent mild encephalitis/encephalopathy with a reversible splenial lesion in two cases. BMC Pediatr. 2022;22(1):17.
3. Maeda M, Shiroyama T, Tsukahara H, Shimono T, Aoki S, Takeda K. Transient splenial lesion of the corpus callosum associated with antiepileptic drugs: evaluation by diffusion-weighted MR imaging. Eur Radiol. 2003;13(8):1902–6.
4. Gao X, Feng Q, Arif S, Liaqat J, Li B, Jiang K. Clinical analysis of reversible splenial lesion syndrome in Chinese adults: a retrospective study of 11 cases. Med (Baltim). 2020;99(36):e22052.
5. Yang Q, Chang CC, Liu M, Yu YQ. Sequential occurrence of eclampsia-associated posterior reversible encephalopathy syndrome and reversible splenial lesion syndrome (a case report): proposal of a novel pathogenesis for reversible splenial lesion syndrome. BMC Med Imaging. 2019;19(1):35.
6. Yamaguchi H, Ishida T, Yokoi T, Tanaka T, Maruyama A, Nagase H, Hasegawa D, Imadome KI, Takeda H, Kosaka Y, Uetani Y. Clinically mild Encephalitis/Encephalopathy with a reversible Splenial Lesion accompanied by Epstein-Barr Virus Hemophagocytic lymphohistiocytosis: a Case Report and Review of the literature. J Pediatr Hematol Oncol. 2017;39(2):e92–6.
7. Kim SS, Chang KH, Kim ST, Suh DC, Cheon JE, Jeong SW, Han MH, Lee SK. Focal lesion in the splenium of the corpus callosum in epileptic patients: antiepileptic drug toxicity? AJNR Am J Neuroradiol. 1999;20(1):125–9.
8. Tada H, Takanashi J, Barkovich AJ, Oba H, Maeda M, Tsukahara H, Suzuki M, Yamamoto T, Shimono T, Ichiyama T, Taoka T, Sohma O, Yoshikawa H, Kohno Y. Clinically mild encephalitis/encephalopathy with a reversible splenial lesion. Neurology. 2004;63(10):1854–8.
9. Starkey J, Kobayashi N, Numaguchi Y, Moritani T. Cytotoxic Lesions of the Corpus Callosum That Show Restricted Diffusion: Mechanisms, Causes, and Manifestations. Radiographics. 2017 Mar-Apr;37(2):562–576.
10. Morishima T, Togashi T, Yokota S, Okuno Y, Miyazaki C, Tashiro M, Okabe N. Collaborative Study Group on Influenza-Associated Encephalopathy in Japan. Encephalitis and encephalopathy associated with an influenza epidemic in Japan. Clin Infect Dis. 2002;35(5):512–7.
11. Tse KH, Lo SS. Mild Encephalitis/Encephalopathy with reversible Splenial and cerebellar lesions (MERS type II) in a patient with Diabetic Ketoacidosis and Hypernatraemia. Hong Kong Acad Med Press. 2015;18(4):293–6.
12. Mirsattari SM, Lee DH, Jones MW, Blume WT. Transient lesion in the splenium of the corpus callosum in an epileptic patient. Neurology. 2003;60(11):1838–41.
13. Narita H, Odawara T, Kawanishi C, Kishida I, Iseki E, Kosaka K. Transient lesion in the splenium of the corpus callosum, possibly due to carbamazepine. Psychiatry Clin Neurosci. 2003;57(5):550–1.
14. Ge YX, Lin YY, Bi QQ, Chen YJ. Reversible Splenial Lesion Syndrome (RESLES) after chemotherapy of oral tegafur-uracil in a female with locally rectal adenocarcinoma. Cogn Behav Neurol. 2020;33(4):283–7.
15. Straeten FA, Meyer Zu Hörste G. Cytotoxic corpus callosum lesion and mild CSF pleocytosis during hantavirus infection: a case report. Ther Adv Neurol Disord. 2022;15:17562864221144808.
16. Fu ML, Han N, Wang W. Cytomegalovirus-Associated mild Encephalopathy/Encephalitis with reversible Splenial Lesion. Neurologist. 2021;26(5):172–4.
17. Soma N, Aizawa Y, Matsunaga M, Saitoh A. Clinically mild Encephalitis/Encephalopathy with a reversible Splenial Lesion Associated with Rhinovirus. Pediatr Infect Dis J. 2021;40(3):e122–5.
18. Li XL, Han J, Yan ZR, Zhang BW, Wang HY. Mild encephalitis/encephalopathy with a reversible splenial lesion associated with respiratory syncytial virus infection in infants. J Neurovirol. 2021;27(4):638–43.
19. Dong X, Cong S. Reversible splenial lesion syndrome associated with acute Mycoplasma pneumoniae-associated encephalitis: a report of four cases and literature review. Exp Ther Med. 2018;16(3):2152–9.
20. Sano F, Fukao T, Tamaru K, Kanemura H, Inukai T, Aihara M. Clinically mild Encephalopathy with a reversible Splenial lesion type 2 caused by human herpesvirus 6 infection. Pediatr Neurol. 2020;113:43–5.
21. Kubo M, Kubo K, Kobayashi KI, Komiya N. Non-severe COVID-19 complicated by cytotoxic lesions of the corpus callosum (mild encephalitis/encephalopathy with a reversible splenial lesion): a case report and literature review. Int J Infect Dis. 2022;125:1–9.
22. Howard-Jones AR, Britton PN, Webster R, Ayer J, Khatami A. Mild encephalitis/encephalopathy with reversible splenial lesion in association with Staphylococcus aureus bacteraemia. J Paediatr Child Health. 2022;58(5):913–7.
23. Avcu G, Kilinc MA, Eraslan C, Karapinar B, Vardar F. Mild encephalitis/encephalopathy with reversible splenial lesion (MERS) associated with Streptococcus pneumoniae Bacteraemia. J Infect Public Health. 2017 Jul-Aug;10(4):479–82.
24. Kageyama S, Hayashi R, Uchida HA. Case of clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) due to Legionella pneumonia. BMJ Case Rep. 2022;15(12):e252994.
25. Li X, Xu D, Zhou Y, Cheng B, Wang Y, Chen Z. Mild Encephalitis/Encephalopathy with Reversible Splenial Lesion Associated with Scrub Typhus in a child: a Case Report. Vector Borne Zoonotic Dis. 2022;22(3):191–4.
26. Morichi S, Kawashima H, Ioi H, Yamanaka G, Kashiwagi Y, Hoshika A. High production of interleukin-10 and interferon-γ in influenza-associated MERS in the early phase. Pediatr Int. 2012;54(4):536–8.
27. Hassel B, Boldingh KA, Narvesen C, Iversen EG, Skrede KK. Glutamate transport, glutamine synthetase and phosphate-activated glutaminase in rat CNS white matter. A quantitative study. J Neurochem. 2003;87(1):230–7.
28. Goursaud S, Kozlova EN, Maloteaux JM, Hermans E. Cultured astrocytes derived from corpus callosum or cortical grey matter show distinct glutamate handling properties. J Neurochem. 2009;108(6):1442–52.
29. Krause KH, Rascher W, Berlit P. Plasma arginine vasopressin concentrations in epileptics under monotherapy. J Neurol. 1983;230(3):193–6.
30. Dai P, Sun J, Yu Z, Zhang T, Wen Z, Jian T, Guo L, Genjiafu A, Kan B, Zhang B, Jian X. Case report: reversible splenial lesion syndrome caused by diquat poisoning. Front Neurol. 2023;14:1178272.
31. Motobayashi M, Fukuyama T, Okuno-Yuguchi J, Tsukahara K, Nagaharu S, Hagimoto R, Kinoshita T, Nakazawa Y, Inaba Y. Subclinical neuroaxonal damage in patients with clinically mild Encephalitis/Encephalopathy with a reversible Splenial Lesion. Pediatr Neurol. 2017;74:e3–4.
32. Shimada T, Sano M, Tsunemi T, Hattori N. Mild Encephalitis/Encephalopathy with a Reversible Splenial Lesion Coincidents with Bickerstaff Brainstem Encephalitis. Neurol India. 2022 Jul-Aug;70(4):1746–1747.
33. Oger V, Bost C, Salah L, Yazbeck E, Maurey H, Bellesme C, Sevin C, Adamsbaum C, Chrétien P, Benaiteau M, Honnorat J, Deiva K. Mild Encephalitis/Encephalopathy with reversible splenial lesion syndrome: an unusual presentation of anti-GFAP astrocytopathy. Eur J Paediatr Neurol. 2020;26:89–91.
34. Kurahashi H, Azuma Y, Masuda A, Okuno T, Nakahara E, Imamura T, Saitoh M, Mizuguchi M, Shimizu T, Ohno K, Okumura A. MYRF is associated with encephalopathy with reversible myelin vacuolizatio. Ann Neurol. 2018;83(1):98–106.
35. Wei R, Mu X, Zhou L. Reversible splenial lesion syndrome in Anti-N-methyl-D-aspartate receptor encephalitis. Neurol Sci. 2024;45(9):4639–41.
36. Li Y, Zhang M, Liu D, Wei M, Sheng J, Wang Z, Xue S, Yu T, Xue W, Zhu B, He J. Case report: autoimmune encephalitis with multiple auto-antibodies with reversible splenial lesion syndrome and bilateral ovarian teratoma. Front Immunol. 2023;13:1029294.
37. Gatto A, Mariotti P, De Rose DU, Curatola A, Mancini G, Lazzareschi I, Ciccone R, Badolato R, Valentini P. Mild encephalitis/encephalopathy with reversible splenial lesion (MERS) in twin sisters with two CD36 frameshift mutations. Neurol Sci. 2020;41(8):2271–4.
38. Kutsuna F, Ueno M, Tokuda M, Iwanaga H, Tsutsumi K. [Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) with a family history: an adult case. Rinsho Shinkeigaku. 2022;62(3):224–30. Japanese.
39. Tuscano A, Zoppo M, Canavese C, Cogoni M, Scolfaro C. Transient blindness associated with mild encephalitis/encephalopathy with a reversible splenial lesion (MERS): a case report and review of literature. Ital J Pediatr. 2020;46(1):152.
40. Shan Z, Qingqing Z, Mingda A. A case of reversible splenial lesion syndrome characterized by increased antithyroid antibodies. Chin J Neurol. 2022;55(2):159–63.
41. Yang J, Ma X, Li R, Ma X, Chen J, Zhang X. Reversible splenial lesion syndrome in sisters with sensorineural deafness as the first manifestation. Heliyon., Zhang Y, Ge D, Jin J, Liu J, Chen Y, He S. M. Clinical and imaging features of reversible splenial lesion syndrome with language disorder. Transl Neurosci. 2020;11(1):210–214.
42. Tang Y, Zhang D, Ge J, Jin J, Liu Y, Chen S, He M. Clinical and imaging features of reversible splenial lesion syndrome with language disorder. Transl Neurosci. 2020 Jun 19;11(1):210-214.
43. Shigeno A, Hiu T, Iwanaga H, Yasu T, Honda R, Nakaoka K, Fukuda Y, Ono T, Kawahara I, Haraguchi W, Ushijima R, Tsutsumi K [A Pediatric Case of Clinically Mild Encephalitis/Encephalopathy with a Reversible Splenial Lesion(MERS) with Recurrent TIA-like Symptoms over a Prolonged Period. No Shinkei Geka., Thabet M, Atig A, Fathallah N et al. Rituximab-induced mild encephalopathy

with a reversible splenial lesion syndrome (MERS): An adverse effect to add to the list. Br J Clin Pharmacol. 2022;88(6):2969–2972.
44. Thabet M, Atig A, Fathallah N, et al. Rituximab-induced mild encephalopathy with a reversible splenial lesion syndrome (MERS): An adverse effect to add to the list. Br J Clin Pharmacol. 2022;88(6):2969-2972.
45. Aoki A, Kobayashi H, Abe S, Kimura T, Taguchi T, Yuuta H. [A case of methotrexate-associated diffuse large B-cell lymphoma with splenial lesions of the corpus callosum on brain MRI after complete remission with chemotherapy]. Nihon Ronen Igakkai Zasshi. 2022;59(1):96–101. Japanese.

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