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Case Report

A Rare Cause of Reversible Splenial Lesion Syndrome: Oropharyngeal Tularemia

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Abstract

Reversible splenial syndrome is a rare syndrome in childhood. Although its etiology is not known distinctly, it includes infections, antiepileptic drug toxicity, prolonged seizure, hyponatremia, and autoimmune diseases. This study aims to present our RESLES case that was caused by F.Tularensis, which is zoonotic that has not been reported before in the etiology of RESLES.

Keywords: Tularemia, RESLES, ataxia

INTRODUCTION

First identified in 2004, Reversible splenial lesion syndrome (RESLES) is a complex situation with rare clinical and radiological findings (1). The clinic consists of many different acute and/or subacute abnormal neurological findings ranging from encephalopathy to ataxia, depending on the underlying cause. Radiologic findings are characterized by hyperintense lesions which show diffusion restriction in the corpus callosum splenium as a result of transient cytotoxic edema on magnetic resonance imaging (2). In recent years, RESLES has specifically been associated with MERS (mild encephalitis/encephalopathy), in which encephalopathy is more prominent. Although the etiology includes infections, antiepileptic drug toxicity, prolonged seizure, hyponatremia and autoimmune diseases, the group of unknown causes is quite large (3).

Tularemia is a zoonotic disease, which is caused by *Francisella Tularensis* and which is clinically manifested by ulceroglandular, glandular, oculoglandular, oropharyngeal, typhodial and pneumonic. Neurological involvement is very rare in tularemia, in which lymph node involvement is common (4). In the etiology of our case with RESLES who presented with ataxia, we detected *F.Tularensis*, which is a very rare agent. Our aim is to present a case of RESLES with a zootonic etiology that has not been reported before in literature.

It is transmitted to humans by vector mediated, infected water and food ingestion, aerosol inhalation and through direct contact with infected animals.

CASE

8-year-old female patient living in the rural area referred to our clinic with complaints of fever, vomiting, headache and unsteady gait that started three days before admission. Her anamnesis showed her neuromotor development was normal and she had had her vaccines. The patient's family history did not have any peculiarities. Physical examination showed pathologically tonsillar hyperemic, painful lymph nodes in the right submandibular region, the largest of which was 4x4cm. Neurological examination showed she was conscious and her cranial nerve examination was normal. Meningeal irritation findings included neck stiffness, positive Brudzinski head and foot sign and ataxic gait. Other cerebellar examination findings were normal. In laboratory examination of the patient, abnormal findings were: 11.300 mm3 (4,300-10,300 mm3) white blood count, 132 mmol/L(136-145 mmol/L) sodium level, 7,5 mg/dL(<0,33 mg/dL) CRP and 59 mm/hour (1-20 mm/hour) sedimentation. Immunoglobulin values, which were evaluated in terms of immunodeficiency, were normal according to the patient's age. Peripheral smear had predominantly neutrophil, and the other series were normal. Cranial MR imaging performed for focal neurological finding revealed T2 and FLAIR hyperintensity in the splenium of corpus callosum, bilateral parietooccipital region subcortical white matter and diffusion restriction in these areas (**Picture 1**). No abnormal findings were seen

in cerebrospinal fluid biochemical and microbiological examinations. Viral serology (*EBV, CMV, Parvovirus, Herpes, Adenovirus, Coxsackie*), Lyme, cat scratch and throat culture were found to be negative in the infectious evaluation. PPD was found to be below 5 mm. Rare causes were evaluated because there was animal contact and Francisella Tularensis (positive at a titre of 1/1280) was detected in the serum through microagglunation method. The patient's antibiotherapy was arranged. Cranial MRI of the patient, whose ataxia and clinical condition improved on the 8th day of the treatment, was evaluated as normal (**Picture 2**). The patient's infected neck lymphadenopathy was drained surgically.

DISCUSSION

Reversible splenial lesion syndrome (RESLES) was first reported in 2004 in 15 cases and it was defined in 2011 by Carlos Garcia-Monco (1). RESLES is a rare clinical and radiological syndrome caused by a reversible lesion localized to the central part of the corpus callosum, easily identifiable by MRI and characterized by the complete disappearance of the lesion usually 1-2 weeks later. Its pathophysiology is not fully known. Signal changes in diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) show that the main pathogenesis of RESLES is transient cytotoxic edema (5). Various hypotheses have been put forward in the past, including intramyelonic or interstitial edema .(6) Recently, some experiments confirmed that there was no significant decrease in fractional anisotropy (FA) value in the splenium of corpus callosum (SCC), which shows that the integrity of myelin sheath and the function of axons in the myelin sheath were hardly ever affected (7,8). Since myelin sheath is not yet developed in babies and since there are babies diagnosed with RESLES, some researchers suggest that the definitive pathogenesis of RESLES may be in astrocytes, rather than inside or under the myelin, as previously thought. (9,10) It has been shown that reversible lesions in SCC may cause cytotoxic edema in astrocytes, by leading to increase in aquaporin 4 (AQP4) level.(11) However, when the diversity of aetiologies is considered, it is possible for more than one mechanism to play a role.

Although case reports associated with this syndrome due to causes such as infection, high altitude cerebral edema (HACE), seizures, antiepileptic drug (AED) toxicity or discontinuation and metabolic disorders have been reported, its etiology is not clear. Viral (adenovirus, rotavirus, influenza(A,B), parainfluenza, sitomegalovirus..) and bacterial agents (*Enterococcus faecalis, staphylococcus aureus*..) have been reported etiologically in literature. **Table 1** summarizes the etiological causes of pediatric cases with RESLES reported in literature between 2016 and 2022. The presence of lymph adenopathy accompanying neurological findings of our case has led us to infectious cases first. When microorganism was not found in microbiological tests and when the animal contact of the case in the rural area was considered, we investigated the possible zootonic agents. As the etiological cause, we identified *F.Tularensisi*, which is a zoonosis that has not been reported before. *Francisella Tularensis,* which is a gram negative coccobacillus, is a zoonosis that is transmitted to humans by arthropod and animal bites, infected animal products, water, aerosol droplets, or through laboratory, especially in the Northern hemisphere and it causes Tularemia. Clinical findings vary depending on the route the bacterium enters the body, inoculation dose of the virulence and the immune status of the host. Central nervous system involvement of tularemia, which mostly causes ulceroglandular disease, is an uncommon complication. The hypothesis that first came to our mind was that the infected lymph nodes in the neck primarily affected the central nervous system due to being adjacent. Immune response of the host can be another possible mechanism that causes complication. However, our case was not found to have signs of immunodeficiency.

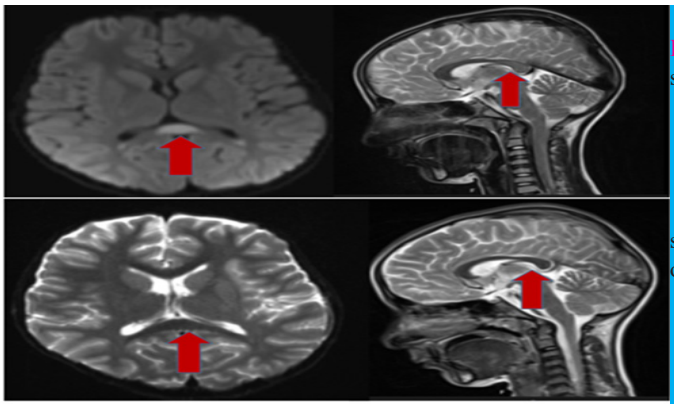
RESLES has a good prognosis depending on the underlying cause (12). However, although rare, there are RESLES cases in literature which have a poor outcome to require ventilator support. The treatment of this syndrome is etiology-oriented treatment. Our case recovered within days with antibiotherapy treatment, with neurological findings improving within days. Complete resolution of corpus callosum edema on cranial imaging taken a week later can provide information to clinicians about the recovery time of the lesion, which is still not clear.

CONCLUSION

In the etiology of RESLES, in addition to viral and

Table 1. Etiological causes of pediatric cases with RESLES reported in literature between 2016 and 2022

Azuma J. (2016), n=4, Rotavirus (2), Influenza (1), Enterococcus faecalis (1)
Chen Wan X. (2016), n=15, Rotavirus(5), Adenovirus(1), nfluenza(1), Campylobacter jejenu(1), Mycoplasma pneumonıa(1)
Landershavn G. (2018), n=1, Influenza tip b
Jiang L. (2019), n=5, Rotavirus(1)
Zhang X. (2020), n=20, HSV(5), Rotavirus(5), EBV(5), E.Coli (2), S.Pneumoniae(2), Epilepsy(7), Respiratory infection(9), Meningitis(3), Adrenal deficiency (2), ALL(1)
Bektaş Ç. (2021), n=2, COVID-19(2)
Vantresca S. (2021), n=1, Influenza tip b
Varol F. (2022), n=1, COVID-19(1)
Limura Y. (2022), n=1, Parachovirus (1)
n: Number of patients
ALL: Acute lympholastic leukemia
E.coli: Escherichia coli
S.pneumoniae: Streptococcus pneumoniae
HSV; Herpes Simplex virus



Picture 1. Diffusion and sagittal MRI sections of the splenial lesion

Picture 2. Recovered diffusion and sagittal MRI sections of the splenial lesion of the case at the time of follow-up

bacterial causes, zootonic rare agents should be examined especially in cases who come from rural area.

DECLARATIONS

Ethics Committee Aproval: Not available

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