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Case Report

VZV Encephalitis with Brucella coinfection—case report

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Abstract

Encephalitis occasionally occurs due to the central nervous system (CNS) infection by Varicella-zoster virus (VZV). The coincidence of herpes Encephalitis-brain infection and brucellosis occurs rarely. In this case, a 56-year-old woman was described with low consciousness, seizures, fever, and mood disorders. The brain CT revealed no pathological lesions, but MR showed non-specific plaques in the periventricular white matter. VZV was detected in molecular tests for the panel of viral Encephalitis in cerebrospinal fluid (CSF). The blood culture and the Wright test revealed the presence of *Brucella spp*. The antiviral treatment of choice was Acyclovir, Levetiracetam to control seizures, and Ampicillin/Sulbactam as prophylaxis antibiotics. Coinfections common poor prognoses makes it crucial to administer antiviral medications immediately. Many clinical challenges require a multidisciplinary team, including involvement of the CNS, resistance to viral strains, reactivation of diseases, and drug toxicity. The early detection of Encephalitis and treatment can promptly prevent exacerbation and complications.

INTRODUCTION

Encephalitis is inflammation of the brain in response to a virus or microorganism. Varicella-zoster virus (VZV), a human α-herpesvirus, can cause primary varicella infection (Chickenpox) or herpes zoster infection (Shingles) after the reactivation of the dormant virus. VZV infection is usually self-limited but can be exacerbated in immune-compromised patients, such as patients with HIV or transplant recipients, and result in VZV reactivation [1]. According to the World Health Organization, VZV causes Encephalitis in an estimated one out of every 33 000–50 000 cases [2].

On the other hand, Brucellosis is a zoonotic infection and a multisystem disease caused by intracellular gram-negative *Brucella spp*, characterized by nonspecific symptoms such as fever, sweats, anorexia, headache, and backache [3]. According to reports, brucellosis incidence in Iran in 2021 ranged from 22 to 59 cases per 100 000 people [4]. This case report indicates how swift recognition and treatment can reduce the infection in a patient suffering from Encephalitis consequence of Shingles and Brucellosis.

CASE PRESENTATION

A 56-year-old female presented to the emergency department of the hospital following to vital signs of generalized clonic seizure, fever (up to 38.3°C), sweating, and aggressive behavior. In neurological examination, a type of seizure with a decreased level of consciousness occurred earlier in the week. Moreover, she has been suffering from a cognitive impairment since a few days ago. Just before hospitalization, the patient underwent phlebotomy (Venipuncture). Then, due to dizziness and fainting, she fell and became unconscious.

The patient had no history of any chronic disease. The physical examination revealed no neck rodor, and the force of organs and cranial nerves were normal, and no skin lesions were identified. Spadework was requested such as Electrocardiography (ECG), binary sequence (BS) tests every 6 h, and computerized tomography (CT) scan, brain MRI (magnetic resonance imaging) with contrast, color doppler sonography of abdominal vessels and pelvic, and Lumbar Puncture (LP). As part of admission to the ward, LP was conducted with the patient's consent with anesthesia consultation. The CSF liquid was sent for culture analysis for the panels of Paraneoplastic, Autoimmune meningitis, and Encephalitis. Immunological tests were ordered for Hbs Ag, Hbs Ab, HCV Ab, ANA, and IgG on CSF. As well, molecular tests were arranged for HSV, CMV, EBV, VZV, Ev and HPeV on CSF.

She has initially prescribed Levetiracetam (Levebel) (500 mg IV every 8 h) to control seizures, and Pantoprazole (40 mg IV) for gastric protection, Captopril (25 mg sublingual once a day) for hypertension urgency. Then for fluids maintenance intravenously, Serum N/S (500 cc with KCl 5 cc + high potassium diet (10 cc KCl in fruit juice)) were added to the patient's daily treatment regime.

There were no pathological lesions in the CT scan result. In MRI, there was SVD (Small vessels disease) as limited and non-specific hyper signal plaques scattered around the periventricular in white matter (Fig. 1). An elevated intracranial pressure (ICP) of 25 cm H_2O appeared in MRI. The viral panel of pathogens in CSF, causing viral Encephalitis are depicted in Table 1, shows a VZV positive PCR test of the CSF sample. Therefore, Acyclovir

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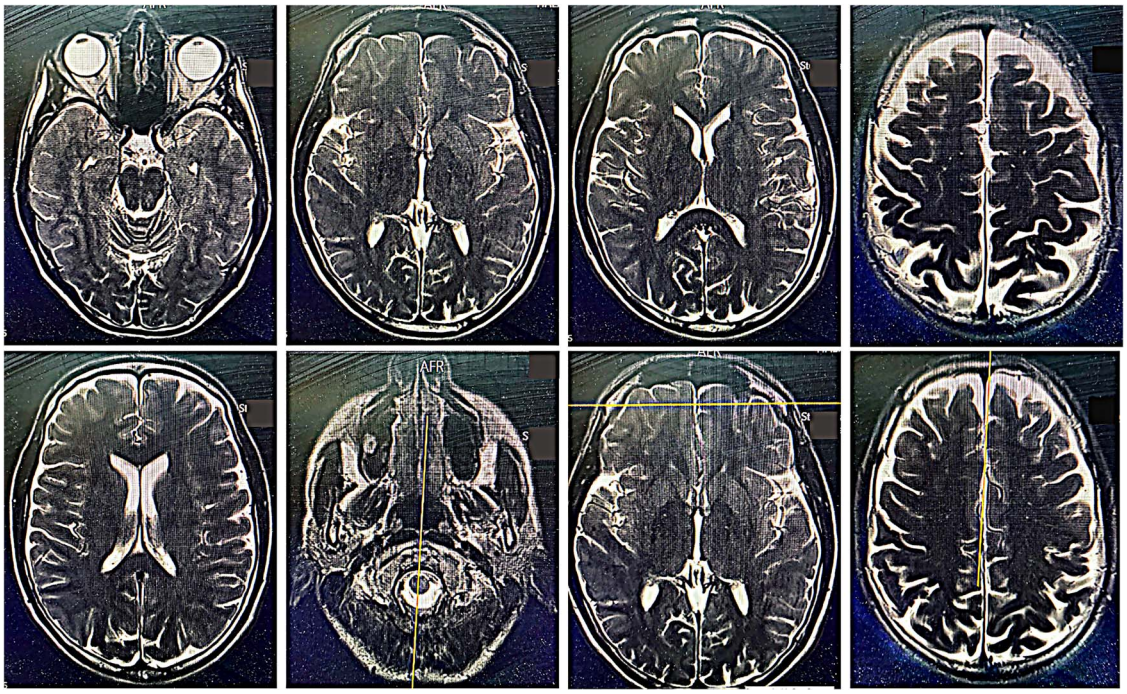

Figure 1. MRI images didn't show pathological lesions.

Table 1. Panel of pathogens in CSF causing viral Encephalitis

Index	Results
HSV-1 *(Herpes Simplex Virus-1)*	Negative
HSV-2 *(Herpes Simplex Virus-2)*	Negative
CMV *(Cytomegalovirus)*	Negative
EBV *(Epstein Barr Virus)*	Negative
VZV *(Varicela-Zoster Virus)*	Positive
EV *(Entrovirus)*	Negative
HpeV *(Pareachovirus)*	Negative

treatment started with the standard dose of 10 mg/kg three times a day (30 mg/kg/day).

Other viral markers of Encephalitis were negative, and IgG, IgM, and ANA were normal, as well as color doppler sonography and abdominal and pelvic ultrasound. HBS-Ag, HCV-Ab, ANA test, and serum toxic panel were all negative. High levels of LFT and ESR in the peripheral blood indicate the presence of inflammation. As a result, additional tests were requested for detecting microbial infection by blood culture.

Blood culture was positive for *Brucella spp*. So, PCR, 2-Mercapto Ethanol reduction (2ME) test, and Wright's test were ordered to confirm. Then PCR, 2ME, and Wright's test were positive and established Brucellosis. Subsequently, antibiotics treatment including Cefotaxime (one gram intravenously twice a day), Doxycycline capsule (100 mg twice a day), and Rifampin capsule (3 mg twice a day) was recommended against *Brucella spp*. The Liver function tests (LFT) were requested due to high level of ESR. The summary of laboratory test results is given in Table 2.

The reduction of liver enzymes appeared to be improving with the recovery of the underlying infectious agent and refining liver condition. Acyclovir continued, while Levetiracetam and Pantoprazole ampoules were replaced by the relevant tablets. The B-complex tablet and Gabapentin (100 mg tablet once a day) were prescribed, and the patient's potassium treatment eliminated.

Ultimately, the patient was discharged after 16 days, with good general condition and a mention of neurological warning signs and medication orders.

DISCUSSION

ICU admission and follow-up decisions were based on some criteria. The patient was admitted to ICU because of a seizure with a decreased level of consciousness. She benefited from receiving the proper medication and treatment for the severity of her illness. A patient with fever, headache, behavioral abnormalities, seizures, or altered mental status, should be suspected of Encephalitis. Patients with suspected Encephalitis should initiate practical Acyclovir therapy, awaiting further diagnostic results. Acyclovir is a small molecule that readily passes through the BBB. However, there were no dermatomal rashes or skin lesions in physical examinations. The general diagnosis methods of VZV Encephalitis may involve a combination of medical history, physical examination, laboratory tests, imaging tests, and pathogen tests [5]. Neuroimaging revealed inflammatory and vascular abnormalities. VZV vasculopathy occurs when VZV replicates within the arterial wall. An early lumbar puncture is crucial to the Encephalitis diagnosis, except for contraindicated patients. In this case, the CT or MRI can indicate elevated ICP. CSF should be tested for cell count, chemistry, stains, fungal and bacterial culture, and viral studies (PCR). In general, diagnostic tests on CSF aren't sensitive enough for slow-growing or uncultivable organisms in the small volume of CSF. Here CSF was examined for the presence of Encephalitis pathogens. In addition to the clinical manifestations, using conventional culture and PCR methods confirmed the result. CSF analysis in patients with viral Encephalitis typically shows normal glucose levels but elevated protein levels. Inflammatory or invading cells may produce protein in CSF [6].

VZV Encephalitis treatment options include intravenous acyclovir, which is the primary treatment, with a duration of

Table 2. Laboratory test

	Index	Results	Units	
CBC	Red blood cell count	3.97×10^6	/μl	
	White blood cell count	6×10^3	/μl	
	Eosinophils	0.01	/μl	Low
	Platelet count	129×10^3	/μl	Low
	PCT (Plateletcrit)	0.1	%	Low
	AST (Aspartate transaminase)	86	U/l	High
	ALT (Alanine transaminase)	168	U/l	High
	ALP (Alkaline phosphatase)	383	U/l	High
	Mg	2.3	mg/dl	
	Na	129	mEq/l	Low
	K	2.8	mEq/l	Low
	HBS Ag	Negative	Mlu/ml	
	HBS Ab	Positive	Mlu/ml	
	HCV Ab	Negative	Mlu/ml	
	ANA (Antinuclear Antibody)	Negative	Mlu/ml	
	CRP	42	mg/l	High
	ESR	71	mm/h	High
	Blood culture	Positive for *Brucella spp.*	Positive	
	Wright	Positive for *Brucella spp.*	Mlu/ml, 1/1280	
	2ME (2Mercaptoethanol reduction)	Positive for *Brucella spp.*	Mlu/ml, 1/640	
CSF	Bacteria	Not seen	Number	
	Glucose	54	mg/dl	Normal
	Protein	157	mg/dl	High
	WBC	0–1	Per Cu/mm	
	RBC	0–1	Per Cu/mm	
	Epithelial cells/hpf	0–1	Per Cu/mm	

seven days in immunocompetent patients and 10–21 days in immunosuppressed patients. Alternative therapies include Valaciclovir and ganciclovir (not common), and adjunctive corticosteroids, which are controversial and should be considered on a case-by-case basis [5].

Brucellosis is an endemic infectious disease in Iran. Microbiological diagnosis of brucella is often challenging. Brucellosis general diagnosis methods involves medical history, physical examination, laboratory tests, imaging, pathogen tests [7]. Blood culture tests are the gold standard for *Brucella* laboratory diagnosis. The Wright and 2ME tests are also of great value. Even so, there is growing evidence that molecular identification can assist in the accurate diagnosis and treatment of Brucellosis. Here, the PCR test for *Brucella spp*. was positive. Antimicrobial regimens and treatment durations for Brucellosis vary widely in the literature. However, it is recommended to prescribe three antibiotics for at least three months [8]. The decision was to use a combination treatment with Rifampin (aminoglycoside), Doxycycline, and Cefotaxime for this patient to reduce the risk of deterioration. However, Trimethoprim-sulfamethoxazole (TMP-SMZ) is a combination antibiotic that may be used as an alternative treatment option for brucellosis [9]. Cefotaxime and TMP-SMZ were equally effective, and no clear preference existed for one.

Briefly, the case presented stands out for the CNS infection/Encephalitis caused by VZV, accompanied by *Brucella* infection. During the initial examination, convulsions and mood swings were the main reasons for suspecting Encephalitis. Then, elevated levels of LFT and ESR in the blood signified the presence of inflammation. The infection agent was diagnosed with Brucellosis following a blood culture test. Brucellosis is responsible for the slight elevation of liver function tests. This case was particularly intriguing because of the coincidence of varicella Encephalitis and Brucellosis.

Eventually, the patient was discharged after 16 days, with acceptable general condition with neurological warning and medication orders. The chronic condition and low physiological capacity made a long-term post-hospital follow-up necessary. The patient follow-up at six months was asymptomatic, and blood cultures were negative. Recurrence occurs in up to 30% of Brucellosis cases and should also be monitored clinically for up to 2 years [10].

Managing VZV encephalitis with Brucella coinfection is difficult because the clinical features are nonspecific and indistinguishable from other viral CNS infections and require specialized testing. The rising incidence of VZV encephalitis highlights the need for proper diagnosis and management. Getting diagnosed and treated with antiviral therapy early on can improve outcomes, but it is important to note that effectiveness can differ from case to case.

The main takeaway lesson illustrates the emerging role of bacterial and viral coinfections in the complexity of illness etiology. Treatment was intricate due to complex drug selection, antibiotics challenges, antiviral toxicity, disease reactivation, and CNS involvement.

CONCLUSION

When Encephalitis is suspected, it is critical to investigate all possible causative agents (bacterial, viral, virions or fungi) to ensure rapid diagnosis and prevent neurological complications. Consideration of various etiological possibilities should also involve the patient's immune status.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflicts of interest relevant to this article.

AUTHOR CONTRIBUTIONS

F.A., J.H.N. and R.H. designed the manuscript, F.A., and J.H.N. collected the data; R.H. and J.H.N. contributed to the analysis tools; F.A. and J.H.N. performed the analysis; J.H.N. and R.H. wrote the paper.

ETHICS APPROVAL/CONSENT TO PARTICIPATE/CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review on request.

THE PATIENT'S CONSENT

The patient's informed consent form is in Farsi, it is not attached to the article, but it will be sent separately upon request.

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