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Case Report

Navigating Treatment Challenges in Pediatric Brucella Infection: A Case Report

Harsh S Patil [1], Dr Midhun Mathew K*[2], Dr Amirtha Tom [3]

1. PharmD, Dr D Y Patil Institute of Pharmaceutical Science and Research.

2 PharmD, Assistant professor, Dr D Y Patil Institute of Pharmaceutical Science and Research.

3 PharmD, Msc Research Ethics, Assistant Professor, Dr D Y Patil Institute of Pharmaceutical Science and Research.

***Correspondence to:** Dr Midhun Mathew K, Assistant professor, Dr D Y Patil Institute of Pharmaceutical Science and Research.

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Abstract

This case report presents the clinical details of a 1-year-old female child who was admitted to the pediatric ward due to a high-grade fever persisting for 15 days, accompanied by abdominal distension. Despite being immunized up to 9 months of age, laboratory tests revealed positive Brucella IgM antibodies. The child underwent a 21-day treatment regimen based on established guidelines for brucellosis, which resulted in the occurrence of drug-related side effects. However, there was no complete resolution of her symptoms at the time of discharge. This case highlights the challenges faced in managing a pediatric patient with brucellosis and emphasizes the need for further investigation and alternative treatment strategies to achieve a successful outcome.

Introduction

One of the most significant zoonoses in the world, Brucella is a bacterium that causes the bacterial illness brucellosis. In addition to a systemic disease characterized by fever, sweats, chills, and exhaustion, brucellosis can also present locally as epididymo-orchitis and spondylodiscitis. Endocarditis and neuro brucellosis are two serious disease manifestations. **(**1**)** The World Health Organization lists brucellosis as one of the seven most neglected illnesses, despite being the most common zoonotic disease in the world. There are 500,000 incident instances but the actual incidence is thought to range from 5,000,000 to 12,500,000 instances each year. **(**2**)** It has seen a significant change in epidemiology over the past ten years due to a variety of hygienic, social, and political factors, as well as the development of international travel. **(**3**)** However, because person-to-person transmission of the illness is exceedingly rare. Mother-to-offspring transmission through placental circulation, exposure to the mother's feces after delivery, breastfeeding, blood transfusion, bone marrow transplantation, and sexual contact have all been linked to the few confirmed cases of acquiring the illness through human sources. **(**4**)**

In general, all age groups are affected the prevalence of brucellosis has been increasing due to growing international tourism, trade, and migration. **(**5**)** Brucellosis in India is yet a very common but often neglected disease. Currently, Brucella melitensis accounts for most recorded cases globally with cattle emerging as an important reservoir with the few cases of B. suis. **(**6**)**

Approach to the Diagnosis of Brucellosis:

Laboratory diagnosis of brucellosis relies on:

1. Positive blood or other sterile body fluid culture, such as synovial fluid, CSF, and plural fluid, for brucella species.
2. Or, a positive brucella serology test of 1:≥160, using the Standard Agglutination Test **(**SAT**)** for patients presenting with symptoms suggestive of brucellosis. For the purpose of screening and in the absence of clinical indicators of active brucellosis, a titer of 1:320 or higher is more specific for the presence of the disease.**(**8**)**

All patients suspected of having brucella should have the following tests done:

1. Complete blood count and differentiation: The result will be normal in most cases; however, in some patients variable affection of different cell lines may be noted such as leukopenia, anemia, thrombocytopenia or a combination of some or all of them.
2. Erythrocyte sedimentation rate: As an acute reactant marker, it will be raised but usually of modest value ranging from 20 to 80 mm/h.
3. Liver function test: A mild to moderate elevation of transaminases can be found in some cases. Increased bilirubin is rare but it can occur.
4. Renal function test: Mostly normal; however, in rare cases, glomerulonephritis may occur with variable elevations of creatinine and BUN.
5. Blood culture
6. Other sterile body fluid, tissue or bone marrow culture as indicated.
7. Brucella serology **(**8**)**

Management of brucellosis relies on adherence to the following criteria:

1. Using an antibiotic that has the ability to act intracellularly and in acidic media.
2. Using combined therapy.
3. Using antimicrobials for a prolonged duration according to the system involved.**(**8**)**.

Drug	**Dosage**
Rifampicin	20 mg/kg/day in two divided doses **(**max. 600 mg**)**
Doxycycline	5 mg/kg/day in two divided doses **(**max. 200 mg**) (**only for children more than 8 year of age**)**
TMP/SMX	10 mg of trimethoprim/kg/day **(**max. 480 mg**)**
Gentamicin	5–7.5 mg/kg/day IM or IV either as a single dose or three divided doses
Streptomycin	15 mg/kg IM or IV once daily **(**max. 1 g/day**) (**only for children more than 8 year of age**)**
Ciprofloxacin	30 mg/kg/day in two divided doses **(**max. 1.5 g**)**
	(8**)**

Case

A 1yr old female child was admitted to the paediatric ward with the chief complaints of high-grade fever from past 15 days and abdominal distension from past 20 days.

The patient's physical examination indicated that her BP was low **(**90/60mm Hg**)** and PR was high **(**138bpm**)**, with rest of her vitals being normal and she was immunized till 9 months of age.

The patient's Provisional diagnosis was made as Acute Febrile Illness under Evaluation.

The hematology and biochemical investigation report indicated that the patient had low Hb, PCV, & MCV levels, along with high platelet, CRP, AST, ALT, ALP and TLC count. Patient's IgM, IgE& Eosinophil

levels were also abnormally raised. Her Sonography and CT reports suggested that she had hepatomegaly, mild splenomegaly along with minimal ascites.

At admission hemoglobin was 6.80 g/dl, TLC was 24100/cu mm with neutrophils 8%, Absolute eosinophils 13,496/µL, platelets 439000/µL, SGPT **(**ALT**)** 40 IU and SGOT **(**AST**)** 138 IU, CRP 50.20 mg/L& her Peripheral blood smear indicated that she had mild hypochromia, mild microcytosis, mild anisocytosis along with marked Eosinophilia and mild leukocytosis.

On the first day the patient had complaints of fever spikes and rashes over face and abdomen, the patient was started on Antibiotics **(**Piperacillin-tazobactam**)** and anti-helmintic **(**Hetrazan**)**, on the next consecutive day they were suspecting the patient of having Brucellosis, Tropical Eosiniophilia and DRESS syndrome since her Total immunoglobulin reports showed IgE – 948 IU/ml and IgM -1200 mg/dl and her uric acid levels were low 1.10 mg/dl for which Inj Doxycycline and Cetrizine was added to the regimen, her vitals were normal. The next day **(**i.e. 4th day of admission **)** she developed cough and cold along with the rashes, her Microbiology test was conducted for checking her Aerobic , Anaerobic and Fungal Culture Sensitivity test which confirmed no growth .On the 5th day of admission the patient was started on Septran, Amikacin and Rifampicin, since they confirmed the patient of having Brucella IgM+ve and she was having c/o 3 fever spikes along with cough her Hb was low 6.90 g/dl WBC count was elevated 27,400/ µL along with her platelet **(**472,000/ µL **)** and Eosinophils **(**15,070/ µL**)**, on the 8th day of admission the c/o rash subsided, SypLumerax was added to the drug regimen on the 12th day, but still the patient was having on & off fever spikes.

On 16thday of admission they diagnosed her with Eosinophilia with Hepatosplenomegaly along with Brucella IgM+ve which was confirmed to be her final diagnosis. Her LFT levels were also elevated which were indicative of her Hepatomegaly and Splenomegaly **(**SGOT **(**AST**)-** 165 U/Lt, SGPT **(**ALT**)-** 45 U/Lt, ALP- 343 U/Lt**)**

The patient was kept under observation for more 6 days and discharged on 22nd day of her admission on medical advice, but she was still facing the complaints of on and off fever spikes for which she was discharged with medications including Tab.Prednisolone, SypOsteocal, Tab HetrazanSyp Uprise D3 &Syp MVBC.

Treatment chart:

SR. NO	FOLLOW UP	DRUG NAME	FREQUENCY
1	DAY 1	INJ. PIPTAZ 100mg/kg/dose INJ. PAN 1.25mg/kg/dose INJ. PCT 15mg/kg/dose INJ. EMSET 0.1mg/kg/dose SYP.HETRAZAN10mg/kg/dose	1-1-1 0-1-0 SOS SOS 1-1-1
2.	DAY 2	INJ. PIPTAZ 100mg/kg/dose INJ. PAN 1.25mg/kg/dose INJ. PCT 15mg/kg/dose INJ. EMSET 0.1mg/kg/dose SYP.HETRAZAN10mg/kg/dose	1-1-1 0-1-0 SOS SOS 1-1-1
3	DAY 3	INJ. PIPTAZ 100mg/kg/dose INJ. PAN 1.25mg/kg/dose INJ. PCT 15mg/kg/dose INJ. EMSET 0.1mg/kg/dose TAB.HETRAZAN100mg/tab SYP. CETRIZINE 2ml LACTO CALAMINE LOTION	1-1-1 0-1-0 SOS SOS 1-1-1 HS LA BD
4	DAY 4	INJ. PIPTAZ 100mg/kg/dose INJ. PAN 1.25mg/kg/dose INJ. PCT 15mg/kg/dose INJ. EMSET 0.1mg/kg/dose TAB.HETRAZAN100mg/tab SYP. CETRIZINE 2ml LACTO CALAMINE LOTION INJ.DOXYCYCLINE2.2mg/kg/dose	1-1-1 0-1-0 SOS SOS 1-1-1 HS LA BD BD
5	DAY 5	INJ. PIPTAZ 100mg/kg/dose INJ. PAN 1.25mg/kg/dose INJ. PCT 15mg/kg/dose INJ. EMSET 0.1mg/kg/dose TAB.HETRAZAN100mg/tab SYP. CETRIZINE 2ml LACTO CALAMINE LOTION INJ. AMIKACIN 15mg/kg/day SYP.RIFAMPICIN15mg/kg/day SYP SEPTRAN 20mg/kg/day	1-1-1 0-1-0 SOS SOS 1-1-1 HS LA BD OD BD BD

6	DAY 6	INJ. PIPTAZ 100mg/kg/dose INJ. PAN 1.25mg/kg/dose INJ. PCT 15mg/kg/dose INJ. EMSET 0.1mg/kg/dose TAB.HETRAZAN100mg/tab SYP. CETRIZINE 2ml LACTO CALAMINE LOTION SYP.RIFAMPICIN15mg/kg/day SYP SEPTRAN 20mg/kg/day INJ. AMIKACIN 15mg/kg/day	1-1-1 0-1-0 SOS SOS 1-1-1 HS LA BD BD BD OD
7	DAY 7	INJ. PIPTAZ 100mg/kg/dose INJ. PAN 1.25mg/kg/dose INJ. PCT 15mg/kg/dose INJ. EMSET 0.1mg/kg/dose SYP. CETRIZINE 2ml LACTO CALAMINE LOTION SYP.RIFAMPICIN15mg/kg/day SYP SEPTRAN 20mg/kg/day	1-1-1 0-1-0 SOS SOS HS LA BD BD BD
8	DAY 8	SYP. CETRIZINE 2ml LACTO CALAMINE LOTION SYP.RIFAMPICIN15mg/kg/day SYP SEPTRAN 20mg/kg/day IV MIDAZ (0.7+0.7NS) SYP.PCM 15mg/kg/dose	HS LA BD BD BD OD SOS
9	DAY 9	SYP. CETRIZINE 2ml LACTO CALAMINE LOTION SYP.RIFAMPICIN15mg/kg/day SYP SEPTRAN 20mg/kg/day SYP.PARACETAMOL15mg/kg/dose TAB HETRAZAN 100mg/TAB	HS LA BD BD BD SOS 1-1-1
10	DAY 10	SYP. CETRIZINE 2ml LACTO CALAMINE LOTION SYP.RIFAMPICIN15mg/kg/day SYP SEPTRAN 20mg/kg/day INJ.PCM 15mg/kg/dose TAB HETRAZAN 100mg/TAB	HS LA BD BD BD OD 1-1-1-1
11	DAY 11	SYP. CETRIZINE 2ml LACTO CALAMINE LOTION	HS LA BD

		SYP.RIFAMPICIN10mg/kg/day SYP SEPTRAN 20mg/kg/day INJ.PCT 15mg/kg/dose TAB HETRAZAN 100mg/TAB	BD BD SOS 1-1-1-1
12	DAY 12	SYP. CETRIZINE 2ml LACTO CALAMINE LOTION SYP.RIFAMPICIN10mg/kg/day SYP SEPTRAN 20mg/kg/day INJ.PCT 15mg/kg/dose TAB HETRAZAN 100mg/TAB SYP LUMERAX 5ml	HS LA BD BD BD SOS 1-1-1-1 OD
13	DAY 13	SYP. CETRIZINE 2ml LACTO CALAMINE LOTION SYP.RIFAMPICIN10mg/kg/day SYP SEPTRAN 20mg/kg/day INJ.PCT 15mg/kg/dose TAB HETRAZAN 100mg/TAB SYP LUMERAX 5ml	HS LA BD BD BD SOS 1-1-1 OD
14	DAY 14	SYP. CETRIZINE 2ml LACTO CALAMINE LOTION SYP.RIFAMPICIN10mg/kg/day SYP SEPTRAN 20mg/kg/day INJ.PCT 15mg/kg/dose TAB HETRAZAN 100mg/TAB SYP LUMERAX 5ml	HS LA BD BD BD SOS 1-1-1 OD
15	DAY 15	SYP. CETRIZINE 2ml LACTO CALAMINE LOTION SYP.RIFAMPICIN10mg/kg/day SYP SEPTRAN 20mg/kg/day INJ.PCT 15mg/kg/dose TAB HETRAZAN 100mg/TAB SYP LUMERAX 5ml	HS LA BD BD BD SOS 1-1-1 OD
16	DAY 16	SYP. CETRIZINE 2.5ml LACTO CALAMINE LOTION SYP.RIFAMPICIN10mg/kg/day SYP SEPTRAN 20mg/kg/day INJ.PCT 15mg/kg/dose TAB HETRAZAN 100mg/TAB	HS LA BD BD BD SOS 1-1-1

		SYP LUMERAX 5ml TAB. PREDNISOLONE 1mg/kg/day SYP. GELUSIL 2.5ml INJ. DOXYCYCLINE 2.2mg/kg/dose	OD BD BD OD
17	DAY 17	SYP.RIFAMPICIN10mg/kg/day SYP SEPTRAN 20mg/kg/day INJ.PCT 15mg/kg/dose TAB HETRAZAN 100mg/TAB TAB.PREDNISOLONE7.5mg/kg/day SYP MVBC 2.5ml SYP. OSTEOCAL 2.5ml	BD BD SOS 1-1-1 BD OD BD
18	DAY 18	SYP.RIFAMPICIN10mg/kg/day SYP SEPTRAN 20mg/kg/day INJ.PCT 15mg/kg/dose TAB HETRAZAN 100mg/TAB TAB.PREDNISOLONE7.5mg/kg/day SYP MVBC 2.5ml SYP. OSTEOCAL 2.5ml	BD BD SOS 1-1-1 BD OD BD
19	DAY 19	INJ.PCT 15mg/kg/dose TAB HETRAZAN 100mg/TAB TAB.PREDNISOLONE7.5mg/kg/day SYP MVBC 2.5ml SYP. OSTEOCAL 2.5ml	SOS 1-1-1 BD OD BD
20	DAY 20	SYP.PCT 15mg/kg/dose TAB HETRAZAN 100mg/TAB TAB.PREDNISOLONE 2mg/kg/day SYP MVBC 2.5ml SYP. OSTEOCAL 2.5ml	SOS 1-1-1 BD OD BD
21	DAY 21	SYP.PCT 15mg/kg/dose TAB HETRAZAN 100mg/TAB TAB.PREDNISOLONE 2mg/kg/day SYP MVBC 5ml SYP. OSTEOCAL 5ml	SOS 1-1-1 BD OD BD

Discussion

The most typical clinical symptom of brucellosis is fever, which is followed by arthralgia, weight loss, a lack of hunger, malaise, and hepatosplenomegaly. Our patient had symptoms of temperature, dry cough, headache, and rash with hepatosplenomegaly along with haematological findings of Mild hypochromia,

anisocytosis, moderate eosinophilia, mild leukocytosis and mild thrombocytosis **(**7**)**

The primary methods for diagnosing brucellosis are serologic studies. In this case the immunoglobulin levels are measured using nephelometry. The key to identification is the isolation of brucella organisms from blood, bone marrow, or other tissue fluids. **(**7**)**

The patient's USG Cranium revealed no abnormalities, and her CT scans of the abdomen and pelvis revealed hepatomegaly with no focal mass lesion, and splenomegaly with minimal ascites in the pelvis. Our case received Piperacillin + Tazobactam, Doxycycline, diethylcarbamazine & Rifampicin for the first 8 days but did not respond, later on only rifampicin was continued till the patient was discharged. Though blood and bone marrow cultures did not grow brucella organisms, Immunoglobulin test by Nephelometry confirmed Brucella IgM+ve in this case.

Pharmacist's interpretation:

The first line treatment of Brucellosis/Brucella involves Rifampicin and TMP/SMX for chidren below 8 years of age as seen in this patient. The patient was on multiple antibiotics for the first week of treatment such as Piptaz **(**Piperacillin+Tazobactum**)** , Amikacin, Co-trimoxazole and also on doxycycline which was a major intervention in this case. The patient had also developed rash on her body along with intermittent fever spikes which were mostly suspected due to Piptaz and Hetrazan**(**Diethylcarbamazine**)** Also the patient was started on Syrup Lumerax**(**Artemether and Lumefantrine**)** which is used in treatment of Malaria and Hetrazan which is an anti-helmintic which in this case both the drugs were not indicated in treatment of Brucellosis

Interaction: Lumerax X Rifampicin **(**X**)** , an interaction was found which suggests that both drugs should not be given together as they decrease the serum conc of active metabolites of Syp Lumerax. When Artemether and Lumefantrine are coadministered with inducers of CYP3A4 **(**Rifampicin**)**,it may result in decreased concentrations of artemether and/or lumefantrine and loss of antimalarial efficacy.

Monitoring Parameters:

1) Efficacy of Treatment:

Monitor the patient's clinical response to the artemether/lumefantrine regimen to ensure that it is effective.

2) Liver Function:

Rifampicin and artemether/lumefantrine can both affect liver function. Regular liver function tests **(**e.g., ALT, AST, bilirubin**)** can help detect liver damage or dysfunction.

3) Electrolyte Levels:

Monitor electrolyte levels, especially potassium and magnesium, as these drugs may affect electrolyte balance.

4) QT Interval on ECG:

Artemether/lumefantrine can potentially prolong the QT interval on an electrocardiogram **(**ECG**)**. Check ECG results to ensure there are no significant QT interval abnormalities.

5) Blood Cell Counts:

Monitor complete blood counts **(**CBC**)** to check for any signs of anemia, leukopenia, or thrombocytopenia, which could be caused by the medications. So in general from a pharmacist's point of view the patient should have been started on selective drugs such as rifampicin and TMP/SMX along with paracetamol, pantoprazole, ondansetron and other multivitamin therapies such as osteocal and MVBC for a better therapeutic outcome.

Conclusion

In summary, our case report sheds light on the persistent symptoms observed in a pediatric patient with brucellosis, despite receiving treatment according to established guidelines and first-line therapies. The prolonged use of multiple antibiotic courses in this case raises concerns regarding the potential consequences of ineffective therapy and the risk of developing antimicrobial resistance. We propose the incorporation of Culture Sensitivity testing as an indispensable tool to guide empirical antibiotic therapy, leading to shorter treatment durations and reduced hospital stays. By advocating for the integration of this diagnostic approach, we aim to improve patient care, minimize the risk of antimicrobial resistance, and optimize treatment outcomes in pediatric brucellosis. Future research endeavors should focus on evaluating

the efficacy and practicality of Culture Sensitivity testing in the management of pediatric cases, providing valuable insights for evidence-based decision-making and improved clinical practices.

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