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Jarisch – Herxheimer Reaction in a Patient with Disseminated Lyme Disease

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Abstract:

A 61-year-old man presented with a 2 week history of intermittent fever, recurrent headaches, arthralgia's and a non-pruritic erythematous macular rash on his right lower abdomen. The patient underwent an uncomplicated lumbar puncture and was commenced on antibiotics for suspected early disseminated Lyme disease. Few hours after the first antibiotic dose he had abrupt onset of high fevers, chills, hypotension and tachycardia requiring fluid resuscitation and antipyretics. Jarisch-Herxheimer reaction (JHR) is a transient shock-like syndrome that typically follows initiation of antibiotics and is classically associated with penicillin treatment of syphilis. We discuss a patient of disseminated Lyme disease who developed JHR after commencing antibiotic therapy.

Key words: Lyme Disease, Spirochaetales, Syphilis, Arthralgia, Exanthema, Hypotension.

Introduction

Jarisch-Herxheimer reaction (JHR) is associated with diseases caused by sphirochetes including syphilis, Lyme disease, tick-borne relapsing fever and babesiosis. We present a case of patient who developed JHR after commencing antibiotic therapy for disseminated Lyme disease. We trust this case will be useful to physicians and students evaluating and managing patients with Lyme disease.

Case Report

A 61-year-old Caucasian man presents to his primary care physician with a 2-week history of recurrent global headaches, generalized arthralgias, myalgias, and a non-pruritic macular rash on his right lower abdomen. He describes headaches with increasing severity and frequency. He also reports having diaphoresis during the nighttime that makes him feel marginally better. He recalls removing ticks off his head for the last few years including a few days prior presentation and stated that it was not unusual for them to appear engorged. He also has frequent mosquito bites and uses insect repellent frequently. He denies any photophobia, neck stiffness, altered mental status, visual deficits, vomiting, chest pain or shortness of breath. Lyme antibody serology performed by the primary care physician is negative and the patient is sent to the Emergency Department for further work up and evaluation.

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Past medical history is significant for migraines, hypertension, hypercholesterolemia, benign prostatic hyperplasia and depression. His medications include gabapentin, atenolol, hydrochlorothiazide, simvastatin and terazosin. He denies any drug allergies. He owns five cats and he no longer owns a dog. The last contact with the dog was approximately 4 years ago. He has no known contact with any other animal and has no prior history of animal bites. He lives near wooded areas and works in road construction and often logs trees.

On examination he is febrile with a temperature of 102.3^{0}F, tachypneic to 25 respirations per minute, pulse 91 beats per minute and blood pressure 116 mmHg systolic and 83 mmHg diastolic. Physical examination is otherwise unremarkable except for a large confluent macular erythematous patch below and to right of umbilicus that is slightly warm and extends across to the flank. It is non-pruritic and has slight evidence of central clearing [Fig. 1].

A complete blood count shows a white blood cell count of 9.5 × 10^9/L with neutrophil predominance (76.2%), hemoglobin of 12.0 g/dl and a hematocrit of 34.5%. A comprehensive metabolic panel reveals an erythrocyte sedimentation rate (ESR) of 100 mm/hr, C-reactive protein of 11.40 mg/dl, normal electrolytes, urea and creatinine. Cerebrospinal fluid analysis revealed pleocytosis with 31 white blood cells, protein of 47.0 mg/dl and glucose of 84 mg/dl.

He is commenced on intravenous ceftriaxone 2 gm daily and intravenous doxycycline 100 mg q12h. However, after receiving his first dose of antibiotics he develops high fevers, chills and diaphoresis. He also develops macular erythematous patches on his right flank and lower limbs [Fig.2,3]. He is resuscitated with intravenous fluids and commences on paracetamol 500 mg orally. A full septic screen including chest X-ray, blood cultures and urinalysis is

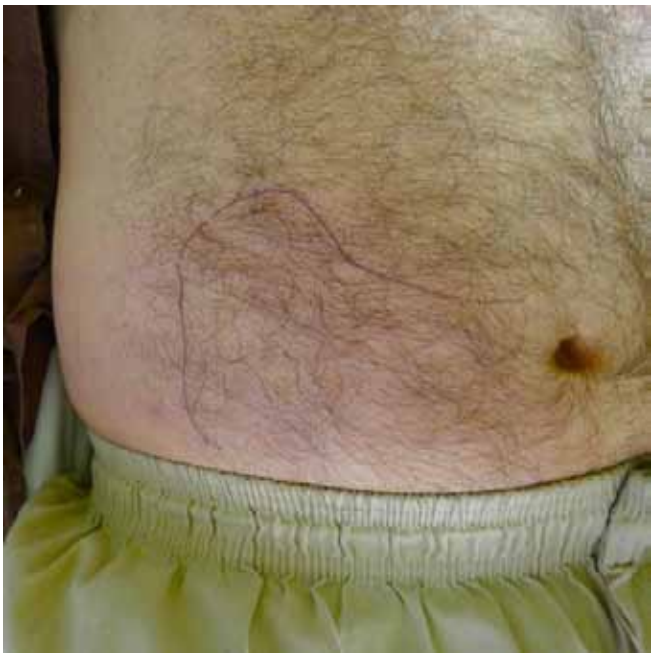

Fig.1: Large confluent erythematous patch, right of umbilicus increasing in size beyond initially marked boundaries.

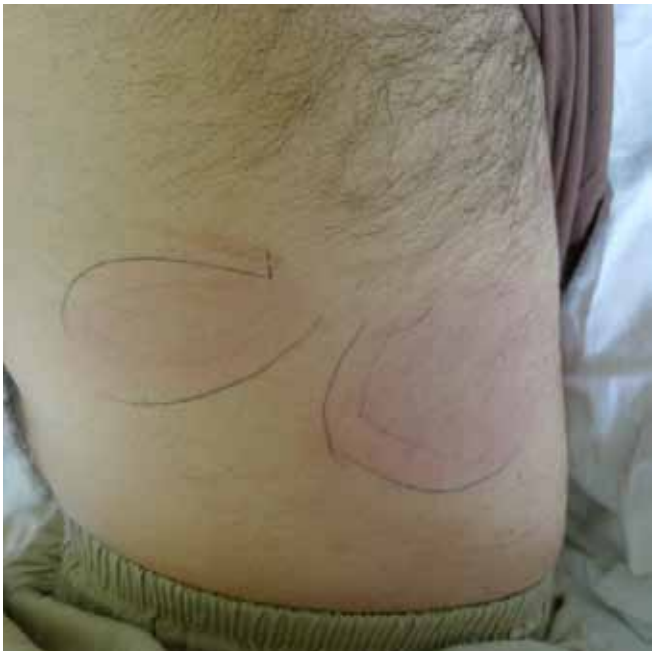

Fig.2: Erythematous non-pruritic patches secondary to antibiotic administration.

performed for presumed bacterial sepsis. The results of the investigation are non-conclusive and he is pre-medicated with ibuprofen and diphenhydramine orally for presumed JHR. His symptoms resolve over the next few days and he is able to tolerate subsequent doses of antibiotics without any further episodes. Repeat Lyme antibodies are strongly positive and he is discharged home on ibuprofen and intravenous ceftriaxone 2g daily for 4 weeks with regular follow up with his primary care physician to monitor progress.

Discussion

Lyme disease is a vector borne disease that is caused by *Borrelia burgdoferi*, a spirochete and is transmitted by infected *Ixodes* tick bites [1]. *Ixodes* ticks are most frequently found in wooded areas and in areas patronized by animals they feed on [1]. The patient had evidence of systemic shock-like symptoms including hypotension, fevers and tachycardia after his first dose of antibiotics. Given his previous history of tick bites, abrupt onset of symptoms following antibiotic administration and a negative septic screen, JHR was the most likely diagnosis. Adolf Jarisch, an Austrian dermatologist first described JHR in 1985 when he observed an exacerbation of lesions in roseolar syphilis patients after they were treated with mercury. Consequently Karl Herxheimer, a German dermatologist identified a similar phenomenon in 1902 [2].

JHR in immunocompetent patients classically occurs after initiation of treatment with antibacterials such as penicillins for the treatment of syphilis. However, it has also been observed in other infections of bacterial, fungal and protozoal origin [2]. Despite medical advances the exact mechanisms of JHR still remains uncertain. Many theories have been postulated to describe the underlying mechanisms of JHR and its relation to spirochetal infections [3]. It has been proposed that following antibiotic treatment there is release of endotoxin like substances

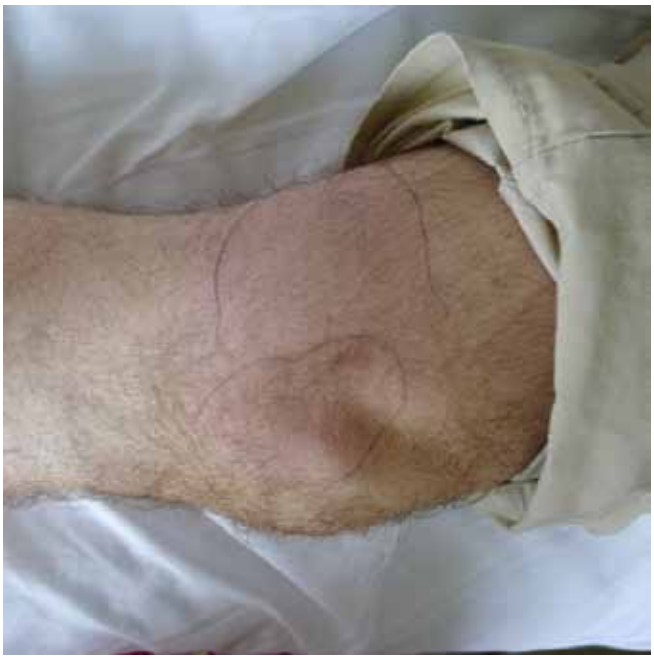

Fig.3: Right lower limb erythematous patch.

(lipoproteins) from spirochetes and an elevation in cytokine levels. Tp47 is a highly immunogenic antigenic component present in abundance with Tp15 and Tp17 present in fewer amounts. This results in phagocytosis of mononuclear cells that release cytokines such as Tumor Necrosis Factor (TNF)-α, Interleukin-8 (IL) and IL-8 resulting in the different symptoms of JHR. This has been reinforced by the favorable response of JHR to corticosteroids, which are recognized to result in down-regulation of TNF, IFN and IL-6 [2,4]. This produces a transient immunological reaction that manifests as fever, rigors, hypotension, headache, vasodilation with flushing, myalgia and exacerbation of skin lesions and anxiety [2,3]. Typically the reaction occurs within two to eight hours of treatment and usually resolves within twenty-four hours without any interventions. The intensity of the reaction indicates the severity of inflammation and it is more severe where the number of organisms is abundant [2]. Moreover appearance of cytokines such as TNF, IL-8 and IL-16 increase the severity of JHR. Conversely antibodies against the inflammatory cytokines have

been shown to reduce the severity of JHR [4].

Since it is a transient clinical reaction no specific testing is required to make a diagnosis. The diagnosis is usually made clinically by presenting symptoms and time course following therapy for the disease. Investigations performed in the setting of JHR would reveal polymorphonuclearleucocytosis, lymphopenia and raised ESR [5]. Skin lesion histopathology would illustrate acute inflammatory changes such as dermal edema, vasodilatation of arterioles and capillaries, perivascular and interstitial polymorphonuclearleucocytic and round cell infiltration. Additionally recovering lesions may exhibit predominance of large mononuclear cells [5].

Most of the time JHR is self limited and benign, however on rare instances the reaction might be severe enough to discontinue treatment [6]. It is crucial to alert patients about the possibility if a reaction and prompt monitoring to avoid any harmful effects from it [7]. In patients with mild systemic features they can be pre-medicated with antipyretics such as aspirin or paracetamol, advised to consume adequate fluids and bed rest. Several dug therapies have been trialed for treatment of JHR in spirochetal infections but their benefit is limited. Minocycline and hydroxy-chloroquine exhibit immuno-modulatory and anti-inflammatory properties however their use has not been well established [8]. However, patients pre-medicated with anti–TNF-α antibodies and opioid analgesics have been shown to have fewer and less severe symptoms. Moreover it has been observed that patients who developed JHR following the first dose of antibiotic did not have further recurrences after subsequent doses [2].

Conclusion

In conclusion, this report is an effort to gain an insight into JHR that is assumed to be a rare occurrence in Lyme disease. JHR is a self-limiting reaction and the treatment is largely supportive. It is still unclear whether a certain class of antibiotics is responsible for triggering JHR. Further clinical studies are required to assess the severity and incidence rates between the various antibiotic classes.

References

1. Hu LT. Lyme disease. Annals of internal medicine 2012;157(3). Pubmed ID 22868858.
2. Belum GR, Belum VR, Arudra SKC, Reddy BSN. The Jarisch Herxheimer reaction: Revisited. Travel Medicine and Infectious Disease (2013). Available from: http://dx.doi.org/10.1016/j.tmaid.2013.04.001.
3. Maloy AL, Black RD, Segurola RJ. Lyme disease complicated by the Jarisch-Herxheirmer reaction. The Journal of Emergency Medicine. 1998;16:437-438.
4. Hoekstra KA, Kelly MT. Elevated Troponin and Jarisch-Herxheimer Reaction in Tick-Borne Relapsing Fever: A Case Report. Case Reports in Infectious Diseases. 2011, Article ID 950314, 3 pages doi:10.1155/2011/950314.
5. Singh G, Jalpota YP. JarischeHerxheimer reaction in early syphilis. Indian Journal of Dermatology Venereology and Leprology. 1995;61:386.
6. Yang C, Lee N, Lin Y, Hung C. Jarisch-Herxheimer Reaction after Penicillin Therapy among Patients with Syphilis in the Era of the HIV Infection Epidemic: Incidence and Risk Factors. Clinical Infectious Diseases 2010; 51:976–979.
7. Guerrier G, D'Ortenzio E. The Jarisch-Herxheimer Reaction in Leptospirosis: A Systematic Review. Public Library of Science ONE. 2013;8:e59266.
8. Fritzsche M. Chronic Lyme borreliosis at the root of multiple sclerosis - is a cure with antibiotics attainable? Med Hypotheses. 2005;64:438-448.