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Case Report

Late Discovery Of Whipple's Disease Complex By Herxheimer-Jarisch Reaction To Ceftriaxone Therapy: A Review Of The Literature And Case Report.

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Abstract

Tropheryma whipplei is the actinomycete that causes Whipple's illness, an uncommon chronic infection. Gastrointestinal problems are frequently reported in patients. We describe a case of classic Whipple's disease that was made worse by a likely Jarisch-Herxheimer reaction after ceftriaxone treatment was started.

Keywords : *Whipple's disease; Jarisch–Herxheimer reaction; antimicrobial treatment.*

INTRODUCTION

First identified by George Hoyt Whipple in 1907, Whipple's disease (WD) is a multi-system illness brought on by infection with the common ambient actinomycete Tropheryma whipplei [1]. With an estimated prevalence of two cases per million people worldwide, the diagnosis is extremely uncommon [2]. With an estimated 10% overall mortality rate, WD can be lethal if therapy is not received; however, response is typically quick with early diagnosis and antibiotic treatment [3, 4].In this case, a 43-year-old man with classic WD had a likely Jarisch-Herxheimer response (JHR) after starting antibiotic medication, and his diagnosis was usually delayed. The latter is a side effect that often appears 24 hours after beginning antibiotic treatment and includes fever, chills, headache, myalgia, and worsening skin rashes. [5] We provide an overview of the research on this side effect and how it relates to WD.

CASE DESCRIPTION

After an upper gastrointestinal endoscopy, a 43-year-old male was referred to the Royal Darwin Hospital's infectious disease division. The patient was a horticultural engineer from Australia who lived in a northern Australian city. He was of European descent, had spent 13 years in Australia's Northern Territory, and had no past medical history or drug sensitivities. He had visited Vietnam, Cambodia, and Indonesia for a few brief vacations. Finasteride, a drug used to treat androgenetic alopecia, was his only prescribed prescription.The patient did not experience gastrointestinal symptoms until the third year of his disease, although he did disclose an 8-year history of erratic and frequently incapacitating malaise. Monthly episodes of subjective fever, chills, and acute tiredness lasting 24 hours were among his earliest symptoms; these went away on their own. Blood cultures, thick and thin blood films for malaria, urine, and chest radiography were all part of the investigations at the time, and they were all normal. The ferritin level was high at 508 µg/L (normal range: 20–220 µg/L), and the erythrocyte sedimentation rate was 25 mm/h (normal: <10 mm/h). Giardia lamblia cysts were discovered during a microscopic stool examination, even though there were no gastrointestinal symptoms. His episodic malaise did not improve after receiving a single dose of tinidazole. He experienced morning stiffness but no signs of arthritis in the second year of his illness, which was accompanied by arthralgia in his hands, wrists, elbows, shoulders, and knees. He had a C-reactive protein (CRP) level of 14 mg/L, which is typical at less than 5 mg/L. An inflammatory arthritis autoantibody screen came out negative. Nonsteroidal anti-

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inflammatory drugs and paracetamol were used to treat the patient.The patient's episodic subjective fevers subsided by the third year of his illness, but he dropped 15 kg of body weight and experienced non-bloody diarrhea (watery bowel movements up to eight times per day) without any abdominal pain. Low hydroxocobalamin, 165 pmol/L (normal range: 200–900 pmol/L), was found during investigations, and G. lamblia cysts were once more found during fecal testing. There was no fecal calprotectin test conducted. Despite being prescribed a three-day treatment of metronidazole, his symptoms persisted. There were no other noteworthy findings on the chest, abdomen, or pelvis computed tomography, although there were slightly enlarged mesenteric lymph nodes.The patient was sent to the infectious diseases unit following confirmation of the WD diagnosis. With a tympanic temperature of 37.0C, a blood pressure of 110/60 mmHg, and a heart rate of 80 beats per minute, the patient looked healthy upon evaluation. He had bilateral quadriceps atrophy, darkening of the skin around the umbilicus, and a body mass index of 21. Other than that, the clinical examination was uneventful. Blood tests showed a hemoglobin level of 129 g/L, which is within the normal range of 135 to 185 g/L, indicating mild normocytic anemia. The CRP level was 21 mg/L, and the total protein level was 58 g/L (normal range: 64–84 g/L). Testing for HIV antigen and antibody was nonreactive. because of T's association.Cerebrospinal fluid was examined in whipplei with disseminated illness, including neurologic infection and endocarditis [3,6,7]. The results indicated that T. whipplei was not discovered by PCR; the white cell count was 2 × 106 (normal: ≤5), the red cell count was 6 × 106, the protein level was 0.33 g/L (normal range: 0.15–0.45 g/L), and the glucose level was 3.6 mmol/L (normal range: 2.7–4.2 mmol/L). Transthoracic echocardiography showed no signs of endocarditis.Ceftriaxone 2 g per day was administered intravenously to the patient. He had severe nausea, vomiting, chills, and sweats within seven hours of the first dose, but no rash or urticaria. Four hours later, his temperature peaked at 38.8C, having risen to 37.7C. Overnight, his symptoms went away entirely without any help from a doctor. He denied having experienced comparable incidents in the past or having a history of cephalosporin or related medicine sensitivities when questioned further.

After receiving ceftriaxone 2 g daily for two weeks without experiencing any further side effects, the patient was given oral trimethoprim–sulfamethoxazole 160/800 mg twice daily. Within a week of beginning antibiotics, his diarrhea had improved, and by the time of his two-month assessment, his arthralgia and gastrointestinal problems had subsided, and he had put on 12 kg. The patient stopped taking antibiotics when he was asymptomatic at 12 months.

DISCUSSION

Weight loss, diarrhea, arthralgia, and abdominal pain are symptoms of classic WD.A sample of infected tissue is necessary for the diagnosis, which is then verified by the presence of T. whipplei identified by PCR and distinctive histological alterations with PAS-stained macrophages [2,3,6]. The gastrointestinal, cardiovascular, neurological, and pulmonary systems are among the many organ systems that are frequently affected by infection [2,3]. There are also descriptions of asymptomatic carriage, self-limiting infections, and localized infections [3].An estimated 4% of Europeans are thought to be infected with T. whipplei, which is widely disseminated in the environment and has been detected in the saliva and feces of asymptomatic people [4,7,8]. Sewage workers have a greater probability of asymptomatic carrying, which is thought to be between 12 and 20% and suggests fecal–oral transmission [4,9].Although the best course of treatment for WD is unknown, it is advised to start with two weeks of intravenous antibiotics and then continue with oral medicine for a longer duration [10]. Immune reconstitution inflammatory disorders have been seen with WD therapy [2,5,11]. A patient receiving intravenous streptomycin and oral trimethoprim-sulfamethoxazole has been reported to have suspected JHR [5]. Relapses of WD are uncommon, but when they do happen, they usually affect the central nervous system and frequently happen years after antimicrobial medication has ended [2].Delays in diagnosis and treatment are frequently caused by the nonspecific character of symptoms, the rarity of the illness, and the challenge of diagnosis. If WD is not identified and treated, it may lead to mortality, irreparable brain damage, sepsis, and nutritional deficits [2]. Indeed, WD was always fatal before it was recognized and treated with powerful antibiotics [5,12,13].

Nevertheless, the prognosis is good with early identification and treatment, with patients getting better two to three weeks after beginning antibiotics [2,6,14].A variety of antimicrobials, such as penicillin, ceftriaxone, carbapenems, trimethoprim–sulfamethoxazole, and doxycycline, can affect T. whipplei. Antibiotics that can reach high concentrations in the central nervous system are preferred since up to 40% of WD patients experience involvement of the central nervous system [6,15]. Since WD relapses can happen years after treatment, therapy is often continued for a minimum of 12 months [2,10,16].Even after thorough rheumatological and infectious illness examinations, our case demonstrates the difficulties in identifying WD. Our patient had vague symptoms at first; arthralgia didn't appear until a year later, and gastrointestinal issues didn't appear until the third year of the illness. It took eight years from the onset of symptoms for the ultimate diagnosis to be made and for effective treatment to start. This trend, which reports 6 to 8 years from

the onset of symptoms to diagnosis, is in line with earlier research [4,17].Despite the fact that G. lamblia was isolated from the patient's feces twice, nitroimidazole treatment did not alleviate his symptoms. According to a prior study, 16% of patients with WD have Giardia, which is far greater than the 0.6% of individuals without WD [18].Our patient experienced an acute febrile reaction that went away on its own after intravenous ceftriaxone was started. Despite the possibility of a ceftriaxone allergy, no additional symptoms that would indicate beta-lactam hypersensitivity were seen, and ceftriaxone was well tolerated after additional dosing. A JHR is the most likely cause of these symptoms. The majority of JHR reports occur in patients who have spirochaete infections after starting intravenous penicillin [11]. Twelve hours after starting antibiotic treatment, a patient with WD had confusion, fever, and retinal vasculitis, according to a 1992 study by Playford et al. [5]. Prednisolone and carbamazepine were used to treat the patient, who recovered while taking antibiotics and was given a JHR diagnosis [5].Because symptoms may be linked to the underlying infection and an exacerbation may be ascribed to the illness rather than a JHR, it is probable that a JHR may frequently go undiagnosed [11]. A JHR seldom results in death and is only temporary, lasting a few hours at most [11]. Crucially, doctors should think about a JHR since first-line antibiotic treatment would be stopped if the symptoms were mistakenly attributed to a drug allergy.

CONCLUSION

Despite being rare, WD is a dangerous persistent illness that is challenging to identify but usually gets better rapidly with the right medications. JHR is a possible side effect of WD that, in the majority of instances, can be treated with supportive care. Patients should be evaluated if their symptoms increase within 4–6 hours of beginning antibiotics.

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