Massive stroke as a consequence of Jarisch-Herxheimer reaction in patient with symptomatic neurosyphilis (case report)

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INTRODUCTION

The Jarisch-Herxheimer reaction (JHR) was first described at the turn of 19th and 20th century by Austrian and German dermatologists in the patients treated for syphilis. It is known as an immunological response to antibiotic treatment of especially spirochetal infections caused by *Treponema pallidum*, *Borrelia spp.* etc. It occurs usually within the first 8 hours after the treatment initiation with a typical flu-like symptoms, such as fever, chills, myalgia, headache.

Some patients, mostly in a late stadium of syphilis, can develop a wide spectrum of neurological, cardiological and other systemic signs, or the present symptoms can be aggravated.

We present a case of an unusual type of JHR that manifested as an ischemic stroke in a patient treated for symptomatic neurosyphilis.

Prof. Dr. Adolf Jarisch (1850 – 1902) ⁸ and Karl Herxheimer (1861 - 1942) ⁹

CASE REPORT

A 53-year-old man was sent by his general practitioner (GP) to the neurology department for confusion, memory lapses and aggression which lasted for several months. He was healthy without any chronic diseases or medication. Because of progression of his neurologic symptoms, he underwent a cranial CT scan, where periventricular atrophy was detected. He refused to undergo further tests.

A month later he had to be brought by a police to a psychiatric department because of suicidal and murdering attempts.

During the stay the psychiatrists obtained a results of the screening blood tests for syphilis from the GP: **VDRL positive 1:16, IgM SPHA borderline 1:4, TPPA positive, TPHA positive, FTA-ABS IgG positive**. The serology test for HIV was negative. The results and the clinical signs led to the diagnosis of probable symptomatic neurosyphilis and the patient was transferred to our department.

At the admission no skin or mucous symptoms of syphilis were present. The patient reported to have only one sexual partner, female, during lifetime. He claimed not to have had any sexual intercourse in the past 10 years.

Because lumbar puncture could not be performed on the date of admission, the treatment according to the IUSTI guideline for the management of syphilis from 2014 with 5 million units of penicillin G intravenously every 6 hours was started.⁶ We controlled our patient's blood pressure and body temperature every 30 minutes after the injection because of the possibility of Jarisch-Herxheimer reaction. Thirty minutes after the first dose, he had a subfebrile temperature 37,8 °C, so we gave him with a 500mg tablet of paracetamol, which decreased the temperature to 37,4 °C. We administered the next dose of antibiotics a 6 hours later, Half an hour after the second injection patient was found lying in the bed with dyspnoea and was reacting with a groan only to a painful stimulus. He had a high blood pressure (197/102 mmHg), tachycardia (112/min), fever (38, 8°C) and the blood oxygen level measured by pulse oximeter was 70 %. We put our patient an oxygen mask with a flow of 4 litres per minute and the saturation increased to 90 %. Also he got an infusion of 100 ml of saline solution with 2 g of metamizol and 80 mg of methylprednisolone. Immediate cranial CT scan revealed a new small hypodense lesion in the frontal lobe of the brain of postischemic etiology. Because of his worsening health state (Glasgow Coma Scale 3, eye pupils isocoric, but deviated to the right side) our patient had to be transferred to the Intensive Care Unit (ICU) and connected to an artificial lung ventilation. The antiedematous therapy did not make any change.

The lumbar puncture detected positive IgM and IgG syphilis antibodies in ELISA and Western Blot tests, which confirmed the diagnosis of neurosyphilis. We recommended to continue in an antibiotic therapy with ceftriaxone 2 g per day intravenously for 14 days.

While investigating in the ICU, the higher levels of myoglobin (252,1 µg/l) and hsTroponinI (10 172 ng/l) were also revealed. The patient developed a secondary nonSTEMI ischemic heart disease for a first time in his life, which led to an administration of dual antiplatelet therapy and therapy of low molecular weight heparin.

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The overall health state of our patient got better after this treatment, he started to fix his eyes to a one place, he cooperated in a simple task, but he had a strong left-sided hemiparesis and confusion. After three days at ICU he was extubated and his spontaneous ventilation was stable. The left-sided hemiparesis got better, he remained confused with intermittent seizures of anxiety. Despite the everyday therapy with tiaprid tablets, the patient was dangerous to himself and other patients, therefore he had to be transferred again to a psychiatric department.

The Jarisch-Herxheimer reaction caused by penicillin G administration to the patient with confirmed neurosyphilis, manifested as an acute ischemic stroke and secondary heart attack in a person, who so far did not have any health problems.

DISCUSSION

Etiology

The JHR is primarily connected with syphilis infection, it occurs in 55 % of seronegative primary syphilis, in 95 % of seropositive primary syphilis and in 95% of secondary syphilis. It is quite rare in latent and late syphilis as well. But patients with neurosyphilis can develop a JHR in 75 %. ⁷

Even though it is less common than in syphilis, the JHR was described in other infectious diseases. It occurs in other bacterial infections, such as the spirochetal infections (Lyme disease, leptospirosis), brucellosis, tularemia, bartonellosis, also in some fungal and protozoal diseases. ^{1-5, 7}

Patophysiology

The exact origin and precise mechanism of the JHR still remains unknown, but the existing studies revealed a role of endotoxin-like lipoproteins, that are released from the dying bacteria after the antibiotic administration. This leads to a massive inflammatory response of phagocytosing mononuclear cells, which are producing cytokines in different stages of the JHR, mostly TNF- α , IL-6 and IL-8. This causes the changes in the symptoms throughout the reaction. Also the presence of these cytokines explains why corticosteroids are effective in the treatment of the reaction (the corticosteroids down-regulate some of the cytokines).

The bigger amount of bacteria leads to a larger immune response with more severe symptoms of JHR. ^{2, 5, 7}

Clinical signs and complications

First symptoms of JHR occur within the first 8 hours after the first dose of antibiotics and usually disappear in 24 hours spontaneously. The reaction consists of an elevation of body temperature to 39 °C – 42 °C with typical flu-like symptoms (headache, chills, sweating, sore throat, lymphadenopathy). This is followed by aggravating of the syphilis symptoms – the skin around the chancre becomes edematous, the rash more prominent. In the late syphilis, the signs of each organ damage can worsen (CNS, heart etc.).

In the beginning the hyperventilation and high blood pressure are present, later because the vasodilatation occurs, it transforms into a hypotension.

In patients with neurosyphilis the JHR manifests as an impairment of the existing neurological signs such as focal neurological deficits, convulsions, hallucination, confusion, coma etc.

The JHR in patients with tertiary syphilis can be lethal – especially if they have gummas in dangerous localizations (brain, larynx), aortic aneurysm and aortitis or optic neuritis. Very serious complications are acute pulmonary hypertension, neuroretinitis with sudden blindness, hepatitis or nephrotic syndrome. ^{1,2,4,5,7}

Treatment

The JHR is a self-limited condition which resolves spontaneously, therefore can be managed symptomatically. We can not prevent the reaction, but we can minimise the symptoms and shorten the duration. This can be achieved by antipyretics such as acetaminophen or aspirin and an adequate amount of fluids.

Some authors recommend a prophylactic administration of corticosteroids because it led to a reduction of febrile responses in every stage of syphilis. The effect of corticosteroid therapy on neurological signs was described in a few case reports only, yet always with a good outcome.²

CONCLUSION

Eventhough the tertiary syphilis with its neurological and psychiatric symptoms is less common thanks to accessible and quality health care, it is still present among patients all over the world. As we can see in our case, the JHR can exceptionally manifest as a severe state with a long-term consequences. Therefore we have to be prepared for a possible harder reaction in these patients and cooperate with colleagues from other specialisations.

DISCLOSURE

Authors have no conflicts of interests to declare.

REFERENCES

- [1] PUNIA V, RAYI A, SIVARAJU A. Stroke after Initiating IV Penicilin for Neurosyphilis: A Possible Jarisch-Herxheimer Reaction. Case Rep Neurol Med. 2014;Article ID 548179, p 4.
- [2] BELUM GR, BELUM VR, CHAITANYA ARUDRA SK, REDDY BS. The Jarisch – Herxheimer reaction: revisited. Travel Med Infect dis. 2013 Jul-Aug;11(4):231-7.
- [3] VAŇOUSOVÁ D, ČERNÝ R, ZÁKOUCKÁ H, KOŽNER P, JILICH D, LISÝ J, HERCOGOVÁ J, MACHALA L. Neurosyphilis. Cesk Slov Neurol N 2012;75/108(3):297-302.
- [4] KADAM P, MOK KT, CYNTHIA CARLYN. Jarisch-Herxheimer Reaction in Patient with Disseminated Lyme Disease. Journ of Case Reports 2013;3(2):362-365.
- [5] BUTLER T. The Jarisch-Herxheimer Reaction After Antibiotic Treatment of Spirochetal Infections: A Review of Recent Cases and Our Understanding of Pathogenesis. Am J Trop Med Hyg. 2017 Jan 11;96(1):46-52.
- [6] JANIER et al. European guideline on the management of syphilis 2014.
- [7] ARONSON, SOLTANI. The enigma of the pathogenesis of the Jarisch-Herxheimer reaction. Br J Vener Dis, 52 (1976), pp. 313-31
- [8] Dunst, Karin Maria et al. "Adolf Jarisch (1850–1902): an important contributor to Austrian dermatology." *Archives of Dermatological Research* 297 (2005): 383-388.
- [9] Weyers, Wolfgang. The discovery of tonofibrils. *Dermatopathology: Practical and Conceptual*. Oct – Dec 2002, Vol. 8, No. 4