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Persisting Hypolipoproteinaemia Following Multiple Wasp Stings

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Short report

Keywords: Wasp Sting, High Density Lipoprotein-cholesterol, Lipid Metabolism

Posted Date: November 23rd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1062834/v1

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Abstract Background

Severe allergic reactions and life-threatening multiple organ injury or failure are common after severe stings. However, reports on wasp stings complicated with continual hypolipoproteinaemia are scarce in the literature and there is no consensus for its therapeutic management.

Methods

This case is a 49-year-old female patient who developed severe allergic reaction and multiple organ failure after severe wasp stings and complicated with sustained hypolipoproteinaemia. Her clinical characteristics and the change of lipid levels are described. During the hospitalization, we did not perform any intervention for dyslipidemia.

Results

The patient's blood lipid levels were decreased after numerous wasp stings. In particular, the HDL-C was linear over all five days(nadir, 0.21mmol/L on day 5), and the level gradually recovered to normal till day 17. At the same time, the patient occurs severe inflammatory response and multiple organ dysfunction syndrome, especially liver failure. The 3 months follow-up of the patient was remarkable with normal lipid level and she was doing well in normal daily activities.

Conclusion

We highlight the hypolipoproteinaemia that might occur in the patient who after severe wasp stings. This study initially confirmed that there is some correlation between abnormal blood lipid metabolism and the evolution of the condition. Whether dyslipidemia in wasp stings is associated with hemolysis and inflammatory reaction is unclear, and further investigation would be required. As far as we know, this is the first report of persisting hypolipoproteinaemia after wasp stings. The clinical research and prolonged follow-up are yet to be concluded, and large-scale clinical studies need to be performed.

Introduction

Wasp stings is a serious and widespread public health concern in the world, especially in developing countries. Severe allergic reactions to wasp venom are common after stings, complications such as massive intravascular hemolysis, liver failure and renal failure follows, which can cause multiple organ failure and death in severe cases[1]. However, Wasp stings complicated with continual hypolipoproteinaemia is rarely reported in the literature and there is no consensus for hypolipoproteinaemia management. Herein, we describe a 49-year-old healthy woman who developed

persisting hypolipoproteinaemia following numerous wasp stings and intend to explore the characteristics and clinical implications of lipid metabolism in wasp stings.

Results

Case presentation and management

A 49-year-old previously healthy female living in the mountainous areas of Hubei China who was presented to the local hospital following numerous wasp stings all over the body 4 hours prior. The patient had features of severe allergic reaction with symptoms of skin flushing, dyspnea, nausea, vomiting, and muscle pain. The vital clinical parameters including blood pressure of 75/53 mmHg, heart rate of 130 beats per minute. She was immediately treated with intravenous (IV) methylprednisolone sodium succinate 80mg and intramuscular (IM) epinephrine 0.5mg in the rescue room before she was transferred to the emergency intensive care unit (EICU). The patient was healthy, with no prior history of hypertension, diabetes, coronary heart disease, chronic kidney disease, chronic liver disease, allergy or prominent family history of genetic and metabolic disorders. On further questioning, she denied recent use of lipid-lowering drugs. After admission, her vital signs were as follows: respiratory rate, 26 breaths/min; heart rate, 88 beats/min; blood pressure, 149/85 mmHg; and temperature, 36.7°C. Chest and abdomen examination were normal, and without lower extremity edema. The patient was stung 85 times in the head, upper limbs, back and hip. The areas that have been stung became red, swollen and central necrosis. Three hours later, gross haematuria was noted from urinary catheter on admission.

Arterial blood gas analysis showed metabolic acidosis with a pH of 7.00, PaCO2: 48.4mmHg, PaO2@79mmHg, HCO ³⁻ 11.9 mmol/L, and Base Excess -19mmol/L. Laboratory test results revealed a white blood cell count of 30.51×10⁹/L, total bilirubin count of 178.6 µmol/L, indirect bilirubin count of 114.2 µmol/l. The serum creatinine level was 189µmol/L, urea level was 12.98mmol/L, alanine aminotransferase level was 8139 IU/L, the aspartate aminotransferase level was 2558 IU/L, and myoglobin level was 1430ng/ml. The creatine kinase level was 820 IU/L, and the creatine kinase-MB isoenzyme level was 92 IU/L with PCT 8.54ng/ml. Blood coagulation function results showed a prothrombin time of 38.1 s, partial thromboplastin time 100 s. Urinalysis identified occult blood (++++), urinary bilirubin (+++), 4 erythrocytes/HPF, and 9 erythrocytes/HPF with specific gravity, 1.025. Blood tests for hepatitis B, Hepatitis C, and HIV were all negative. A chest X-ray showed pulmonary oedema. Her electrocardiogram showed sinus tachycardia. Blood lipid tests revealed a total cholesterol (TC) level of 0.67 mmol/l, triglyceride (TG) level of 0.85 mmol/l, high-density lipoprotein cholesterol (HDL-C) level of 0.41 mmol/l, a low-density lipoprotein (LDL-C) level of 0.8 mmol/l, apolipoprotein A1 (Apo-A1) level of 0.23 g/L, and apolipoprotein B (Apo-B) level of 0.74g/L (Table 1).

Laboratory data.							
Test	Reference interval	D1	D3	D5	D8	D10	D17
WBC(x10 ⁹ /L)	3.5-9.5	30.51	39.52	23.1	27.47	24.47	11.01
RBC(x10 ¹² /L)	3.8-5.1	4.16	2.91	3.12	3.05	2.89	1.97
Hb(g/L)	115-150	124	88	91	89	86	57
PLT(x 10 ⁹ /L)	125-350	167	35	20	61	116	161
PCT(ng/ml)	<0.25	8.54	15.61	17.09	5.23		
T-Bil(µmol/L)	3.42-20.5	178.6	105.5	74	56.7	63.7	20.1
U-BiL(µmol/L)	1-17.0	114.2	80.1	47.5	35.6	40.6	8.2
ALT(IU/L)	0-40	2558.3	843	807.3	504.7	295.8	59
AST(IU/L)	0-35	8139.5	1718.3	1414.8	203	93.9	21.2
Alb(g/L)	40-55	38.1	35	36.3	30.1	30.8	28.8
BUN(mmol/L)	1.7-7.5	12.68	34.4	16.85	33.36	24.85	23.18
Cr(µmol/L)	44-120	189	553.1	204.9	443	424.4	599.9
PT(s)	9-13	38.1	15.6	15		13	
APTT(s)	25-37	>100	>100	27.8		29	
TC(mmol/L)	2.8-5.68	0.67	0.5	0.42	0.48	2.51	3.21
TG(mmol/L)	0.28-1.80	0.85	0.73	0.85	0.54	3.15	2.01
HDL-C(mmol/L)	0.9-1.60	0.41	0.26	0.21	0.28	0.34	1.12
LDL-C(mmol/L)	1.5-3.11	0.81	0.92	0.87	0.84	2.39	2.54
ApoA⊠(mmol/L)	1.06-1.80	0.25	0.33	0.2	0.28	0.39	1.32
Apo-B(mmol/L)	0.6-1.14	0.74	0.43	0.65	0.55	0.85	0.98

Table 1

Based on the above characteristics, her admission diagnosis was severe wasp sting complicated with anaphylactic shock, intravascular hemolysis, rhabdomyolysis, hepatitis, acute kidney injury, acute pulmonary edema and coagulation abnormality. The patient was treated with large doses of hormonal, optimal hydration, alkalization of urine, microcirculation improvement and correction of coagulopathy. The patient received mechanical ventilation for aggravated gradually pulmonary edema during the hospitalization, and continuous renal replacement therapy (CRRT) was used for acute kidney injury more than 72h. On day 7, the patient was weaned from the ventilator and transferred to the general ward in a stable condition. However, her renal function did not improve with urine output less than 400ml/day. She

received dialysis for renal failure 4 times with approximately 3 to 4 hours of treatment time. After 20 days of treatment, the patient's condition improved with peak creatinine of 450.6mmol/L, and she was transferred back to the rural hospital for further dialysis. The three months clinical follow-up of the patient was remarkable with normal lipid level and renal function, and she was doing well in normal daily activities. During the hospitalizations, her blood lipid levels were decreased, in addition to TG. In particular, the decrease of the HDL-C was linear over all five days(nadir, 0.21mmol/L on day 5), and the level gradually recovered to normal till day 17. During the hospitalization, for the patient with dyslipidemia, she was under neither infusion of fat emulsion nor application of drugs that might interfere with blood lipids level such as propofol.

Discussion

Whether dyslipidemia would occur in patients after wasp stings is unknown, and the mechanism for this and the clinical implications remain unclear. At present, questions stated above have not been reported in previous studies and this article might be the first study to explore the impact of the wasp venom on the human from the perspective of dyslipidemia. In our case, the patient after mass wasp stings developed hemolysis and rhabdomyolysis with multiple organs dysfunction of the heart, lungs, liver, kidney, and hematological system. A highly significant correlation was found between the declining serum lipid levels trends and the patient's condition change. From day 5 to day 7, the patient developed severe multiple organ failure with the lowest level of HDL-C. After active treatment, the damage of multiple organ gradually improved, and the HDL-C concentration gradually increased and return to normal after two weeks.

The patient's past medical history was unremarkable. She had no history of a high-fat diet, no history of smoking or alcohol consumption, and no history of taking any medication. In addition, her blood lipid tests were normal in the community health screening 1 year previously. Requestioning the patient about her previous history and performing relevant laboratory examinations, including endocrine investigations, revealed no abnormalities, and we therefore rule out the chronic diseases which might induce the decline of the HDL-C concentration, including endocrine diseases and family genetic diseases. Before the first blood purification, the levels of blood lipid were significantly decreased. Thus, we speculated that dyslipidemia, including the persisting low level of HDL-C, has a close relationship with the patients after numerous wasp stings.

The changes in blood lipid levels play various important roles in the clinical observation of the critical patient's condition change, prognostic assessment, and treatment task. Decreased lipoprotein levels contribute to poor outcomes in patients with sepsis[2]. The application of exogenous lipids can significantly increase the lipoprotein level, especially in lipoprotein cholesterol. Furthermore, cholesteryl ester transfer protein (CETP) inhibitors can preserve HDL levels and improve outcomes for individuals with sepsis[3]. The hemolysis and systemic symptoms can be alleviated by the addition of exogenous cholesterol in sickle cell disease (SCD) patients who have chronic hemolytic anemia[4]. The cholesterol content of the cell membrane is critical for red blood cells(RBCs) membrane stability. The

supplementation of cholesterol during ex vivo erythropoiesis can strengthen the stability and integrity of RBCs membrane[5]. In this way, the hemolysis of red blood cells induced by melittin can be effectively alleviated.

The possible mechanisms of the decreased level of lipoprotein in this patient are listed below. Cholesterol inhibits the toxicity of wasp venom and causes lipid depletion. The patient after severe wasp stings, a large amount of wasp venom goes into the blood. The cholesterol in the cell membrane can combine with wasp venom and inhibit the hemolysis induced by wasp venom. Hence, lipid depletion occurs at an early stage of the disease[6]. Severe wasp stings induces sepsis-like syndrome. HDL-C can bind and clear bacterial toxins, such as lipopolysaccharide (LPS), which also has the functions of anti-inflammatory, anti-apoptotic, or antioxidant effects. Subsequently, the level of HDL-C decrease because it is excessively consumed in the persistent inflammation response. During the clinical course in this patient, rapid increase in WBC and PCT levels with the persistent decrease of HDL-C, indicating that the HDL-C has a significant correlation with the expressions of the inflammation. Lipid synthesis disorders are closely related to liver failure. Generally, the liver is considered an essential organ in lipid metabolism and synthesis. Phospholipase A2 (PLA2), which is the component of wasp venom, can cause lipid deposition, hepatic edema, and intrahepatic cholestasis, and finally, the necrosis of hepatocytes and liver failure occurs [8]. With the decline of the liver capacity (biosynthetic and catabolic) and the apparent reduction in hepatic enzyme activity, the HDL-C synthesis decrease in the patient with severe wasp stings.

Conclusions

In conclusion, the HDL-C level of this patient gradually recovered to normal till day 17. The patient suffered up to 85 needles of wasp stings, which means a large amount of wasp venom entered into the body. Subsequently, the patient occurs severe inflammatory response and multiple organ dysfunction, especially liver failure. This study initially confirmed that there is some correlation between abnormal blood lipid metabolism and the evolution of the condition. However, whether dyslipidemia in wasp stings is associated with hemolysis and inflammatory reaction need further investigation. As far as we know, this is the first report of persisting hypolipoproteinaemia after wasp stings. In our study, one of the limitations of this report is that is a case report, and further studies with a large sample are needed in the future.

Abbreviations

HDL-C: High Density Lipoprotein-cholesterol; EICU: Emergency Intensive Care Unit; TC: Total Cholesterol; TG: Triglyceride; LDL-C: Low Density Lipoprotein; Apo-A1: Apolipoprotein A1; Apo-B: Apolipoprotein B; CRRT: Continuous Renal Replacement Therapy; CETP: Cholesteryl Ester Transfer Protein; SCD: Sickle Cell Disease; RBCs: Red Blood Cells; LPS: Lipopolysaccharide; PLA2: Phospholipase A2

Declarations

Ethics approval and consent to participate

Notes Ethics approval and consent to participate The hospital ethics committee approval was granted of this case report. The patient provided signed consent forms. The subject in figure 1 provided consent for the use of her photographic images.

Consent for publication

The patient provided signed consent forms. The subject in figure 1 provided consent for the use of her photographic images.

Availability of data and materials

All data generated or analysed during this study are included in the published article.

Competing interests

The authors declare that they have no competing interests.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or notfor-profit sectors.

Authors' contributions

Zhenglin Quan were responsible for analyzing the data, organizing the manuscript and literature review in the introduction and discussion; Huanchao Zeng and Zhicheng Fang were responsible for interpreting the results. Xianyi Yang was responsible for drafting the introduction and conclusions, in addition to finalizing the writing. The author(s) read and approved the final manuscript.

Acknowledgements

The authors thank the patient and his family for their valuable contribution to this study.

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References

- Chinese Society Of Toxicology Poisoning And Treatment Of Specialized Committee, Hubei Emergency Medicine Committee Of Chinese Medical Association, Hubei Provincial Poisoning And Occupational Disease Union, Yang X, Xiao M. [Expert consensus statement on standardized diagnosis and treatment of wasp sting in China]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2018 Sep;30(9):819-823. Chinese. doi: 10.3760/cma.j.issn.2095-4352.2018.09.001. PMID: 30309405.
- 2. Cirstea M, Walley KR, Russell JA, et al. Decreased high-density lipoprotein cholesterol level is an early prognostic marker for organ dysfunction and death in patients with suspected sepsis. J Crit Care. 2017 Apr;38:289–294.
- Trinder M, Wang Y, Madsen CM, et al. Inhibition of Cholesteryl Ester Transfer Protein Preserves High-Density Lipoprotein Cholesterol and Improves Survival in Sepsis. Circulation. 2021 Mar 2;143(9):921-934.
- 4. Yalcinkaya A, Unal S, Oztas Y. Altered HDL particle in sickle cell disease: decreased cholesterol content is associated with hemolysis, whereas decreased Apolipoprotein A1 is linked to inflammation. Lipids Health Dis. 2019 Dec 20;18(1):225.
- 5. Bernecker C, Köfeler H, Pabst G, et al. Cholesterol Deficiency Causes Impaired Osmotic Stability of Cultured Red Blood Cells. Front Physiol. 2019 Dec 20;10:1529.
- 6. Raghuraman H, Chattopadhyay A. Cholesterol inhibits the lytic activity of melittin in erythrocytes. Chem Phys Lipids. 2005 Apr;134(2):183–9.
- 7. Barker G, Leeuwenburgh C, Brusko T,et al.Lipid and Lipoprotein Dysregulation in Sepsis: Clinical and Mechanistic Insights into Chronic Critical Illness. J Clin Med. 2021 Apr 14;10(8):1693.
- 8. Barr-Nea L. Neuman MG. Eschar J. et al. Histopathological changes in rat liver following repeated vespine envenomation.Liver1985;5(6):335

Figures



The patient after mass wasp stings. Day 1, the wounds were swelling and redness. Day 3, this was followed by the gradual emergence of suppuration and ulceration. Day 7, the scabs formed on the wound in wounds.



Figure 2

The change of HDL-C during the patient's hospitalization.