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A Case of Investigation and Diagnosis of Immune Thrombocytopenic Purpura After Vaccination of COVID-19 Inactivated Vaccine

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Abstract: *Objective:* Analyze the relationship between inoculating one case of the COVID-19 inactivated vaccine (Vero cell) and immune thrombocytopenic purpura to provide a reference for the standardized handling of adverse events following immunization. *Methods:* According to the "National Monitoring Program for Suspected Adverse Reactions to Vaccinations," an on-site investigation, data collection and analysis, expert group diagnosis, and medical association assessment were conducted on a case of immune thrombocytopenic purpura in District A of Chongqing after vaccination with the inactivated COVID-19 vaccine. The assessment report was delivered to the three relevant parties, the case was reviewed, and the experience was summarized. *Results:* The investigation and diagnosis by the district-level vaccination abnormal reaction expert group concluded that the disease that occurred after vaccination with the COVID-19 inactivated vaccine was secondary immune thrombocytopenic purpura, an abnormal reaction to the vaccination. The medical damage was classified as Level II Grade B. The vaccine production enterprise raised objections to this conclusion. After re-assessment by the municipal-level medical association, the conclusion was consistent with that of the district-level medical association. The vaccine production enterprise did not raise any further objections. *Conclusion:* Through active collaboration among district and municipal-level medical associations, disease control institutions, and vaccination units, the recipients have been promptly and effectively treated, providing financial support for their subsequent treatment and safeguarding their rights. The investigation and disposal procedures for adverse events following immunization in Chongqing are clear, and the mechanism is sound. It is necessary to continue strengthening the monitoring of adverse events following immunization according to the existing plan and to ensure timely and standardized handling. Simultaneously, it is crucial to strengthen vaccine management and vaccination management.

Keywords: Adverse events following immunization; Immunizations; COVID-19 inactivated vaccine (Vero cell); Immune thrombocytopenic purpura; Investigation and diagnosis

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1. Introduction

Vaccination is the most economical and effective measure to prevent infectious diseases [1]. Vaccination with the coronavirus vaccine can effectively reduce the risk of severe illness and death after infection with the coronavirus. After the outbreak of the coronavirus in 2020, the country launched the research, development, production, and vaccination of the coronavirus vaccine to protect the lives of the people, achieving emergency vaccination within just five months [2].

According to the official website of the Chinese Center for Disease Control and Prevention, from December 15, 2020, to April 30, 2021, a total of 265 million doses of the coronavirus vaccine were reported in China, with an incidence of adverse reactions of 11.86 per 100,000 doses. Among these, general reactions accounted for 83%, with a reported incidence of 9.84 per 100,000 doses; abnormal reactions accounted for 17%, with a reported incidence of 2.02 per 100,000 doses. The incidence of severe abnormal reactions was 0.07 per 100,000 doses, an extremely rare probability (less than one in 10,000). The incidence of general reactions and abnormal reactions to the coronavirus vaccine in China is lower than the average reporting level for other types of vaccines in 2019.

Nevertheless, concerns about the safety, effectiveness, and adverse reactions of the coronavirus vaccine are the main reasons people are unwilling to receive it [3,4]. Wong WHS *et al*. (2022) found that among those unwilling to receive the new coronavirus vaccine, 79% of respondents expressed concerns about its safety [3]. This indicates that the public is highly concerned about adverse reactions and the effectiveness of the new coronavirus vaccine. To address this, Chongqing City issued the *"Notice on Printing and Distributing the Guidelines for the On-site Investigation of Severe Suspected Abnormal Reactions to New Coronavirus Vaccines in Chongqing"*, which guides the on-site investigation of severe suspected abnormal reactions to new coronavirus vaccines in Chongqing.

Immune thrombocytopenic purpura (ITP), or idiopathic thrombocytopenic purpura, is an immune-mediated acquired disease that can occur in adults and children. It is clinically characterized by transient or persistent thrombocytopenia, and as the platelet count decreases, the risk of bleeding increases accordingly [5].

In May 2021, District A in Chongqing reported a case of immune thrombocytopenic purpura after vaccination with the inactivated COVID-19 vaccine. The district's disease control agency immediately launched an investigation and organized an expert meeting on the diagnosis of abnormal reactions to vaccination. An investigation and diagnosis conclusion was formed, and after assessment by the district and city medical associations, an assessment conclusion was given.

2. Materials and methods

2.1. Definition

The National Monitoring Program for Suspected Adverse Event Following Immunization (AEFI) defines an AEFI as a reaction or event that occurs after vaccination and is suspected to be related to vaccination.

2.2. Sources

Information is collected using case report cards, case survey forms, investigation reports, and other data from vaccine recipients. Recipients provide medical records such as physical examination records, prenatal examination records, and hospital admission and discharge records. The vaccination unit provides the Chongqing New Coronavirus Vaccine Informed Consent Health Inquiry and Medical Advice, medical institution practice license, vaccination qualification certification documents, pre-examination personnel and vaccination personnel practice certificates, vaccine transportation record forms, cold chain equipment registration forms, temperature record sheets for cold chain equipment, syringe entry and exit registration forms, and vaccination certificates. The vac-

cine manufacturer provides batch vaccine inspection reports and vaccine instructions.

2.3. Survey method

Upon receiving a telephone report about an AEFI following the administration of the inactivated COVID-19 vaccine, the disease control agency in District A immediately organized staff and members of the district-level expert group to investigate and diagnose abnormal reactions to vaccination to conduct an on-site investigation. The investigation included on-site inquiries, observations, data collection, and recommendations for the next treatment step, followed by the preparation of an investigation report. The collected data were organized, and an expert meeting was convened to investigate and diagnose abnormal reactions to vaccination.

The expert meeting consisted of one member from the municipal expert group and four members from the district expert group, specializing in internal medicine, surgery, haematology, and epidemiology. The experts provided their opinions independently, based on the principles of association with abnormal reactions to vaccination and the clinical course of the disease, and finally formed an investigation and diagnosis conclusion.

The vaccine manufacturer raised objections to the investigation and diagnosis conclusion of the district-level expert meeting and applied for assessment by the district-level medical association. When the vaccine manufacturer raised objections to the district-level medical association's assessment conclusion, they applied for re-assessment by the municipal medical association. The assessment conclusions of the medical associations at both the municipal and district levels were collected.

3. Results

3.1. Basic information about the recipient

The recipient, born on June 19XX, was 35 years old at the time of vaccination. She is female and has one son. Physical examination records from 2018 to 2020 indicate that the recipient had no underlying diseases. There were no abnormalities in her body shape or physical condition at the time of vaccination.

3.2. Survey on vaccination and vaccine storage and transportation

Information on the inactivated COVID-19 vaccine administered to the recipient is shown in **Table 1**. The recipient was required to stay for observation for 30 minutes after each vaccination and left after no abnormalities were found. The two temporary COVID-19 vaccination sites where she received the vaccine were approved by the Health and Wellness Administrative Department of District A, Chongqing. The vaccination-related personnel underwent professional vaccination training organized by District A's health and wellness administrative department and obtained COVID-19 vaccination training certificates. The inactivated COVID-19 vaccines at the two sites were delivered by the disease control agency of District A, Chongqing, using cold chain vehicles, maintaining a storage temperature of 2–8 ℃. The vaccine storage and transportation process and the pre-examination and vaccination implementation process met all requirements. The syringes used for vaccination were packaged intact and were within their validity period.

Table 1. List of recipients of inactivated COVID-19 vaccines

Vaccination dose	Vaccine batch number	Vaccine specifications	Dosage	Validity	The use of vaccine batch	AEFI report	AEFI classification
First dose	2021030258	0.5 mL/vial	0.5 mL/vial	2023/3/7	10797	5	4 cases of normal reaction and 1 case of abnormal reaction
Second dose	2021040037C	0.5 mL/vial	0.5 mL/vial	2023/4/9	20796	1	1 case of general reaction

3.3. Diagnosis and treatment of the disease

After receiving the second dose of the inactivated COVID-19 vaccine at a temporary site in District A, Chongqing, at around 10 a.m. on May 202X, small red spots appeared on the recipient's instep around 4 p.m. that afternoon, but no treatment was taken. One day after vaccination, blood blisters appeared in the recipient's oral cavity, but again, no treatment was given. The condition gradually worsened, with multiple bleeding spots and blood blisters appearing in the oral cavity. Two days after vaccination, she went to the emergency department of Chongqing A District People's Hospital in the early morning. A blood routine examination showed platelets at 5×10^9/L (low), white blood cells at 8.3×10^9/L, red blood cells at 4.51×10^{12}/L, and haemoglobin at 139 g/L. The hospital's emergency department admitted her to the Department of Nephrology and Hematology for thrombocytopenia treatment. Physical examination revealed ecchymoses of 0.1–1.0 cm in diameter on the limbs and trunk, which did not fade when pressed. Multiple blood blisters were seen in the oral cavity, and there was local bleeding on the gums. The preliminary diagnosis was thrombocytopenia. After admission, relevant examinations showed platelets at 1×10^9/L (low). She was treated with platelet transfusion, sodium chloride carbazochrome sulfonate, lancehead agkistrodon haemocoagulase, and Sodium glycinate.

Three days after vaccination, the recipient was transferred to another hospital and diagnosed with idiopathic thrombocytopenic purpura. She was given intravenous human immunoglobulin and dexamethasone, along with symptomatic treatments such as hemostasis, liver protection, and lipid-lowering medications. Her skin and mucosal ecchymosis subsided, and no discomfort was reported. Seven days after vaccination, her total platelet count was 224×10^9/L, and she was discharged with a diagnosis of primary immune thrombocytopenia (idiopathic thrombocytopenic purpura).

Within six months after vaccination, the recipient had her platelet count rechecked several times and was hospitalized for treatment after it dropped to a dangerous level, a total of nine times. During hospitalization, she received platelet-raising treatment, with her platelet count increasing and then decreasing after discharge. Until the expert meeting for investigation and diagnosis was held, she had been taking avatrombopag to maintain her platelet count.

3.4. Investigation and diagnosis conclusions

Based on the medical information provided by the recipient, including laboratory test results, imaging data, clinical manifestations, and physical examinations, the investigation and diagnosis expert group concluded that the recipient's main disease was secondary immune thrombocytopenic purpura. The conclusions were based on the following:

(1) A temporal correlation between the recipient's vaccination and the onset of the disease.

(2) The presence of bleeding symptoms.

(3) Multiple thrombocytopenia episodes.

(4) Bone marrow showing megakaryocyte hyperplasia with maturation disorder.

(5) Elevated platelets after immune-related treatment.

It was determined to be an abnormal reaction caused by vaccination, and the medical damage was classified as Class II B. The disease control agency in District A promptly delivered the investigation and diagnosis to the recipient and the vaccine manufacturer. The vaccine manufacturer objected to the investigation and diagnosis results and applied for an assessment by the district medical association.

3.5. District Medical Association's assessment conclusion

After receiving the assessment application, the District Medical Association of District A collected the required information from the recipient, the vaccination unit, and the vaccine manufacturer. The recipient's representa-

tive selected five professional assessment experts in forensic medicine, endocrinology, medical testing, haematology, and pharmacy (later replaced by epidemiology with the recipient's consent) and signed for confirmation. During the meeting, representatives of the recipient, the vaccination unit, and the vaccine manufacturer each presented their opinions and reasons. The experts then discussed and formed the assessment conclusion after a secret ballot. The district medical association concluded that it could not be ruled out that it was an abnormal reaction caused by vaccination. The diagnosis was immune thrombocytopenic purpura, and the medical damage was graded as Grade II B. The vaccine manufacturer objected to this conclusion and applied for re-assessment by the municipal medical association.

3.6. Municipal Medical Association's assessment conclusion

After receiving the re-assessment application and related materials, the Chongqing Municipal Medical Association collected the identification materials submitted by the three parties and the municipal and district disease control agencies. The vaccine recipient and the staff of the municipal medical association then randomly selected the identification experts from the national medical identification management system of the Chinese Medical Association. The expert identification group consisted of three haematology experts, one endocrinology expert, and one epidemiology expert. The vaccine recipient had no objection to the expert group. During the meeting, each party stated their facts and opinions separately, and the experts conducted on-site inquiries and investigations. After the parties left the venue, the experts deliberated and voted by secret ballot. The expert group concluded that abnormal reactions caused by the inactivated COVID-19 vaccine could not be ruled out, and the degree of damage was Grade II B.

4. Discussion

The Vaccine Management Law of the People's Republic of China defines vaccines as preventive biological products used for human immunization to prevent and control the occurrence and spread of diseases. Vaccines are the most economical and effective means of preventing and controlling diseases and protecting health. They are crucial for public health security. Vaccines allow humans to take proactive measures against infectious diseases [6]. Since the implementation of planned immunization in China in 1978, the incidence and mortality of vaccine-preventable diseases such as poliomyelitis, hepatitis B, diphtheria, measles, meningitis, and Japanese encephalitis have significantly decreased, with the number of cases declining year by year [7-10]. The widespread adoption of vaccination has built a strong barrier to protecting the health of the population.

By the end of 2020, COVID-19 vaccination efforts had commenced, and by July 31, 2023, the National Health Commission reported that 3.497 billion doses of COVID-19 vaccines had been administered nationwide, with 1.31 billion people vaccinated. The large-scale COVID-19 vaccination campaign has presented numerous challenges. In response, District A has implemented various measures to address these challenges, such as increasing personnel and outpatient configurations through training, setting up temporary vaccination points, and deploying mobile vaccination vehicles to alleviate the pressure on existing vaccination facilities. Community mobilization efforts have expanded vaccination coverage, creating an immune protection barrier. Relevant documents on AEFI (Adverse Events Following Immunization) monitoring work have been issued to standardize the handling process and effectively protect public interests. As the number of COVID-19 vaccinations increases, so does the number of reported AEFIs, necessitating that staff involved in AEFI monitoring be familiar with the handling process, improve efficiency, and manage each AEFI in a timely and standardized manner as per the guidelines.

In this case, after receiving the report, the disease control agency in District A promptly organized an ex-

pert group to conduct an on-site investigation, collect clinical data, vaccine data, and vaccination data, and write an investigation report. Staff maintained communication with the recipients throughout the process, updated medical information promptly, and organized an expert meeting for investigation and diagnosis. A member of the municipal expert group was invited to participate in the meeting and provide opinions, forming an investigation and diagnosis conclusion. After the vaccine manufacturer raised objections, it cooperated with the district and municipal medical associations to complete the assessment work, ultimately achieving a satisfactory outcome for all parties involved. This case highlights the importance of effective AEFI monitoring.

Currently, passive monitoring is the main method for AEFI monitoring, where feedback from the vaccine recipient or their family members is reported by vaccination unit staff to higher authorities. The professional level and business ability of the vaccination unit staff directly affect the sensitivity of AEFI monitoring. A survey on the awareness of AEFI by primary healthcare personnel conducted by Sun L *et al*. (2012) found that only 34.8% of respondents could correctly respond to the relevant laws and regulations related to AEFI treatment [11]. Additionally, an investigation of the human resource status of the Huizhou AEFI monitoring system revealed a significant shortage of monitoring personnel, with an average staffing rate of only 0.84 people per 10,000, and the quality of personnel was uneven [12]. The primary difficulties encountered in AEFI monitoring include staff shortages and unfamiliarity with the work. Therefore, it is necessary to increase human resource investment, strengthen team building, improve the quality of monitoring work, and ensure the normal operation of AEFI monitoring.

In future work, disease control agencies should enhance their study of AEFI monitoring, master on-site investigation, report writing, data collection, communication skills, expert diagnosis meetings, and writing investigation diagnosis reports. They should also ensure proper vaccine storage and transportation management. Vaccination units should standardize vaccination services, communicate effectively with vaccine recipients, master various on-site first aid measures, and cooperate with higher authorities to carry out related work. Vaccine manufacturers should assume greater social responsibility by providing safer and more effective vaccines, and actively cooperating with disease control agencies and vaccination units for AEFI monitoring. The whole society should vigorously promote the importance of vaccination to protect public health, creating a positive atmosphere of common concern and active participation. Finally, to carry out AEFI monitoring more efficiently, especially for serious AEFIs and those with significant social concerns, it is recommended that the government establish a special department or team to lead AEFI handling. This would ensure timely response, rapid contact, information exchange, efficient communication, standardized handling, and reduction of unnecessary contradictions and disputes.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Pan F, 2019, Vaccination is the Most Effective Measure to Prevent Infectious Diseases: Interview with Professor Zeng Guang of the Chinese Center for Disease Control and Prevention. Contemporary Chinese Medicine, 26(5): 1–3.

[2] Ma C, An Z, Wang F, et al., 2021, Prevention First Serves the Health and a Century of Building an Immune Wall: A Review of Immunization Planning Work and Achievements Since the Founding of the Communist Party of China 100 Years Ago. Chinese Journal of Vaccines and Immunization, 27(6): 609–614 + 638.

[3] Wong WHS, Leung D, Chua GT, et al., 2022, Adolescents' Attitudes to the COVID-19 Vaccination. Vaccine, 40(7):

967–969.

[4] Cheng X, Yan W, Wang X, et al., 2023, Comparative Analysis of Factors Affecting COVID-19 Vaccine Hesitancy in China. Chinese Journal of Social Medicine, 40(4): 431–436.

[5] Rodeghiero F, Stasi R, Gernsheimer T, et al., 2009, Standardization of Terminology, Definitions and Outcome Criteria in Immune Thrombocytopenic Purpura of Adults and Children: Report from an International Working Group. Blood, 113(11): 2386–2393.

[6] Ma L, Yang Z, Wang Y, 2024, Current Status and Prospects of Global Vaccine Research and Development. Journal of China Pharmaceutical University, 55(1): 115–126.

[7] Chai F, Zhang R, Cao L, et al., 1995, Analysis of the National Poliomyelitis Epidemic Situation in 1994. Chinese Journal of Epidemiology, 16(6): 338–342.

[8] Ma C, Luo H, An Z, et al., 2008, Analysis of Epidemiological Characteristics of Measles and Measures to Eliminate Measles in China from 2006 to 2007. Chinese Vaccines and Immunization, 2008(3): 208–213.

[9] Hao L, Ma C, Ma J, et al., 2010, Analysis of Epidemiological Characteristics of Measles in China from 2008 to 2009. Chinese Journal of Vaccines and Immunization, 16(4): 293–296 + 370.

[10] Fu Y, Bie F, He L, et al., 2021, Implementation Results of the Immunization Program in China. Chinese Journal of Clinical Research, 34(11): 1599–1601.

[11] Sun L, Shi Y, Xu W, 2012, Investigation on the Cognition of Suspected Abnormal Reactions to Vaccination Among Primary Health Care Workers in a Certain District. Modern Preventive Medicine, 39(2): 340–341 + 344.

[12] Liu X, Xiao W, Gong F, et al., 2010, Investigation and Analysis of Human Resources Status of Huizhou City's Adverse Reaction Monitoring System for Immunization. Chinese Journal of Medicine, 12(4): 714–715.