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CASE REPORT

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Unexpected hypereosinophilia after Sinopharm vaccination: a case report

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Abstract

Background COVID-19 vaccines have been pivotal in the management of the recent pandemic. However, despite their safety and efficacy, apprehension regarding possible adverse effects has always been raised. Most of the vaccine-related side effects are mild. However, serious complications like anaphylaxis and thromboembolic events have also been reported. Various hematological disorders, including hypereosinophilia, have been reported following COVID-19 vaccination, the exact mechanisms of which remain unclear.

Case presentation We report a 66-year-old male who developed hypereosinophilia (absolute eosinophil count: 4063 cells/μL) and lymphadenopathy two months after receiving the third dose of the BBIBP-CorV (Sinopharm) COVID-19 vaccine. Extensive investigations failed to identify an alternative cause for these findings.

Conclusions This case report underscores the potential for unexpected hematological adverse events following COVID-19 vaccination, even with inactivated vaccines. While a definitive causal relationship cannot be established, the temporal association between vaccination and symptom onset warrants further investigation. This case emphasizes the importance of continued surveillance for rare adverse events and additional research to elucidate the potential mechanisms underlying vaccine-associated eosinophilia.

Keywords Hypereosinophilic syndrome, Sinopharm COVID-19 vaccine, Vaccine adverse events, Lymphadenopathy, Case report

Introduction

Covid-19 vaccines have been instrumental in controlling the recent pandemic. Despite their overall safety and efficacy, concerns about potential adverse effects have persisted since their widespread implementation [1, 2]. While most vaccine-related side effects are mild and self-limiting (e.g., injection site pain, fatigue, headache) [3], severe complications such as anaphylaxis and thromboembolic events have also been documented [3–5]. Furthermore, Covid-19 vaccines have been associated with a range of adverse effects affecting various organ systems, including the hematological system. Lymphadenopathy and autoimmune disorders are among the reported side effects [3, 6]. Hematological disorders, including hypereosinophilia, have also been documented [7]. While the exact mechanisms linking vaccines to eosinophilic disorders are not fully understood, potential pathways include immune dysregulation, delayed-type hypersensitivity reactions, or cross-reactivity with vaccine components. To date, there have been limited reports of eosinophilic complications associated with mRNA-based COVID-19 vaccines. This report presents the first documented case of hypereosinophilia following the third dose of the inactivated Sinopharm COVID-19 vaccine.

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Case presentation

A 66-year-old man with type 2 diabetes mellitus (treated with metformin 500 mg three times daily) and benign prostatic hyperplasia (treated with tamsulosin 0.4 mg daily) presented to the emergency department with a two-month history of progressively worsening fever, night sweats, significant weight loss, and non-productive cough. These symptoms began two months after receiving the third dose of the BBIBP-CorV (Sinopharm) COVID-19 vaccine (Beijing Bio-Institute of Biological Products, China) [8]. The patient had no known allergies.

On admission physical examination, the patient was febrile (38.5 °C) with palpable, mobile, tender cervical and axillary lymphadenopathy. In the initial laboratory evaluation, eosinophilic leukocytosis was seen in complete blood count test (Table 1) (absolute eosinophil count of 4063 cells/μL).

To evaluate palpable lymph nodes, a neck and axillary ultrasound was performed. Due to respiratory complaints, a non-contrast chest computed tomography (CT) scan revealed mediastinal lymphadenopathy (Fig. 1).

To investigate the cause of leukocytosis, lymphadenopathy and increased inflammatory markers, the patient underwent additional assessments with microbiological, viral studies, serum angiotensin converting enzyme level measurement, and evaluation of rheumatological indices, which did not reveal any specific diagnostic diagnosis (Table 2).

A hematology consultation was performed, and according to their recommendation, to investigate the possibility of lymphoproliferative disorders, an excisional biopsy of the axillary lymph node was performed. Histopathological evaluation did not reveal any findings suggesting these disorders. In the next step, according to the hematologist's recommendation, the patient underwent bone marrow aspiration and biopsy, which did not reveal any malignancy.

Table 1 Initial Complete Blood Count (CBC)

Parameter	Value	Reference Range
WBC (cells/uL)	15.63×10^3	4.5—11.0×10^3
Eosinophil (%)	26	1—6
Neutrophil (%)	39	40—70
Lymphocyte (%)	28	20—40
Monocyte (%)	7	2 – 10
Hemoglobin (g/dL)	9.2	13.5—17.5 (men)
MCV (fL)	95.1	80—100
Platelet (cells/uL)	630000	150000—450000

Abbreviations: MCV Mean Corpuscular Volume, *WBC* White Blood Cell Count

Table 2 Laboratory Investigations to Rule Out Differential Diagnoses

Test	Result	Test	Result
Blood Culture	Negative	RF	Negative
Sputum Culture	Negative	ANA	Negative
Influenza PCR	Negative	Anti-ds DNA	Negative
COVID-19 PCR	Negative	CH50	Negative
Brucella IgM Ab	Negative	Anti-CCP	Negative
Brucella IgG Ab	Negative	P-ANCA	Negative
Brucella agglutination test	Negative	C-ANCA	Negative
2ME	Negative	Serum ACE level	Negative
Stool ova and parasite test	Negative		
Sputum MTB PCR	Negative		
HBS Ag	Negative		
HIV Ag-Ab	Negative		
Anti-HCV Ab	Negative		
HTLV I – II Ab	Negative		

Abbreviations: 2ME 2-Mercaptoethanol, *ACE* Angiotensin-Converting Enzyme, *ANA* Antinuclear Antibody, *Anti-ds DNA* Anti-double stranded DNA, *Anti-HCV Ab* Anti-Hepatitis C Virus Antibody, *C-ANCA* Cytoplasmic Antineutrophil Cytoplasmic Antibody, *HBS Ag* Hepatitis B Surface Antigen, *HIV Ag-Ab* Human Immunodeficiency Virus Antigen–Antibody, *HTLV I – II Ab* Human T-lymphotropic virus type 1 and 2 antibodies, *MTB* Mycobacterium tuberculosis, *P-ANCA* Perinuclear Antineutrophil Cytoplasmic Antibody, *PCR* Polymerase Chain Reaction, *RF* Rheumatoid Factor

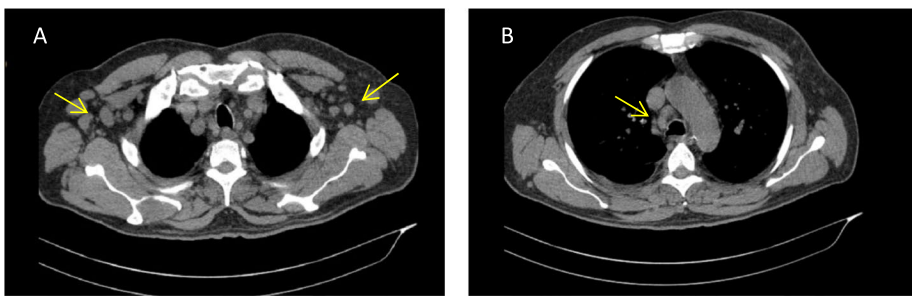

Fig. 1 Chest CT scan showing: **A** Enlarged axillary lymph nodes; **B** Enlarged mediastinal lymph nodes

Following consultation with an infectious disease specialist, the patient was hospitalized in the Respiratory Department on December 12, 2022, with suspected pneumonia. Empiric antibiotic therapy consisted of intravenous ceftriaxone 2 g twice daily and clindamycin 900 mg three times daily. Supportive care included fever management with paracetamol 500 mg orally four times daily, adequate hydration, and thromboembolism prophylaxis with subcutaneous heparin 5000 IU twice daily. Vital signs were closely monitored. With these interventions, the patient showed significant clinical improvement, fever resolved, and he was subsequently discharged from the hospital in good general condition.

It is worth noting that a follow-up chest CT scan performed after 10 days demonstrated a significant decrease in the size and number of mediastinal lymph nodes (Fig. 2). After three months, the patient's general condition remained good, and his initial complaints had resolved.

Discussion

This case report describes a patient with hypereosinophilia and lymphadenopathy following the third dose of the BBIBP-CorV (Sinopharm) COVID-19 vaccine. While post-vaccination lymphadenopathy is typically reported within weeks of vaccination [9], late presentations are increasingly well-recognized. For instance, El-Sayed et al. [10] reported reactive lymphadenopathy up to 10 weeks following mRNA and adenovirus-based COVID-19 vaccination, highlighting that immune-mediated lymphadenopathy may be prolonged beyond the early post-vaccination timeframe. Similarly, Yu et al. [11] escribed reactive lymphadenopathy 4–5 months after CoronaVac (Sinovac) vaccination, even later than in our patient. These findings support our hypothesis that inactivated vaccines such as BBIBP-CorV (Sinopharm) may pose delayed immune-mediated effects. Also, Westreich et al. [7] reported the onset of eosinophilia at 5–224 days following mRNA vaccinations, highlighting the desynchrony between vaccine platforms. These reports support the claim that adverse events such as lymphadenopathy and eosinophilia can appear months after vaccination, probably due to delayed stimulation or hypersensitivity reaction.

Causality assessments

To assess the potential causal relationship between the BBIBP-CorV (Sinopharm) COVID-19 vaccine and the patient's symptoms, we employed the WHO-UMC system for standardized case causality assessment [12]. This system provides a structured framework for evaluating the likelihood of an adverse drug reaction, considering factors such as temporal relationship, alternative explanations, and response to withdrawal. Based on the WHO-UMC criteria, the causality assessment in this case was categorized as "Possible" (Supporting information: Supplementary File 1).

Evaluation of other possible etiologies

To investigate potential underlying causes, a comprehensive evaluation included:

Infections: Blood/sputum cultures, viral PCRs (including COVID-19, influenza), and parasitic stool testing were negative.

Autoimmune diseases: Rheumatologic serologies (ANA, anti-dsDNA, RF, ANCA) were non-reactive.

Malignancies: Lymph node and bone marrow biopsies showed no evidence of neoplasia.

Medications: The patient had been on stable, long-term therapy with metformin (500 mg three times daily) for type 2 diabetes mellitus and tamsulosin (0.4 mg daily) for benign prostatic hyperplasia for five years prior to symptom onset, with no prior adverse effects. Although a rare case of metformin-associated eosinophilic interstitial lung disease has been reported [13], the temporal dissociation (five years of uneventful use) and lack of prior hypersensitivity reactions made drug-induced eosinophilia highly

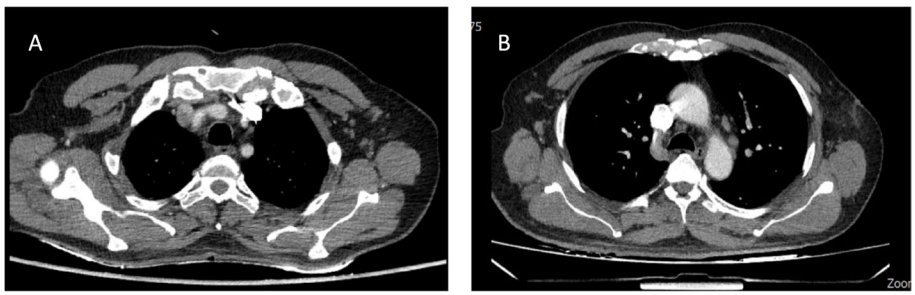

Fig. 2 Chest CT scan showing significant improvement in lymphadenopathy after 10 days

unlikely in this context. Tamsulosin has no established association with eosinophilia.
Exposures: No recent travel, occupational hazards, or environmental triggers were identified.

Review of relevant literature

Several reports have documented the occurrence of lymphadenopathy following COVID-19 vaccination. For example, Cocco et al. reported some patients who developed lymphadenopathy after receiving Pfizer, Moderna and AstraZeneca Covid-19 vaccines [9]. This happened within a few days to weeks after receiving the vaccine, and it mostly resolved itself in the follow-up of the patients [9].

A recent study by Westreich et al. identified 16 cases of peripheral eosinophilia in approximately 41,000 individuals vaccinated with the Pfizer or Moderna COVID-19 vaccines. The study found that eosinophilia was associated with various clinical manifestations, including respiratory symptoms, skin conditions, and systemic involvement. Some patients required treatment with oral corticosteroids or anti-IL-5 biologics. Additionally, several patients had underlying conditions like asthma or atopy [7].

A case report by Doman et al. described a 61-year-old male who, after the second administration of the BNT162b2 mRNA COVID-19 vaccine, developed watery diarrhea with hypereosinophilia. This case highlights the diverse spectrum of eosinophilic complications that can arise following COVID-19 vaccination, including colitis with hypereosinophilia. Furthermore, the Doman et al. review identified various eosinophilic disorders following COVID-19 vaccination, including myocarditis, EGPA, and skin manifestations, across different vaccine platform [14].

Furthermore, a recent case report described a patient who developed refractory hypereosinophilia and eventually rheumatoid arthritis following the first dose of inactivated BBV152 COVID-19 vaccine [15]. This case illustrates that rare and unexpected autoimmune complications, including the induction of autoimmune diseases, might be possible post-COVID-19 vaccination, even with inactivated vaccine platforms.

Table 3 presents a collection of reported cases where individuals experienced eosinophilic events following COVID-19 vaccination [16–22]. The data highlights the diversity of eosinophilic conditions observed, including unexplained hypereosinophilia, hypereosinophilic syndrome, eosinophilic pneumonia, and eosinophilic granulomatosis with polyangiitis (EGPA).

The reported cases involve individuals of varying ages, ranging from teenagers to adults, suggesting that eosinophilic complications can occur across a wide age spectrum. Both males and females are represented in the data, indicating that these complications can affect individuals of both sexes.

The table also details the types of vaccines involved. While the majority of cases involve mRNA-based vaccines (e.g., Pfizer-BioNTech, Moderna), one case involved the inactivated BBIBP-CorV (Sinopharm) COVID-19 vaccine, highlighting the potential for eosinophilic complications to occur with various vaccine platforms.

The onset of symptoms varied widely, ranging from days to weeks to even months after vaccination. In our case, the two-month interval between vaccination and symptom onset might initially appear atypical. However, recent data on mRNA COVID-19 vaccines demonstrated that vaccine-associated eosinophilia can have a delayed onset, with the time between dose 1 and initial eosinophilia ranging from 5 to 224 days in one study. Furthermore, in this study, 38% of the patients developed clinical sequelae that needed treatment, indicating the clinical relevance of delayed-onset eosinophilia [7]. Although the data presented here relates to mRNA vaccines, it supports the concept of a delayed-onset vaccine-related adverse event, even for other vaccine platforms.

The primary treatments administered to patients in these cases include corticosteroids (e.g., methylprednisolone), immunosuppressants (e.g., cyclophosphamide, rituximab), and supportive care. In most cases, patients experienced clinical improvement following treatment. However, it is essential to note that the long-term outcomes of these cases may vary, and further follow-up is necessary to assess the durability of the responses.

Possible pathophysiological mechanisms

Lindsley et al. [23] reviewed the role of eosinophils in COVID-19 and coronavirus vaccination. Though eosinophils may exert antiviral properties, their role in COVID-19 is poorly understood. Eosinopenia has been described in some COVID-19 patients; this may be a secondary phenomenon and not directly contribute to the disease course [24]. Importantly, the review by Lindsley et al. discussed the possibility of vaccine-induced immunopathology, especially TH2-skewed responses, as seen in some preclinical SARS-CoV-1 vaccine studies [23]. These studies demonstrated that certain vaccine formulations, particularly those using whole viruses or some protein subunits, can induce eosinophilic pulmonary disease in animal models [25, 26]. This emphasizes the importance of careful vaccine design and safety monitoring to minimize the risk of vaccine-associated immunopathology.

A possible explanation for the eosinophilia observed in our patient and other reported cases could involve a vaccine-induced TH2-skewed immune response [23, 27].

Table 3 Summary of reported eosinophilic events following COVID-19 vaccination

Study, Year, Country	Age, Sex	Vaccine	Onset	Clinical Manifestations	Diagnosis	Main Treatments	Outcome
Our case, 2024, Iran	66, M	BBIBP-CorV (Sinopharm)	2 months	Fever, night sweats, weight loss, non-productive cough	UE	Antibiotics Supportive care	CI
Hoxha et al. [16], 2023, Italy	48, M	BioNTech/Pfizer	5 days	Inguinal adenopathy, erythematous dermatitis	HES	Methylprednisolone Anticoagulation ASA Mepolizumab	CI
Piqueras et al. [17], 2021, Sapin	37, M	Pfizer-BioNTech	2 days	Fever, dyspnea, wheezing, chest pain, cough, palpitations, arthralgia	AEP	-	CI
Miqdadi et al. [18], 2021, Casablanca	66, M	AstraZeneca	5 h	Chest tightness, wheezing, polypnea, fever, asthenia, muscle weakness	Acute respiratory distress, and eosinophilia (25%) on CBC	Methylprednisolone	CI
Mahdi et al. [19], 2024, Qatar	Middle-aged, M	Pfizer-BioNTech	10 days	Hand clumsiness, fatigue, myalgia, non-pruritic skin rash	EGPA	Methylprednisolone Rituximab Cyclophosphamide IVIG	CI
Hwang et al. [20], 2023, Korea	71, F	Pfizer-BioNTech	After receiving	Shoulder pain, motor weakness, generalized rash	EGPA	Methylprednisolone Cyclophosphamide	CI
Nappi et al. [21], 2022, Italy	63, M	Moderna	1 day	Diplopia, headache, scotoma, impaired color vision, dry cough	EGPA	Methylprednisolone Cyclophosphamide	CI
Ramezanzade et al. [22], 2022, Iran	15, M	BBIBP-CorV (Sinopharm)	1 month	Colic-like flank pain	AAV	Prednisolone Cellcept	CI

Abbreviations: AAV ANCA-associated vasculitis, *AEP* Acute eosinophilic pneumonia, *ANA* Antinuclear antibodies, *ANCA* Antineutrophil cytoplasmic antibodies, *ARD* Acute respiratory distress, *ASA* Acetylsalicylic acid, *CI* Clinical improvement, *CTX* Cyclophosphamide, *EGPA* Eosinophilic granulomatosis with polyangiitis, *HES* Hypereosinophilic syndrome, *IVIG* Intravenous immunoglobulin, *M* Male, *UE* Unexplained eosinophilia

This mechanism, akin to the previously observed vaccine-associated enhanced disease, has been noted in vaccine trials for other viruses, such as dengue virus, respiratory syncytial virus, and measles, where certain vaccines have been shown to promote exaggerated TH2 responses and exacerbate disease after subsequent infection [7].

Further research is needed to investigate the specific mechanisms underlying eosinophilia in this case and to determine the potential role of the BBIBP-CorV vaccine in its development.

Conclusion

This case highlights the importance of continued surveillance for unexpected adverse events following vaccination. Further research is crucial to elucidate the potential mechanisms underlying this phenomenon, including the possibility of vaccine-induced immune dysregulation. Larger studies are necessary to assess the prevalence and clinical significance of eosinophilic events following COVID-19 vaccination, including those associated with inactivated vaccines like BBIBP-CorV (Sinopharm).

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-025-10990-8.

Supplementary Material 1.

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Not applicable.

Clinical trial number
Not applicable.

Authors' contributions
Behnam Dalfardi: Data curation; Methodology; Writing—original draft Niloofar Khoshnam Rad: Methodology; Project administration; Writing—original

draft; Writing—review & editing Tayebe Mohammad Alizade: Validation; Writing—original draft Maryam Edalatifard: Supervision Sanaz Asadi: Data curation Besharat rahimi: Conceptualization; Supervision; Validation.

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Data availability
The data that support the findings of this study are available from the corresponding author, [B.R], upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki, and all procedures were approved by the Institutional Review Board at Imam Khomenini Hospital Complex. Informed consent was obtained from the patient prior to participation.

Consent for publication
The patient provided written consent for the publication of this case report.

Competing interests
The authors declare no competing interests.

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