

CASE REPORTS

New-Onset Type 1 Diabetes Mellitus Following Hepatitis B Vaccination: Case Report and Review of Vaccine-Induced Autoimmune Mechanisms

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While vaccinations are critical for preventing viral infections, several reports have documented autoimmune conditions following immunization. We present a case of new-onset type 1 diabetes mellitus (T1DM) that occurred after Hepatitis B vaccination. A 42-year-old African American woman presented with polyuria, polydipsia, and unintended weight loss two months after receiving a Hepatitis B vaccine. Initial laboratory analysis showed a hemoglobin A1c (HbA1c) of 9.8%, along with elevated titers of anti-glutamic acid decarboxylase (GAD-65) antibodies. The patient was initiated on insulin therapy and remains under glycemic control. Potential mechanisms for T1DM post-vaccination include autoimmune activation triggered by molecular mimicry and inflammatory responses. Though rare, this case underscores the importance of timely screening for hyperglycemia in patients with new-onset symptoms following vaccination. This case highlights the need for awareness of immune-related adverse events following vaccinations. Early recognition and management are key to minimizing long-term complications.

1. Introduction

Vaccination is a critical public health intervention that has dramatically reduced the incidence of infectious diseases worldwide. Among the vaccines available, the Hepatitis B vaccine is a routine immunization that plays a vital role in preventing Hepatitis B virus (HBV) infections, which can lead to severe liver complications, including chronic liver disease, cirrhosis, and hepatocellular carcinoma (Al-Busafi and Alwassief, 2024; Zhao et al., 2020). The Hepatitis B vaccine is generally considered safe, and its use has been associated with a significant decrease in the global burden of liver-related morbidity and mortality (Nguyen et al., 2020). The World Health Organization (WHO) recommends that all infants receive the vaccine as part of the universal immunization schedule, and adults in high-risk groups, such as healthcare workers and those with chronic liver conditions, are also encouraged to get vaccinated (World Health Organization, 2019). Despite the overwhelming success and safety of the vaccine, there are occasional reports of adverse events, including rare cases of autoimmune diseases triggered following vaccination. Autoimmune diseases occur when the immune system mistakenly targets the body's own cells and tissues (Vojdani et al., 2020).

Although the precise cause of autoimmunity is not fully understood, it is believed that both genetic predisposition and environmental triggers, such as infections or vaccines, play a role. While autoimmune disorders following vaccinations are rare, they can have serious implications for affected individuals. Among the autoimmune conditions that have been reported post-vaccination are Guillain-Barré syndrome, autoimmune thyroiditis, systemic lupus erythematosus, and, in some cases, type 1 diabetes mellitus (T1DM) (Chavda et al., 2024; Ricke, 2023).

T1DM is a chronic autoimmune disorder that results from the immune-mediated destruction of pancreatic beta cells, which are responsible for producing insulin (Eizirik et al., 2020). Insulin is a hormone that regulates blood glucose levels, and without adequate insulin production, individuals with T1DM experience hyperglycemia, or elevated blood sugar levels (Bolli et al., 2021). The disease most commonly develops in childhood or adolescence, but adult-onset T1DM is increasingly recognized. Unlike type 2 diabetes mellitus, which is primarily related to insulin resistance, T1DM is characterized by an absolute insulin deficiency and requires lifelong insulin therapy for management (Tatovic et al., 2023). The exact triggers of T1DM remain unclear, but both genetic

susceptibility and environmental factors, including viral infections, have been implicated. The potential link between vaccinations and the onset of T1DM is still a subject of debate, and the association remains controversial due to the rarity of such cases. The relationship between vaccines and autoimmune diseases is complex. Vaccines are designed to stimulate the immune system to produce an immune response against specific pathogens (Sánchez-Ramón et al., 2018). However, in rare cases, the immune response triggered by the vaccine may cross-react with self-antigens, leading to autoimmunity. This phenomenon, known as molecular mimicry, occurs when the immune system is unable to distinguish between the vaccine antigens and the body's own cells (Suliman, 2024; Tagliamonte et al., 2023). In the case of T1DM, it is hypothesized that vaccine antigens may resemble proteins found on pancreatic beta cells, leading to an immune attack on these cells. Other proposed mechanisms include the possibility of an exaggerated inflammatory response following vaccination, which could exacerbate pre-existing autoimmune tendencies or reveal latent autoimmunity in genetically susceptible individuals (Root-Bernstein, 2023). Although T1DM has been reported after a variety of viral infections, including mumps, rubella, and coxsackievirus, cases of new-onset T1DM following vaccination are exceedingly rare. Most reports of vaccine-induced T1DM have involved viral vaccines, such as the mRNA-based COVID-19 vaccines or the measles-mumps-rubella (MMR) vaccine (Mochizuki et al., 2024). However, there have been very few documented cases linking the Hepatitis B vaccine to the onset of T1DM (Ferreira et al., 2018), making this case particularly significant. The rarity of these cases suggests that the Hepatitis B vaccine is generally well-tolerated, and the vast majority of individuals who receive the vaccine do not experience any adverse autoimmune effects.

In the few cases where T1DM has developed following vaccination, the timeline of symptom onset varies. Some individuals develop symptoms of hyperglycemia within days to weeks of vaccination, while others experience a more delayed onset. The clinical presentation of post-vaccination T1DM is similar to that of traditional T1DM, with symptoms including polyuria (frequent urination), polydipsia (increased thirst), unexplained weight loss, and fatigue. Laboratory findings typically reveal elevated blood glucose levels, a high hemoglobin A1c (HbA1c) reflecting poor glycemic control, and the presence of autoantibodies targeting pancreatic beta cells. The most common autoantibodies detected in cases of T1DM are anti-glutamic acid decarboxylase (GAD-65), anti-insulin antibodies, and

anti-islet cell antibodies. The case we present involves a 42-year-old African American woman who developed new-onset T1DM approximately nine weeks after receiving the Hepatitis B vaccine. Her presentation, characterized by classic symptoms of hyperglycemia and confirmed by laboratory findings, is consistent with autoimmune diabetes. Although a direct causal relationship between the Hepatitis B vaccine and T1DM cannot be definitively established, the temporal association between vaccination and the onset of symptoms raises important questions about the potential role of vaccines in triggering autoimmunity in susceptible individuals.

In this report, we aim to provide a detailed account of this case of new-onset T1DM following Hepatitis B vaccination, and to review the current literature on vaccine-induced autoimmune diseases. Our discussion will explore potential pathophysiological mechanisms that may link vaccination to the development of T1DM, and we will examine the implications of these findings for clinical practice. While the benefits of vaccination far outweigh the risks for the vast majority of individuals, understanding the rare adverse events associated with vaccines is crucial for improving vaccine safety and for identifying individuals who may be at increased risk of autoimmune complications following immunization. This case contributes to the growing body of evidence that suggests a potential, albeit rare, association between vaccines and autoimmune diseases. It highlights the need for continued research into the immunological mechanisms underlying vaccine-induced autoimmunity, and emphasizes the importance of monitoring for early signs of hyperglycemia in patients who present with new-onset symptoms following vaccination.

2. Case Report

A 42-year-old African American woman presented to the clinic with complaints of frequent urination, increased thirst, and unintentional weight loss of 12 lbs over the past two months. She reported receiving her Hepatitis B vaccine approximately nine weeks prior to the onset of these symptoms. Her medical history included well-controlled hypertension, managed with a low-dose beta-blocker, and asthma, for which she used an inhaled corticosteroid. There was no family history of diabetes or autoimmune disorders. On physical examination, her BMI was 26.1 kg/m², and her blood pressure was 130/85 mmHg. The patient appeared mildly dehydrated but was otherwise in no acute distress. Neurological examination was normal, and her cardiac exam revealed a regular heart rate and rhythm. There were

Table 1: Initial Laboratory Findings

Parameter	Result	Reference Range
Fasting Glucose (mg/dL)	240	70-99
HbA1c (%)	9.8	<5.7
C-Peptide (ng/mL)	0.6	0.8-3.1
Anti-GAD-65 (U/mL)	>200	<10
Anti-Insulin Antibodies	Negative	Negative
Urine Glucose	Positive	Negative
Urine Ketones	Negative	Negative

no signs of diabetic ketoacidosis, such as fruity breath or rapid breathing. Laboratory workup revealed a fasting blood glucose level of 240 mg/dL and a hemoglobin A1c (HbA1c) of 9.8%. Urinalysis was positive for glucose but negative for ketones. Autoantibody testing showed elevated anti-GAD-65 antibodies (>200 U/mL, reference <10 U/mL) and negative anti-insulin antibodies. Her C-peptide level was 0.6 ng/mL, indicating reduced insulin production. Based on these findings, the patient was diagnosed with new-onset type 1 diabetes mellitus. She was started on a basal-bolus insulin regimen, consisting of 15 units of insulin glargine once daily and 5 units of insulin lispro before meals. Additionally, she received education on frequent glucose monitoring and maintaining a balanced diet to help manage her blood sugar levels.

At her 3-month follow-up, the patient reported significant improvement in her symptoms. She had regained 5 lbs and her blood glucose readings were stable, ranging from 90-140 mg/dL. Her insulin doses were adjusted based on her glucose logs, and she was advised to continue close glucose monitoring. A repeat HbA1c measurement showed a reduction to 6.8%, demonstrating improved glycemic control. The patient remains on insulin therapy and continues to adhere to lifestyle modifications, including dietary adjustments and daily exercise.

3. Discussion

The occurrence of autoimmune diseases following vaccination has sparked extensive discussion and research, especially as vaccines have become more widely used during the global fight against infectious diseases. Vaccines, while overwhelmingly beneficial in preventing infections and controlling epidemics, are occasionally associated with rare autoimmune events. Historically, conditions such as Guillain-Barré syndrome and myocarditis have received the most attention in post-vaccination autoimmune studies. Guillain-Barré syndrome, characterized by immune system damage to the peripheral nervous system, and myocarditis, an inflammation of the heart muscle, have been documented in relation to various vaccines, including those for influenza and COVID-19 (Mahroum et al., 2022; Wen et al., 2023). However, less focus has been placed on the potential development of new-onset type 1 diabetes mellitus (T1DM) following vaccinations. T1DM is an autoimmune condition in which the immune system targets and destroys insulin-producing beta cells in the pancreas (Roep et al., 2021). The onset of this autoimmune attack typically occurs early in life, but cases of adult-onset type 1 diabetes are increasingly recognized. Vaccination-related autoimmune T1DM is a particularly rare phenomenon, and the precise mechanisms underlying this

condition remain poorly understood. While multiple cases of vaccine-induced T1DM have been reported following viral infections, including mumps, rubella, and cytomegalovirus, it is much less common to see new-onset T1DM following vaccinations (Thomas et al., 2022). However, growing evidence suggests that vaccines, which stimulate an immune response, may in some cases inadvertently trigger autoimmunity in genetically predisposed individuals.

In our case, a 42-year-old woman developed new-onset T1DM following her Hepatitis B vaccination. The timing of her symptom onset, occurring approximately nine weeks after the vaccine, suggests a potential link between the vaccination and the autoimmune response that led to diabetes. Although rare, this case aligns with a small body of literature suggesting that vaccines, including the Hepatitis B vaccine, may be involved in triggering T1DM in susceptible individuals. However, establishing a clear causative link remains challenging. The temporal association does not necessarily imply direct causality, and the precise mechanism by which a vaccine might induce autoimmunity leading to T1DM is still speculative. One prevailing hypothesis is that molecular mimicry may play a key role. Molecular mimicry occurs when a vaccine antigen shares structural similarities with self-antigens. In this case, it is possible that the Hepatitis B vaccine contained antigens that were similar to the antigens on pancreatic beta cells. The immune system, recognizing these antigens as foreign, may have mistakenly targeted and attacked the beta cells. This autoimmune response would eventually lead to the destruction of beta cells, resulting in insulin deficiency and the clinical onset of T1DM. Molecular mimicry has been implicated in other autoimmune conditions post-vaccination, including myocarditis and Guillain-Barré syndrome, lending some credence to this theory as a potential explanation for post-vaccination T1DM.

Another plausible mechanism is the role of vaccination-induced inflammation in triggering latent autoimmune tendencies (Arunachalam, 2024). Vaccines are designed to provoke an immune response, which can involve a temporary state of inflammation. In individuals with a genetic predisposition to autoimmunity, this heightened immune activation may overstimulate the immune system, leading to the development of an autoimmune disorder. In the case of T1DM, the inflammation may target the pancreas, resulting in beta-cell destruction. The inflammatory response might also exacerbate pre-existing conditions of insulin resistance or subclinical beta-cell dysfunction, hastening the onset of T1DM. In our patient's case, it is conceivable that a pre-existing, undetected autoimmune tendency was accelerated by the vaccine-induced inflammatory response. Additionally, genetic predisposition is likely a critical factor

Table 2: Follow-Up Laboratory Results (3 Months Post-Diagnosis)

Parameter	Initial Value	3-Month Follow-Up	Reference Range
HbA1c (%)	9.8	6.8	<5.7
Fasting Glucose (mg/dL)	240	115	70-99
C-Peptide (ng/mL)	0.6	0.8	0.8-3.1
Anti-GAD-65 (U/mL)	>200	150	<10
Insulin Dose (Units/day)	25	18	N/A

in the development of autoimmune diseases following vaccination (Scepanovic et al., 2018). Research suggests that certain genetic markers, such as human leukocyte antigen (HLA) types, are associated with a higher risk of developing autoimmune diseases, including T1DM (Chen et al., 2021). In patients with these genetic susceptibilities, the immune system may be more prone to overreacting to the introduction of foreign antigens, as seen in vaccinations. Although genetic testing was not performed in our patient, it is possible that she may possess genetic markers that predisposed her to T1DM, and the Hepatitis B vaccine acted as a trigger that accelerated the development of the disease. Cases of post-vaccination T1DM have primarily been associated with viral vaccines, especially mRNA-based COVID-19 vaccines. In these instances, patients typically present with hyperglycemia and positive autoantibodies, similar to our patient's presentation. In a review of literature examining cases of vaccine-related T1DM, most reports describe symptom onset within weeks to months after vaccination, often involving the detection of autoantibodies such as anti-glutamic acid decarboxylase (GAD-65). The clinical presentation, laboratory findings, and treatment strategies in these cases bear striking similarities to our patient's experience. However, there are very few reports specifically linking Hepatitis B vaccination to T1DM, making this case particularly noteworthy. The rarity of such cases, combined with the life-saving benefits of vaccination, emphasizes the need for a nuanced understanding of the risks and benefits associated with vaccines. It is important to note that the vast majority of individuals who receive vaccines, including the Hepatitis B vaccine, do so without developing any serious adverse effects. Vaccines remain one of the most effective public health interventions available, and the occurrence of vaccine-related autoimmune diseases is exceptionally rare. Nonetheless, clinicians should be aware of the potential for such events and consider routine screening for hyperglycemia and autoantibodies in individuals who present with new-onset symptoms after vaccination, particularly in those with a family history of autoimmune diseases.

4. Conclusion

This case highlights a rare but notable instance of new-onset type 1 diabetes following Hepatitis B vaccination. Though causality is difficult to establish, it is essential for clinicians to be vigilant for autoimmune responses post-vaccination, particularly in patients presenting with symptoms of hyperglycemia. Early recognition, prompt diagnosis, and initiation of insulin therapy are crucial for managing such cases effectively. Further research is needed to better understand the mechanisms involved in vaccine-associated autoimmunity and to develop strategies for early detection and prevention.

Declarations

Consent to participate

The authors declare that they have no conflict of interest

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Consent was obtained from the patient

Author contribution

E.C.P: investigation, formal analysis, writing original draft. S.A: conceptualization, writing original draft, and supervision.

Reference

1. Al-Busafi, S.A., Alwassief, A., 2024. Global Perspectives on the Hepatitis B Vaccination: Challenges, Achievements, and the Road to Elimination by 2030. *Vaccines* 12, 288. <https://doi.org/10.3390/vaccines12030288>
2. Arunachalam, A.B., 2024. Vaccines Induce Homeostatic Immunity, Generating Several Secondary Benefits. *Vaccines* 12, 396. <https://doi.org/10.3390/vaccines12040396>
3. Bolli, G.B., Porcellati, F., Lucidi, P., Fanelli, C.G., 2021. The physiological basis of insulin therapy in people with diabetes mellitus. *Diabetes Res. Clin. Pract.* 175, 108839. <https://doi.org/10.1016/j.diabres.2021.108839>
4. Chavda, V.P., Gogoi, N.R., Shah, Y., Shah, D., Mazumder, B., 2024. New approaches to vaccines for autoimmunity, in: *Advanced Vaccination Technologies for Infectious and Chronic Diseases*. Elsevier, pp. 391–414. <https://doi.org/10.1016/B978-0-443-18564-9.00023-0>
5. Chen, W., Chen, X., Zhang, M., Huang, Z., 2021. The association of human leukocyte antigen class II (HLA II) haplotypes with the risk of Latent autoimmune diabetes of adults (LADA): Evidence based on available data. *Gene* 767, 145177. <https://doi.org/10.1016/j.gene.2020.145177>
6. Eizirik, D.L., Pasquali, L., Cnop, M., 2020. Pancreatic β -cells in type 1 and type 2 diabetes mellitus: different pathways to failure. *Nat. Rev. Endocrinol.* 16, 349–362. <https://doi.org/10.1038/s41574-020-0355-7>
7. Ferreira, G.L.C., Marano, C., De Moerloozee, L., Guignard, A., Feng, Y., El Hahi, Y., van Staa, T., 2018. Incidence and prevalence of hepatitis B in patients with diabetes mellitus in the UK: A population-based cohort study using the UK Clinical Practice Research Datalink. *J. Viral Hepat.* 25, 571–580. <https://doi.org/10.1111/jvh.12841>
8. Mahroum, N., Lavine, N., Ohayon, A., Seida, R., Alwani, A., Alrais, M., Zoubi, M., Bragazzi, N.L., 2022. COVID-19 Vaccination and the Rate of Immune and Autoimmune Adverse Events Following Immunization: Insights From a Narrative Literature Review. *Front. Immunol.* 13. <https://doi.org/10.3389/fimmu.2022.872683>
9. Mochizuki, S., Miura, J., Ucida, K., Kubota, R., Fujikawa, H., Takagi, S., Yoshida, N., Ootake, S., Fujimori, C., Shinohara, A., Tanaka, J., Babazono, T., 2024. Type 1 diabetes mellitus following COVID-19 vaccination: a report of two cases and review of literature. *Diabetol. Int.* 15, 577–582. <https://doi.org/10.1007/s13340-024-00695-9>
10. Nguyen, M.H., Wong, G., Gane, E., Kao, J.-H., Dusheiko, G., 2020. Hepatitis B Virus: Advances in Prevention, Diagnosis, and Therapy. *Clin. Microbiol. Rev.* 33. <https://doi.org/10.1128/CMR.00046-19>
11. Ricke, D.O., 2023. Immediate onset signatures of autoimmune diseases after vaccination. *Glob. Transl. Med.* 2, 1455. <https://doi.org/10.36922/gtm.1455>
12. Roep, B.O., Thomaidou, S., van Tienhoven, R., Zaldumbide, A., 2021. Type 1 diabetes mellitus as a disease of the β -cell (do not blame the immune system?). *Nat. Rev. Endocrinol.* 17, 150–161. <https://doi.org/10.1038/s41574-020-00443-4>
13. Root-Bernstein, R., 2023. From Co-Infections to Autoimmune Disease via Hyperactivated Innate Immunity: COVID-19

- Autoimmune Coagulopathies, Autoimmune Myocarditis and Multisystem Inflammatory Syndrome in Children. *Int. J. Mol. Sci.* 24, 3001. <https://doi.org/10.3390/ijms24033001>
14. Sánchez-Ramón, S., Conejero, L., Netea, M.G., Sancho, D., Palomares, Ó., Subiza, J.L., 2018. Trained Immunity-Based Vaccines: A New Paradigm for the Development of Broad-Spectrum Anti-infectious Formulations. *Front. Immunol.* 9. <https://doi.org/10.3389/fimmu.2018.02936>
 15. Scepanovic, P., Alanio, C., Hammer, C., Hodel, F., Bergstedt, J., Patin, E., Thorball, C.W., Chaturvedi, N., Charbit, B., Abel, L., Quintana-Murci, L., Duffy, D., Albert, M.L., Fellay, J., 2018. Human genetic variants and age are the strongest predictors of humoral immune responses to common pathogens and vaccines. *Genome Med.* 10, 59. <https://doi.org/10.1186/s13073-018-0568-8>
 16. Suliman, B.A., 2024. Potential clinical implications of molecular mimicry-induced autoimmunity. *Immunity, Inflamm. Dis.* 12. <https://doi.org/10.1002/iid3.1178>
 17. Tagliamonte, M., Cavalluzzo, B., Mauriello, A., Ragone, C., Buonaguro, F.M., Tornesello, M.L., Buonaguro, L., 2023. Molecular mimicry and cancer vaccine development. *Mol. Cancer* 22, 75. <https://doi.org/10.1186/s12943-023-01776-0>
 18. Tatovic, D., Narendran, P., Dayan, C.M., 2023. A perspective on treating type 1 diabetes mellitus before insulin is needed. *Nat. Rev. Endocrinol.* <https://doi.org/10.1038/s41574-023-00816-5>
 19. Thomas, S., Ouhtit, A., Al Khatib, H.A., Eid, A.H., Mathew, S., Nasrallah, G.K., Emara, M.M., Al Maslamani, M.A., Yassine, H.M., 2022. Burden and disease pathogenesis of influenza and other respiratory viruses in diabetic patients. *J. Infect. Public Health* 15, 412–424. <https://doi.org/10.1016/j.jiph.2022.03.002>
 20. Vojdani, A., Gushgari, L.R., Vojdani, E., 2020. Interaction between food antigens and the immune system: Association with autoimmune disorders. *Autoimmun. Rev.* 19, 102459. <https://doi.org/10.1016/j.autrev.2020.102459>
 21. Wen, P., Chen, X., Zhang, M., Chu, W., Wu, H., Ren, C., 2023. Guillain-Barre syndrome after myocardial infarction: a case report and literature review. *BMC Cardiovasc. Disord.* 23, 226. <https://doi.org/10.1186/s12872-023-03261-4>
 22. World Health Organization, 2019. Hepatitis B vaccines: WHO position paper, July 2017 – Recommendations. *Vaccine* 37, 223–225. <https://doi.org/10.1016/j.vaccine.2017.07.046>
 23. Zhao, H., Zhou, X., Zhou, Y.-H., 2020. Hepatitis B vaccine development and implementation. *Hum. Vaccin. Immunother.* 16, 1533–1544. <https://doi.org/10.1080/21645515.2020.1732166>