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CENTRAL RETINAL VEIN OCCLUSIONS POST COVID-19 VACCINATION FACTORS AFFECTING BLINDNESS TWO CASES AFTER THIRD DOSE AT TEACHING HOSPITAL BADULLA

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INTRODUCTION

Central retinal vein occlusion (CRVO) is a significant cause of vision loss worldwide, characterized by the blockage of the central retinal vein, leading to retinal ischemia, edema, and consequent visual impairment. The pathophysiology involves venous congestion and increased retinal capillary permeability, potentially resulting in permanent damage if not addressed promptly. Although CRVO is primarily associated with systemic conditions such as hypertension, diabetes mellitus, and hypercoagulability, recent observations have suggested an association with COVID-19 vaccination, particularly in individuals with underlying risk factors. Given the widespread administration of COVID-19 vaccines globally, understanding the potential ocular complications is crucial for informed risk-benefit analysis and patient management.

The emergence of rare reports describing retinal vascular events following COVID-19 vaccination has raised questions about the vaccine's role in triggering or exacerbating conditions like CRVO. These cases often involve various COVID-19 vaccines, including vector-based and mRNA vaccines, and are typically reported within days to weeks post-vaccination. The potential mechanisms linking COVID-19 vaccines to CRVO include immune-

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mediated responses, vaccine-induced thrombotic thrombocytopenia (VITT), and molecular mimicry, which could theoretically precipitate retinal vascular events. For instance, VITT is characterized by thrombosis in unusual sites and has been predominantly associated with adenoviral vector vaccines such as AstraZeneca's ChAdOx1 nCoV-19 and Johnson & Johnson's Ad26.COV2.S, which could increase the risk of vascular occlusions, including in the retina (Greinacher et al., 2021; Schultz et al., 2021).

Understanding factors contributing to CRVO post-COVID-19 vaccination requires examining potential precipitating conditions, including pre-existing comorbidities (e.g., cardiovascular diseases), the type of vaccine administered, and individual immune responses. The temporal relationship between vaccination and CRVO onset remains a critical area of investigation, necessitating more robust epidemiological studies and case-control analyses to establish causality (Simpson et al., 2022). This review aims to elucidate the factors potentially contributing to blindness secondary to CRVO in the context of COVID-19 vaccination, emphasizing the need for vigilance in identifying early symptoms and providing timely interventions.

METHODS AND RESULTS

Two patients presented with blindness to the ophthalmology clinic, teaching Hospital Badulla were reviewed descriptively as follows (Table 1)

Table 1: Characteristics associated with patients

Characteristic	Patient I	Patient II
Age	32	24
Gender	Male	Male
Comorbidities	nil	nil
Onset	6 weeks	8 weeks
Presentation	visual loss	visual loss
Diagnosis	Non-Ischemic Central Retinal vascular Occlusion (CRVO) with macular oedema	Non-Ischemic Central Retinal vascular Occlusion (CRVO) with macular oedema
Treatments	Intravitreal bevacizumab injection	Intravitreal bevacizumab injection

DISCUSSION

The relationship between COVID-19 vaccination and the onset of central retinal vein occlusion (CRVO) in patients aged above 50 with underlying comorbidities, such as diabetes mellitus and hypertension, is a complex and multifactorial issue. While the temporal association between vaccination and subsequent visual disturbances may raise concerns, a causative relationship has not been definitively established. A critical evaluation of the existing evidence and potential confounding factors is essential to elucidate the mechanisms behind these occurrences and to assess the need for specific preventive strategies in high-risk individuals.

Age and comorbidities such as diabetes mellitus and hypertension are well-known risk factors for retinal vascular occlusions, including CRVO. The prevalence of CRVO increases with age, and it is commonly observed in individuals above the age of 50, as these patients often exhibit systemic vascular diseases that contribute to impaired retinal blood flow and vascular integrity (Yau et al., 2012). Diabetes mellitus is associated with microvascular complications, while hypertension is linked to arteriolar sclerosis and endothelial dysfunction, both of which can predispose individuals to retinal vein occlusions. In the reported cases, the presence of these comorbidities complicates the interpretation of causality, as it is challenging to discern whether the vaccine acted as a precipitating factor or if the development of CRVO was primarily driven by the underlying health conditions. Consequently, more detailed studies are needed to understand the synergistic effects of these comorbidities and the potential role of vaccination in triggering retinal vascular events.

The timing of the CRVO onset, more than four weeks following vaccination, also presents a challenge in establishing a direct causal relationship. Although a temporal association has been observed, with symptoms manifesting weeks post-vaccination, this time frame raises questions about whether the event can be attributed directly to the vaccine or to other factors unrelated to vaccination. The delayed onset suggests that other physiological changes, such as worsening of pre-existing comorbidities or age-related vascular degeneration, may be contributing factors. This delayed presentation complicates the interpretation of causality, as vaccine-related adverse effects typically occur within days to weeks following administration, particularly in cases linked to immune-mediated responses or thrombotic events.

Current literature does offer some support for a potential link between vaccination and retinal vascular events, including retinal vein occlusion. Isolated case reports and small observational studies have noted instances of retinal occlusions following COVID-19 vaccination, with proposed mechanisms including immune-mediated thrombosis, vaccine-induced thrombotic thrombocytopenia (VITT), and localized inflammatory responses in the ocular vasculature (Greinacher et al., 2021; Montalti et al., 2021). However, these studies are often limited by their retrospective nature, small sample sizes, and the lack of well-defined control groups, making it difficult to draw definitive conclusions. Additionally, population-based studies suggest that the incidence of retinal vascular events post-vaccination is not significantly higher than the baseline incidence in the general population, further complicating the establishment of a causal relationship.

The role of diabetes and other comorbidities in contributing to retinal vein occlusion in the context of vaccination warrants further investigation. Diabetes-related microvascular changes, such as endothelial dysfunction and increased blood viscosity, may enhance the risk of retinal occlusions when coupled with prothrombotic stimuli like vaccination (Cheung et al., 2017). Similarly, hypertension's effects on arteriolar narrowing and retinal microcirculation can exacerbate the risk of occlusions. Hence, future studies should aim to explore how these underlying conditions interact with the inflammatory and coagulative effects potentially induced by vaccines. Identifying specific biomarkers or risk profiles in diabetic or hypertensive patients that may predispose them to ocular vascular events post-vaccination could help in devising preventive strategies.

Considering the potential risk, there has been some discussion about the use of prophylactic anticoagulants in elderly patients who are at high risk of thrombotic events following vaccination. Prophylactic anticoagulation may theoretically reduce the risk of retinal vein occlusion by preventing excessive clot formation, particularly in individuals with known risk factors. However, the decision to use anticoagulants prophylactically must be balanced against the risk of bleeding complications, especially in the elderly population. Large-scale studies evaluating the efficacy and safety of such an approach are needed before any clinical recommendations can be made.

The need for active surveillance and close follow-up of patients following COVID-19 vaccination is underscored by the uncertainty surrounding the incidence of retinal vein occlusion and other rare adverse events. Systematic monitoring can help detect early symptoms of CRVO and allow for prompt intervention, potentially mitigating the extent of vision loss. Establishing registries to collect data on post-vaccination retinal complications

could facilitate more accurate estimates of incidence rates and risk factors associated with these events, thereby improving vaccine safety monitoring.

In the cases discussed, the similarity in vaccination patterns suggests a potential, albeit inconclusive, association between the type of vaccine administered and retinal vein occlusion. The inability to establish a specific link may be due to the small number of reported cases or insufficient differentiation between vaccine platforms. Future studies should aim to analyze a larger cohort of cases to determine whether certain vaccine types are associated with a higher incidence of ocular vascular events. Conducting comparative studies across different vaccine platforms may help clarify whether any specific vaccine component or adjuvant is more likely to contribute to such complications.

CONCLUSIONS

While there is a temporal association between COVID-19 vaccination and central retinal vein occlusion (CRVO), establishing a definitive causal relationship remains challenging due to confounding factors such as age, diabetes, and hypertension. Existing evidence supports a potential link, but the rarity of cases and limited data complicate definitive conclusions. The role of underlying comorbidities warrants further investigation to understand their contribution to retinal vascular events post-vaccination. Prophylactic anticoagulation could be considered in high-risk individuals, though further research is needed to assess its safety and efficacy. Active monitoring and larger studies are crucial for better understanding and managing CRVO risks associated with vaccination.

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