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Case Report

Tracheal Calcification Following Warfarin Administration: A Case Report

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ABSTRACT

Warfarin ought to be utilized for an extended duration in individuals with a predisposition to thromboembolism, such as those with atrial fibrillation or aortic valve replacement. While the primary complication of long-term warfarin usage is the potential for bleeding, there are also infrequent complications like vascular and tracheal calcification. We present a case of a patient who experienced diffuse tracheal calcification as a result of long-term warfarin usage.

A 74-year-old female patient, who had been receiving chronic warfarin treatment for atrial fibrillation, required intubation and was admitted to the intensive care unit due to aspiration pneumonia. As the patient was unable to be extubated during the hospital stay, she became a candidate for Percutaneous dilution tracheostomy (PDT). It was discovered during the PDT procedure that all available spaces of the trachea above the sternum were calcified, preventing the passage of the trach needle. The presence of tracheal calcification was confirmed by both a radiologist and ultrasound examination.

Currently, individuals are compelled to employ oral anticoagulants, like warfarin, in order to avert thromboembolic diseases. Nevertheless, the protracted utilization of warfarin is linked with infrequent adverse outcomes, such as disseminated calcification. Consequently, meticulous scrutiny of these side effects is requisite for patients with enduring warfarin consumption.

Introduction

Percutaneous dilatation tracheostomy (PDT) is a standardized protocol frequently employed in the management of critically ill individuals necessitating prolonged mechanical ventilation in order to promote the process of weaning from ventilatory support, effectively supplanting the need for surgical tracheostomy. The technique of Percutaneous Dilatational Tracheostomy (PDT) entails the act of puncturing the trachea through the utilization of the adapted Seldinger technique, namely, the expansion of the tracheostomy pathway using a guiding wire [1]. PDT is a procedure frequently conducted on patients in critical condition within the confines of intensive care units, necessitating a prolonged employment of an artificial airway. This particular method for the establishment of a tracheostomy is executed within specialized care facilities as well as at the patient's bedside. Nevertheless, PDT does have the potential to give rise to significant complications, including hemorrhaging, the formation of a tracheoesophageal fistula, as well as the perforation of the posterior tracheal wall. Furthermore, there exist instances in which the accurate localization of the tracheostomy is rendered difficult due to the absence of

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discernible anatomical markers. On the contrary, due to the absence of visual feedback, the surgeon is unable to directly manipulate the position of the needle, hole, guide wire, or dilating forceps during the procedure [2].

Anticoagulant medications are utilized effectively in order to mitigate complications and mortality rates in patients afflicted with arterial thromboembolism and venous thromboembolism. Given the increasing average age of the global population and the subsequent rise in cardiovascular disease risk, the utilization of these medications poses a challenge. Among these medications, warfarin stands out [3]. Warfarin, an oral anticoagulant, competitively inhibits vitamin K epoxide reductase complex 1 (VKORC1), an enzyme that is vital for the activation of vitamin K. Consequently, this inhibition disrupts the synthesis of various coagulation factors, including factors II, VII, IX, and X, as well as regulatory factors. Furthermore, it also interferes with coagulants such as protein C and protein S [4]. Commonly employed in the treatment and prevention of thromboembolic disorders, warfarin's long-term utilization is associated with several rare complications, such as cholesterol microembolization, nephropathy, vascular calcification, osteoporosis, calciphylaxis, skin necrosis, and vasculitis [5].

In this report, we present a case of a patient who is a potential candidate for photodynamic therapy (PDT) and who has diffused calcification. This patient has been on long-term warfarin anticoagulation therapy due to atrial fibrillation (AF).

Case Report

A 74-year-old female patient was admitted to the intensive care unit due to shortness of breath and respiratory distress with a diagnosis of aspiration pneumonia. He had a history of diabetes and AF since 2 years ago, and since then he has been treated with warfarin, and he has regularly monitored the INR level during the treatment and adjusted the drug dose based on the INR value. During the period of taking warfarin, the patient did not suffer from complications such as bleeding and was asymptomatic. During the hospitalization, due to the drop in spo2, respiratory distress and tachypnea, the patient needs intubation. Due to the long intubation and the inability to extubate, the patient is a candidate for PDT. During PDT, all the available spaces of the trachea above the sternum were calcified and it was not possible to enter the tracheostomy needle. (Fig 1) Considering the patient's condition and the inability to move for imaging, the radiologist colleague They came to the patient's bedside for an ultrasound, and tracheal calcification was confirmed by ultrasound.

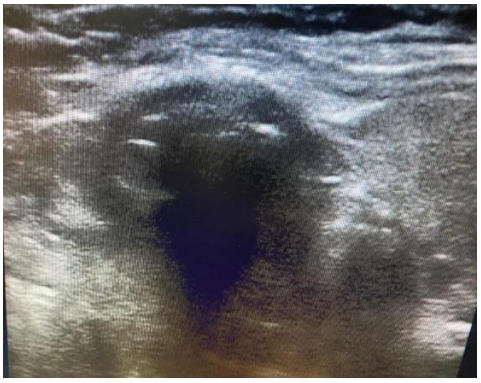

Figure 1- Unavailable spaces of the trachea above the sternum were calcified and it was not possible to enter the tracheostomy needle.

Discussion

We present a potential complication of prolonged prophylactic administration of warfarin, specifically disseminated calcification. Warfarin is commonly utilized for the management and prevention of thromboembolic disorders. As an oral anticoagulant, warfarin serves as a primary approach for clinical anticoagulation and effectively mitigates various thromboembolic conditions. Among anticoagulants, this medication is effectively employed to prevent ailments such as pulmonary embolism and deep vein thrombosis following mechanical heart valve replacement [6]. The extended usage of warfarin is linked to several potential adverse reactions including cholesterol microembolization, nephropathy, vascular calcification, osteoporosis, calciphylaxis, skin necrosis, and vasculitis, albeit the incidence of these complications is relatively infrequent. However, one of the lesser-known long-term side effects is the escalation in systemic arterial calcification [13,7]. Moreover, clinical and animal investigations have demonstrated that prolonged utilization of warfarin can provoke calcification in multiple tissues throughout the body, consequently leading to augmented stiffness of the vessel wall and diminished compliance. These pathological side effects may induce severe complications such as arteriosclerosis, valvular calcification, and coronary artery calcification [6-7]. In the case we present, the patient exhibited diffuse calcification in the trachea, which was confirmed via ultrasound.

The complexities of warfarin-associated vascular calcification are intricate and remain incompletely comprehended. One specific protein, known as matrix gamma-carboxyglutamate-glutamate protein (MGP), is implicated in the process of vascular calcification. MGP, an extracellular matrix protein, is firmly attached to minerals and is predominantly secreted by chondrocytes and vascular smooth muscle cells within the arterial

tunica environment [8,13]. The reason why long-term warfarin use is associated with increased vascular calcification is due to warfarin's competitive inhibition of VKORC1, whereas MGP-inhibitory vascular calcification relies on the active form of vitamin K. Therefore, decreased activation of vitamin K decreases the number of MGPs. and leads to vascular calcification [9,12].

In our patient, due to aspiration pneumonia and the inability to extubate during PDT, all available spaces of the trachea above the sternum were calcified and it was not possible to enter the trachea needle.

A prominent feature of calcifications is extensive calcification in the tracheobronchial tree. Tracheobronchial calcification is common among the elderly and can be caused by a number of diseases such as tracheopathy, osteochondroplasty, polychondritis, and amyloidosis. Although the association between long-term use of warfarin and progressive tracheobronchial calcification is well established, only limited cases have been reported [10-11]. To date, the exact mechanism of how warfarin causes calcification of the tracheobronchial tree is unclear, but previous studies have suggested a similar mechanism with vascular calcification, as tracheobronchial calcification has also been observed in a patient with Keutel syndrome, a genetic syndrome with a mutation in a gene that it regulates the function of MGP protein [11-12]. However, tracheobronchial calcification caused by warfarin is usually widespread, but it is always asymptomatic and is not a contraindication for continuing warfarin treatment.

Conclusion

Our case presented a patient who exhibited diffuse tracheal calcification that could potentially be attributed to the prolonged administration of warfarin. Despite the myriad adverse effects associated with the prolonged usage of warfarin, patients akin to our subject are compelled to utilize this anticoagulant. Consequently, it is imperative to exercise diligent surveillance in order to detect and manage these adverse effects in patients undergoing long-term warfarin therapy.

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