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A Case of Medication-Induced Diffuse Alveolar Hemorrhage in Neurofibromatosis Type I

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Introduction

- Amiodarone, an antiarrhythmic and apixaban, an anticoagulant have been associated with diffuse alveolar hemorrhage (DAH).
- Cases have been documented demonstrating DAH in the setting of amiodarone and apixaban treatment, however there are few cases examining DAH in combination therapy.
- We present a case of diffuse alveolar hemorrhage in the setting of amiodarone and apixaban treatment for paroxysmal atrial fibrillation.
- NF1 is know to have higher risk for major bleeds due to their friable vasculature.

Case Presentation

- A 69-year-old African American female with a past medical history of heart failure with preserved ejection fraction, hypertrophic obstructive cardiomyopathy, neurofibromatosis type 1 and permanent atrial fibrillation (On Amiodarone and Apixaban) was admitted for shortness of breath and hemoptysis.
- chest x-ray showed new bilateral patchy infiltrates worse on the right lower lobe, which were not present on previous study from 2 weeks prior
- On the first night of admission, the patient had severe hemoptysis for which the patient required two units of packed red blood cell transfusion.

Intervention

- Amiodarone and Eliquis were discontinued
- TB, autoimmune and viral panel and blood cultures were negative
- Despite extensive workup, she continued to have shortness of breath, hemoptysis, and worsening cough.
- Repeat chest x-ray showed improved aeration in the right lower lung field but mildly increased diffuse alveolar opacities.
- She had minimal improvement on IV Furosemide and IV Solumedrol
- Bronchoscopy was performed and showed blood clots in the upper airways and tracheo-bronchial tree. Diffuse alveolar hemorrhage hemorrhagic bronchitis was noted primarily in the right middle, and lower lobes and left lingula with no frank purulence or abnormal secretions.
- After her bronchoscopy, the patient had improvement in her shortness of breath, oxygenation and cough. She was aerating on room air, and the hemoptysis resolved.
- Given the patient's coincident atrial fibrillation, it was felt that the benefit of anticoagulation outweighed the risk of recurrent bleeding, and the patient was continued on aspirin alone at discharge.

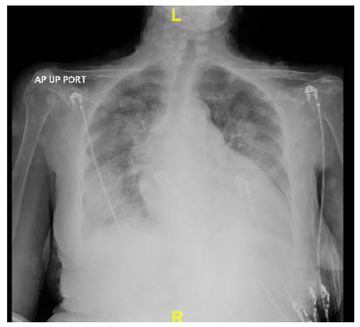

Figure 1: Xray on admission

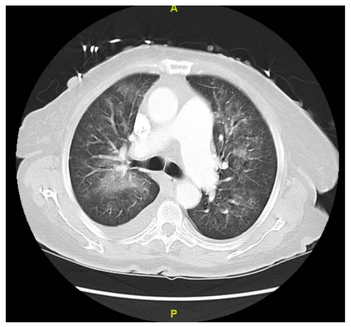

Figure 2: CT scan of DAH before patient got his bronchoscopy

Discussion

- DAH is a potentially life-threatening complication arising from the pulmonary microcirculation and has variable presentations including but not limited to hemoptysis, anemia, and hypoxic respiratory failure and diffuse lung involvement.
- Amiodarone is historically associated with alveolar and interstitial pneumonitis, and reports of amiodarone induced DAH is limited.
- In this case because the patient was taking amiodarone and apixaban, there is the potential for drug-drug interaction that could have contributed to the severity of the DAH.
- For instance, amiodarone is a known CYP3A4 inactivator (Ohyama, 2001). Apixaban has been shown to have increased levels in the blood when given with strong inhibitors such as itraconazole.
- Since apixaban is broken down via CYP34A, an inactivator such as amiodarone could potentially cause an increase in the amount of circulating apixaban which could increase the risk of DAH
- Pulmonary complications are a rare occurrence in NF1 is also known to lead to complications such as interstitial fibrosis and emphysema; which both can raise the risk of DAH. (Ngygen 2018; Park 2013). However, there appear to be few published studies that show correlation between NF1 and DAH.

Conclusion

- When considering anticoagulant therapy, clinicians should assess the risks and benefits of starting the medical therapy, specifically bleeding complications.
- Apixaban related bleeding complications should be addressed especially when the medication is administered concomitantly with CYP3A4 inhibitors such as amiodarone. NF1 patient are knows to have increased bleeding risk, anti-coagulation should be started under careful supervision.
- DAH is one of the potential bleeding complications of non-vitamin K antagonist oral anticoagulants, which requires prompt intervention including discontinuation of the offending medications, steroid administration, and close respiratory monitoring.
- Overall, careful monitoring and follow up should be a cornerstone when implementing apixaban therapy.

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