

**Case Report****Case of Remdesivir associated Atrial Fibrillation**Anand Naik<sup>1</sup>, Prashant Patil<sup>2</sup>**ABSTRACT**

Remdesivir has emerged as one of very important anti-viral drug against, COVID-19 during the pandemic. Cardiac involvement in patient's in COVID is mostly attributed to myocarditis or flare up of underlying heart disease. Remdesivir has an important cardiac side effect profile which is often overlooked. We present a case of 65 year old man with COVID 19 pneumonia with recent onset transient atrial fibrillation with fast ventricular rate secondary to remdesivir administration.

**Introduction :**

World has witnessed the most horrific pandemic in the century because of COVID-19 virus outbreak. Remdesivir has emerged as one of the important drugs in the management of SARS COV-19 virus infection. Remdesivir is included in most of the management protocols for COVID-19 disease. Therefore, remdesivir has been used rampantly in last 2 years. However much effective remdesivir is, it comes with it's side effects as well. Here we discuss a case admitted in our hospital, who developed atrial fibrillation during remdesivir therapy and eventually recovered on it's own after discontinuation of the therapy .

**Case Report :**

65 year old man admitted in the hospital with chief complaints of cough, fever and breathlessness since 5 days. He was a known case of hypertension and diabetes, however there was no history of any kind of heart disease. Patient was eventually tested positive for COVID 19 by RTPCR testing and HRCT Thorax revealed a CT Severity score of 20/25. Patient was admitted in ICU setup and treatment was given in the form of oxygen support via face mask and reservoir bag, Inj. Remdesivir, iv antibiotics, Inj. Methylprednisolone , Low molecular weight heparin in standard doses. Patient also

continued to take his regular medications for diabetes and hypertension. His blood sugar levels and blood pressure was within normal range throughout the hospital stay. With above treatment patient's condition improved in 3 days and therefore patient was shifted out of ICU to High Dependency Unit (HDU) for further care. Patient's oxygen requirement also decreased from 15l/min to 3l/min.

Patient started experiencing sudden onset palpitations after 5 days of admission. On examination, patient had irregularly irregular pulse with an apex pulse deficit of 15. Blood pressure was within normal limits and on auscultation, except for changing intensity of S1, rest examination was within normal limits. An emergency ECG was done which revealed Atrial Fibrillation with fast ventricular rate. Since patient did not have any history of heart disease or atrial fibrillation, thorough investigations were done for knowing the cause of atrial fibrillation. Serum electrolytes (Sodium, Pottasium, Ionic Calcium and Magnesium) were done which were in normal limits. Sr. TSH, Free T3 and Free T4 levels were also done to rule out ant thyroid disease. Since cardiac involvement in COVID 19 is a known entity, Sr. CPKMB levels and 2D echo were done to rule out Myocarditis, both were normal. The fast ventricular rate was controlled by administrating Inj. Diltiazem 12.5 mg iv and rate was controlled, patient was then shifted on oral Tb Diltiazem 30 mg TDS. Further hospital stay of the patient was uneventful and patient was discharged on oral medications.

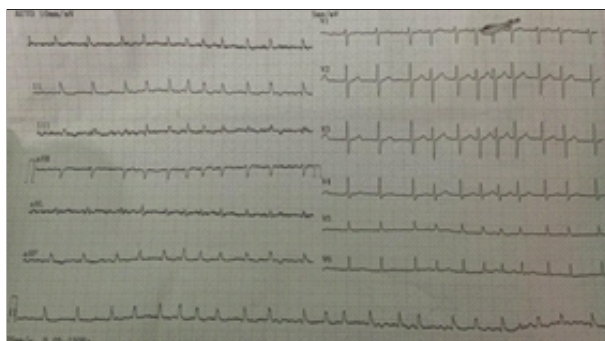
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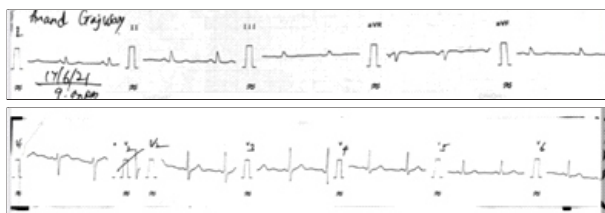
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(ECG of Atrial Fibrillation during Hospitalization)

On 15 days follow up it was observed that patient’s general condition was better and Repeat ECG was suggestive of a normal sinus rhythm. All the relevant investigations were done again and everything was within normal limit. 2D echo was done by a senior cardiologist which was normal.

So the case was studied thoroughly, all the reports and investigations were reviewed and literature was reviewed and the cause of atrial fibrillation with fast ventricular rate was attributed to Remdesivir.



(ECG at 15 days follow up showing sinus rhythm)

**Discussion :**

The expanding epidemic of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome has posed a serious threat to the global public health. There is an urgent demand for safe and effective therapeutics. Remdesivir, a broad-spectrum antiviral drug, emerges as a potential candidate for fighting against COVID-19 because of its potent in vitro anti-SARS-CoV-2 activity<sup>1</sup>. However, with increasing application, adverse effects of remdesivir have been detected and become a concern of clinicians.

Renal and hepatic derangements are a known entity due to remdesivir therapy and that is why routine renal function tests and liver function tests are

recommended in all the protocols of administering remdesivir. However, the side effect profile of remdesivir drug has more to it than just nephrotoxicity and hepatotoxicity. Other systems involved in the side effects are gastrointestinal, respiratory, reproductive and cardiovascular. **Table 1** describes the various side effects of remdesivir.

**Table 1 : Side effect Profile of Remdesivir Drugs**

System Involved	Adverse effect	Reference study
1) Hepatic	Hepatic enzymes increased.	1) J. Grein, et al. (2) 2) Y. Wang, et al. (1)
2) Gastrointestinal	Constipation, nausea, diarrhoea, vomiting, poor appetite and	1) The COVID-19 Investigation Team (3) 2) Grein, et al. 3) Y. Wang et al.
3) Respiratory	Acute respiratory distress syndrome, pneumothorax	1) J. Grein, et al. 2) Y. Wang, et al.
4) Cardiovascular	Hypotension, atrial fibrillation, cardiac arrest.	1) J. Grein, et al.
5) Renal Toxicity	Acute Kidney Injury	1) J. Grein, et al.

In *Grein et al.*'s study, hypotension (8%), **atrial fibrillation (6%)** and hypernatremia (6%) were observed in COVID-19 patients treated with remdesivir<sup>2</sup>.

**Table 2 : Cardiovascular side effects of Remdesivir**

Cardiovascular toxicity		
Hypotension	J. Grein, et al. [2] <sup>a</sup>	4/53
Atrial fibrillation	J. Grein, et al. [2] <sup>a</sup>	3/53
Hypernatremia	J. Grein, et al. [2] <sup>a</sup>	3/53
Cardiac arrest	Y. Wang, et al. [6] <sup>a</sup>	1/155

Management of atrial fibrillation should be like any other atrial fibrillation, the principles being same i.e. 1) rate control at earliest 2) Identifying the aetiology of atrial fibrillation and if reversible then correct the underlying cause 3) After ruling out Left atrial clot or after anticoagulation, rhythm control (Electrical or pharmacological). In our patients since it was a transient atrial fibrillation, only rate was controlled and during follow up, the patient had sinus rhythm.

The current safety profile of remdesivir is still incomplete. Increasing evidence has witnessed COVID-19 is implicated in injuries of multiple organs including lung, liver, gastrointestinal tract, heart and kidney<sup>4,5,6,7</sup>, hence it is complex to distinguish the underlying causes of adverse events

during remdesivir treatment. Since the experience of remdesivir application in the newly emerging COVID-19 is still limited, adverse drug effects need to be paid much attention to.

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