

Dear editors and reviewers,

Thank you for considering our manuscript. The reviewers have made a great effort in reviewing our manuscript and have given appropriate suggestions, which significantly improved the quality of this manuscript. About the quality of figures in this manuscript: We have edited the figures and the quality has improved. However, some of the figures' quality may not be high enough due to technology disadvantages. We think the figures we provide this time meet the publication standards. We have revised the manuscript and attached point-by-point responses to the reviewers' comments below. Don't hesitate to get in touch with me if there are any further questions.

Yours Sincerely,

Jun Teng

Department of Emergency, Qingdao Central Hospital

E-mail: owen-145@163.com

Replies from the authors to reviewers

To Reviewer #1:

Specific Comments to Authors: I. Advantages Grave is an autoimmune illness, also known as Basedow's disease, that is characterized by a variety of symptoms. It is relatively frequent in Endocrine disorder and is thought to be the reason of an increase in frequency on T3 and T4 lines. Graves' disease affects around 2% of women, with a female to male ratio of 7:1 to 8:1. However, hyperthyroidism symptoms can be caused by a variety of different factors (single goiter, multinodular goiter, viral thyroiditis, etc.). As a result, there are several treatment options available, depending on the exact cause and the problems caused by the condition. From an initial symptom of paralysis, a manifestation of hyperthyroidism that led the patient to the hospital, the author demonstrated logical thinking in diagnosing the disorder, finding causes, complications, and treatment outcomes (near and far) and use the CARE protocol checklist. The diagnostic criteria are clear: 1. Diagnosis of Grave's disease (or Basedow - quantitative hormone, differential diagnosis); 2. Diagnosis of myocarditis (cardiac enzymes, and use of CTA, magnetic resonance); 3. Diagnosis of junctional tachycardia (P wave loss, frequency 91 l/min, range 60 – 130). 4. Differential diagnosis: cerebral stroke, other hyperthyroidism of the thyroid gland, myocardial infarction Internists, cardiologists, and intensive care unit doctors learn diagnostic thinking skills from this clinical case => As a result, the paper is quite useful in clinical practice. Grave's disease has a number of cardiovascular complications, including sinus tachycardia, atrial fibrillation, premature ventricular contraction, and hypertension. However, even though this illness results in acute myocarditis, junctional tachycardia is a very uncommon occurrence in practice=> The article has contributed to world literature The paper concludes, "Graves' disease in combined with acute myocarditis and extreme hypokalemia." The echocardiogram with accelerated junctional rhythm often demonstrates the lack of P waves and a heart rate of 60-130 beats per minute, which are characteristic features and novel results of the study II. Some suggestions 1. Title: "Acute myocarditis presenting as accelerated junctional rhythm in Graves' disease: a case report and review of the literature". The study of the literature, on the other hand, is insufficient to emphasize the rarity, diagnosis, and treatment approaches. As a result, the reviewer requested clarification from the author (one table). 2. Annotated acronym (highlighted in blue): EMB?, ST? PR? CMR?.... 3. Introduction: sketchy (should write about 250-300 words): definition,

epidemiological characteristics, research in the world? What contribution does the article make to clinical practice and world literature? 4. EMB to determine myocardial damage. So according to the author, should this method be specified? What are the risks and hazards? Because of the fact, there must be specific indications according to the recommendation 5. Certain comments are unfounded and should be omitted from the conclusion, for example: "Usually misdiagnosed as myocardial infarction, Graves' disease combined with acute myocarditis is a rare manifestation, and the etiology thereof is due to an autoimmune process" => This statement belongs in the INTRODUCTION or DISCUSSION section only. - "Usually seen in young males, Graves' disease can manifest as thyrotoxic periodic paralysis, in which sudden paralysis and extreme hypokalemia will be experienced" => OK - "The etiology may be attributed to high carbohydrate intake" => should be discarded due to the lack of solid proof - "The correction of hypokalemia and hyperthyroidism will relieve the symptoms. The electrocardiograph of accelerated junctional rhythm usually shows an absence of P waves and a heart rate with 60-130 rates per minute, which is a manifestation of acute myocarditis" => OK III. Conclusion This is a rare clinical case, good diagnostic logic, significant in clinical practice. Reviewers agree to accept BUT need major additions and corrections before posting.

I. Advantages Grave is an autoimmune illness, also known as Basedow's disease, that is characterized by a variety of symptoms. It is relatively frequent in Endocrine disorder and is thought to be the reason of an increase in frequency on T3 and T4 lines. Graves' disease affects around 2% of women, with a female to male ratio of 7:1 to 8:1. However, hyperthyroidism symptoms can be caused by a variety of different factors (single goiter, multinodular goiter, viral thyroiditis, etc.). As a result, there are several treatment options available, depending on the exact cause and the problems caused by the condition. From an initial symptom of paralysis, a manifestation of hyperthyroidism that led the patient to the hospital, the author demonstrated logical thinking in diagnosing the disorder, finding causes, complications, and treatment outcomes (near and far) and use the CARE protocol checklist. The diagnostic criteria are clear: 1. Diagnosis of Grave's disease (or Basedow - quantitative hormone, differential diagnosis); 2. Diagnosis of myocarditis (cardiac enzymes, and use of CTA, magnetic resonance); 3. Diagnosis of junctional tachycardia (P wave loss, frequency 91 l/min, range 60 – 130). 4. Differential diagnosis: cerebral stroke, other hyperthyroidism of the thyroid gland, myocardial infarction Internists, cardiologists, and intensive care unit doctors learn diagnostic thinking skills from this clinical case => As a result, the paper is quite useful in clinical practice. Grave's disease has a number of cardiovascular complications, including sinus tachycardia, atrial fibrillation, premature ventricular contraction, and hypertension. However, even though this illness results in acute myocarditis, junctional tachycardia is a very uncommon occurrence in practice=> The article has contributed to world literature The paper concludes, "Graves' disease in combined with acute myocarditis and extreme hypokalemia." The echocardiogram with accelerated junctional rhythm often demonstrates the lack of P waves and a heart rate of 60-130 beats per minute, which are characteristic features and novel results of the study.

Replies from the authors: First of all, thank you for your careful review and affirmation of our manuscript. You have pointed out the flaws of this manuscript and we have

revised them following your comments. Let us reply to your suggestions in the following parts.

1. Title: "Acute myocarditis presenting as accelerated junctional rhythm in Graves' disease: a case report and review of the literature". The study of the literature, on the other hand, is insufficient to emphasize the rarity, diagnosis, and treatment approaches. As a result, the reviewer requested clarification from the author (one table).

Replies from the authors: Thank you for this suggestion. We have attached three tables separately in the discussion part as "Table 1, Table 2, Table3" We listed most related research and clarified this case's diagnosis, differential diagnosis, treatment process and uniqueness.

2. Annotated acronym (highlighted in blue): EMB?, ST? PR? CMR?....

Replies from the authors: We have given the sequence of the full words before abbreviating them in the manuscript. ST-segment and PR segment are the terms in the electrocardiography, and there are no full words.

3. Introduction: sketchy (should write about 250-300 words): definition, epidemiological characteristics, research in the world? What contribution does the article make to clinical practice and world literature?

Replies from the authors: We have revised the introduction part. We have written the definition, epidemiological characteristics and cited the researches in the world. We have also addressed the importance of this case.

4. EMB to determine myocardial damage. So according to the author, should this method be specified? What are the risks and hazards? Because of the fact, there must be specific indications according to the recommendation.

Replies from the authors: According to the latest guidelines by ESC (Alida L P Caforio, Sabine Pankuweit, Eloisa Arbustini, Cristina Basso, Juan Gimeno-Blanes, Stephan B Felix et al. Current State of Knowledge on Aetiology, Diagnosis, Management, and Therapy of Myocarditis: A Position Statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J.* 2013 Sep;34(33):2636-48, 2648a-2648d.), EMB is strongly suggested. EMB should be the gold standard for the diagnosis of myocarditis. However, this implies that all patients with suspected myocarditis should undergo an EMB which is not routine practice; moreover, current guidelines recommend EMB only in a limited number of clinical scenarios that do not include some common presentations of myocarditis, in particular, pseudo-infarction. The guideline gives the highest levels of recommendations for EMB in life-threatening clinical presentations. Thus, EMB is specified to certain kinds of patients. According to the latest guidelines, the complication rate of EMB is low (0-0.8) if experienced teams perform it. Therefore, we think this procedure has no risks and hazards for this patient. The patient will otherwise benefit from this procedure. The patient's symptoms of myocarditis were atypical. Therefore he met the indications for EMB according to the guideline. Besides, EMB is the gold standard for the diagnosis of myocarditis. It can detect the histologic characteristics of this patient, especially beneficial in defining the type of myocarditis, which can give us a clear answer for the cause of the patient's disease. That's the reason we persuaded him to accept this procedure.

5. Certain comments are unfounded and should be omitted from the conclusion, for example: "Usually misdiagnosed as myocardial infarction, Graves' disease combined with acute myocarditis is a rare manifestation, and the etiology thereof is due to an autoimmune process"

=> This statement belongs in the INTRODUCTION or DISCUSSION section only. - "Usually seen in young males, Graves' disease can manifest as thyrotoxic periodic paralysis, in which sudden paralysis and extreme hypokalemia will be experienced" => OK - "The etiology may be attributed to high carbohydrate intake" => should be discarded due to the lack of solid proof - "The correction of hypokalemia and hyperthyroidism will relieve the symptoms. The electrocardiograph of accelerated junctional rhythm usually shows an absence of P waves and a heart rate with 60-130 rates per minute, which is a manifestation of acute myocarditis" => Replies from the authors: We have revised the conclusion part. "Usually misdiagnosed as myocardial infarction, Graves' disease combined with acute myocarditis is a rare manifestation, and the etiology thereof is due to an autoimmune process" We have put this sentence in the introduction part. "The etiology may be attributed to high carbohydrate intake" We have deleted this sentence.

To Reviewer #2:

Please, review all your abbreviations, and give the full words sequence before abbreviating them; for example: EMB, ED. The Introduction reviewed the case, instead of giving a background summary with references to the relevant literature. Why was the patient given beta blocker at the ED, since the rhythm was below 100? What was the target? Or was it for symptomatic reasons? Please, provide better figures quality, especially the ECGs and CMR.

Replied from the authors: Thank you for the careful review of our manuscript. Your comments are pretty helpful for us. We have given the sequence of the full words before abbreviating them in the manuscript. We have also written this case's definition and epidemiological characteristics and cited the related study in the introduction part. The beta-blocker was used for the following reasons: Firstly, the patient was initially considered myocardial infarction; beta-blocker is demonstrated to reduce myocardial oxygen consumption, which is beneficial for the patient. Secondly, the patient would be performed coronary CTA. The heart rate requirement for this procedure is below 65bpm. The patient heart rate did not meet the requirement at that time. Therefore a beta-blocker was administered based on these considerations. We have edited the figures and made the best effort to provide the highest quality of figures. We think the figures we provided this time are of higher quality. However, some of the figures' quality may not be high enough due to technology disadvantages, especially the ECG of accelerated junctional rhythm. But we think the figures we provide this time meet the publication standards.