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A rare case of steroid responsive Torsades de pointes

Asha Ramsakal, Vadin Lall Dass

CASE REPORT

A 37-year-old female with sarcoma on pembrolizumab experienced lightheadedness during hospitalization. Telemetry revealed Torsades de pointes (TdP) that lasted 3.8 seconds (Figure 1). Her potassium, magnesium and troponin were normal. Admission EKG was sinus bradycardic at 44 bpm with a QTc of 478 ms. Cardiac MRI revealed subtle focal myocardial edema in the left ventricular septal wall suspicious for mild myocarditis likely secondary to pembrolizumab. The patient was given 2 grams of intravenous magnesium sulfate and initiated on methylprednisolone 1 mg/kg intravenously daily. She had no further lightheadedness or episodes of TdP. She was discharged on a course of tapering oral prednisone. Patient was also instructed to avoid all QT prolonging medications. Her pembrolizumab was discontinued. The patient was still asymptomatic at follow-up in five weeks and her QTc had decreased to 388 ms.

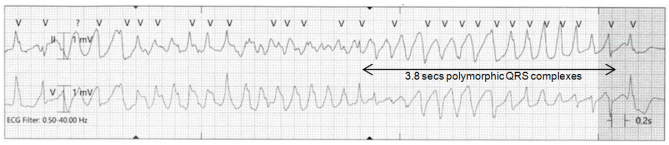

Figure 1: Telemetry strip showing Torsades de pointes.

DISCUSSION

Pembrolizumab is a highly selective programmed cell death receptor-1 (PD-1) blocking antibody which reverses T-cell suppression and in doing so promotes antitumor responses [1]. The incidence of myocarditis is rare (<1%). The most common etiology of TdP is QT prolonging medications [2]. Other risk factors include bradycardia, electrolyte abnormalities (hypokalemia, hypomagnesemia and hypocalcemia), female sex, underlying structural heart disease and advanced age. Patients with multiple risk factors present with the greatest risk [3]. Our patient was female, had baseline bradycardia at 44 bpm and was on ondansetron plus metoclopramide both of which can prolong the QT interval.

The key to management of TdP in stable patients is to identify and treat the potentially reversible risk factors. In our patient's case, it was to discontinue the pembrolizumab, ondansetron and metoclopramide. Another therapy with proven benefit is intravenous magnesium sulfate even in patients with normal magnesium levels [4]. In addition, the initial management of immune mediate myocarditis is a course of steroids [5]. Our patient responded quite favorably to methylprednisolone 1 mg/kg intravenously daily initially and then was successfully transitioned to an oral prednisone taper without further lightheadedness or episodes of TdP.

CONCLUSION

Pembrolizumab is a programmed cell death receptor-1 blocking antibody. To our knowledge this is the first reported case of Torsades-de-pointes associated with pembrolizumab immune-mediated myocarditis that was successfully responsive to steroids. The authors recommend telemetry monitoring of patients on pembrolizumab and avoidance of concomitant QT prolonging medications. If patients develop pembrolizumab-induced TdP, intravenous magnesium sulfate is indicated even in the absence of hypomagnesemia plus prednisone 1 mg/kg daily with a subsequent taper.

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SUGGESTED READING

- https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm608253.htm.
- www.crediblemeds.org/

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Author Contributions

Asha Ramsakal – Conception of the work, Design of the work, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Vadin Lall Dass – Conception of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

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Consent Statement

Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.