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Brief Report

Myocarditis after COVID-19 Vaccination in Pediatrics: Opportunities for Improvement

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ABSTRACT

The surge of pediatric admissions for myocarditis after COVID-19 vaccination has waned since 2021. Our experience has provided opportunities to improve our current understanding and future response. First, we must continue to search for risk factors in addition to age and sex. Overweight or obese status, a known risk factor for COVID-19 disease severity in adults, has been observed frequently in our unpublished experience in pediatrics and is worthy of further attention. Second, to aid in diagnosis, strong consideration should be given to establishing one uniform troponin isoform and range across centers instead of utilizing multiple isoforms and ranges. Third, developing a systematic and organized method for tracking deviations from proposed pathways such as ours will be essential in refining future recommendations and may help develop clinical equipoise to help justify future randomized controlled trials for treatment. With a deliberate and methodical approach, we can improve our understanding and management of myocarditis after COVID-19 vaccination and of myocarditis in general.

Keywords: Myocarditis; COVID-19 Vaccine; Pediatric; Pathway

DESCRIPTION

The surge of pediatric admissions for myocarditis after COVID-19 vaccination in children ages 12 and older has waned considerably since summer and fall of 2021 with just two additional admissions observed in 2022 by our group (compared with 8 cases in 2021). According to the American Academy of Pediatrics, as of January 18, 2023, only 58% of children adolescent ages 12-17 years (15.2 million) completed the 2-dose vaccination series [1]. Compared to historical data from December 29, 2021 (~ 1 year ago) showing a 53% vaccination completion rate (13.1 million), the rate of vaccine uptake appears to be decelerating towards an asymptote. The vaccination completion percentage is even lower for children ages 5-11 years (32%) and only 11% of children ages 6 months-4 years had received "at least one dose." Post-vaccine myocarditis in children under 12 years appears to be an even rarer adverse event, [2,3] and to date, we have not encountered any cases of post vaccine myocarditis in this age group.What will happen to these vaccinated children who receive vaccine boosters at age 12 years onwards? Despite uncertainty about whether future post-vaccine myocarditis cases will arise, it is unlikely that this phenomenon will be completely eradicated. As more data is gathered, our approach to management will likely need modification as well [4].

During this relative "lull" in cases, we must critically reflect on our experience to improve our current understanding and future response. Currently, the Centers for Disease Control and Prevention (CDC) have made a blanket recommendation for individuals who experienced "myocarditis or pericarditis after a dose of COVID-19 vaccine" to "not receive a subsequent dose of any COVID-19 vaccine" [5]. While such caution is presently justifiable, we as care providers must continue to analyze data that will aid the CDC in refining this recommendation to apply only to those at highest risk of developing recurrent myocarditis after COVID-19 vaccination and not all individuals as it currently stands. Age (12-29 years) and gender (male predominance) were quickly established as demographic risk factors [6]. While race and ethnicity have also been discussed, multiple investigators have wisely cautioned about other confounding socioeconomic variables such as variations in vaccination rate [7,8]. Looking beyond, we noted in our own

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unpublished experience that most patients (8 of 10 from 2021-2022) had a Body-Mass Index (BMI) percentile >85th percentile at least meeting the definition of overweight, with 7 of those 8 at the 95th percentile or higher meeting the definition of obesity. This trend was not convincingly borne out in other case series [9,10] and in multiple other studies BMI was not reported [7,8,11-13]. Obesity is a known risk factor in adults with COVID-19 for developing severe critical illness; interestingly, longer hospital stay was correlated with BMI, with the risk increasing when combined with younger age and male sex [14]. Hence, it seems plausible that a similar correlation could exist between BMI and risk of myocarditis after COVID-19 vaccination. Given the rarity of myocarditis, the small sample sizes in existing case series may not yield sufficient statistical power to establish elevated BMI percentile as a potential risk factor. However, this limitation alone should not justify ignoring such a possible emerging trend altogether.

As we developed our pathway, the impediments from lack of standardization were evident to no greater degree than in serum troponin evaluation. Covering multiple community hospitals in western Washington State provided us a unique vantage point into the variability of troponin testing at centers just tens of miles away from one another. An abnormal value in one center would result normal elsewhere and likely influence a different management plan. Further, multiple outpatient laboratories analyzed troponin T isoform instead of the troponin I followed while inpatient. These differences, evident nationwide in the USA, make direct comparisons of myocardial injury difficult within multi-center analyses [8,10] as well as between single-center studies [9,12,13]. Perhaps for these reasons, the CDC definition of probable and confirmed cases of myocarditis does not specify a specific troponin isoform or numerical cutoff [15]. However, this degree of variability is suboptimal especially for a disease entity such as myocarditis, which remains a clinical diagnosis relying on a constellation of supporting findings. Now is the time for the cardiology community to strongly consider uniformity. Utilizing one mutually agreed upon troponin isoform and normal range would simplify long-term analysis and also allow for easier pooling of data and eventual mathematical modeling and regression analysis that could aid in risk forecasting.

The goal of our pathway was to improve consistency, reduce mixed messaging, and to improve overall resource utilization. In 2010, a novel method with similar goals in mind was proposed as an innovative and systematic approach to gathering and acting on clinical data [16]. This Standardized Clinical Assessment And Management Plan (SCAMP) recognizes the uncertainty in medical decision-making for diverse patient populations, allows for differences based on clinical heterogeneity to emerge, and affords the opportunity to understand why practice deviations, which are inevitable, occur. Analysis of these deviations helps to reduce ineffective resource utilization and can also lead to important discoveries. The SCAMP methodology, proposed by pediatric cardiologists, has already found multiple uses within our field and would be well-suited for studying myocarditis after COVID-19 vaccination. For instance, one unanswered question is regarding if/when immunosuppressing agents are needed. While the treatment approach for adult and pediatric post-vaccine myocarditis patients has been very similar, there is a clear divergence regarding Intravenous Immunoglobulin (IVIG), which has been used predominantly in pediatric patients and much less frequently in adults [17]. There is no clear evidence demonstrating an improvement in clinical course and outcome with Intravenous Immune Globulin (IVIG). Truthfully, there is likely not an obvious consensus regarding how such improvement should be defined. Do we seek swift normalization of troponin, shorter hospital length of stay, faster recovery of ventricular systolic function, or something else? We hope that our pathway will help provide insights regarding the necessity of IVIG by raising the threshold at which its use is considered.

CONCLUSION

In conclusion, the current severity level of the COVID-19 pandemic, generalized pandemic fatigue, and on-going vaccine hesitancy have impacted the general public's risk-benefit calculus regarding COVID-19 vaccination, and it is unclear with what frequency and degree we will see future cases of myocarditis after COVID-19 vaccination. There are opportunities now to reflect on our prior experience to improve our future response. We must continue working to identify those at highest risk of developing post-vaccine myocarditis to make the best recommendations for our patients' safety. Strong consideration should be given to reducing or even eliminating the existing variability regarding how troponin testing is used to define myocardial injury as this will aid both in diagnosis and long-term analysis of these patients. Finally, while encouraging a standardized approach for triage and treatment, practice deviations should also be tracked and analyzed systematically, such as with a SCAMP methodology, to help uncover valuable insights and improve future guidance for providers. The gains achieved in managing myocarditis after COVID-19 vaccination will help improve overall management of myocarditis in general.

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