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COMMENTARY

Timely pediatric cancer diagnoses: An unexpected casualty of the COVID-19 surge

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The waiting room and halls of the pediatric outpatient clinic at the Dana-Farber Cancer Institute are tempered by an unfamiliar calm. A thick plexiglass shield guards the front desk, floor tape demarcates a safe distance, and patients and families float in and out of invisibly bound spheres of social isolation. The quiet is unsettling, while partially by design and the product of rapid implementation of virtual visits and direct-to-floor admissions to limit exposures and clinic volume, there is the unspoken recognition of a decline in new patient diagnoses correlating all too closely with the coronavirus disease 2019 (COVID-19) quarantine.

Limited published and institutional data suggest a surprisingly mild clinical course and low asymptomatic carriage rates for pediatric oncology patients infected with COVID-19.[1–5] In light of this, the care of pediatric oncology patients on active therapy has remained relatively unchanged with life-saving inpatient and outpatient chemotherapy courses delivered as scheduled except, perhaps, for patients requiring high-dose chemotherapy or stem cell transplant conditioning. As COVID-19 testing becomes increasingly available, decisions surrounding administration of chemotherapy to COVID-positive patients and the conservative management of patients with COVID-positive fever and neutropenia will continue to evolve. But what about the data affecting the prediagnostic course of a pediatric oncology patient? What is the impact of COVID-19 on the delivery of pediatric primary care, this being at the very core of early detection of pediatric cancer-related symptoms? The American Academy of Pediatrics and the Center for Disease Control have posted guidelines surrounding continued in-person well-child visits and consistent administration of childhood vaccinations.[6,7] Despite these recommendations, the reality finds great variation in regional pediatric primary care provided; many primary care clinics have restricted hours, others have converted to virtual or drive-through vaccination-only visits, and some find themselves under-resourced in the ability to care for traditional patient volumes. In addition, families remain fearful of leaving their homes during quarantine, particularly to go to a doctor's office, and even if offered an appointment, are unable or unlikely to attend. As more literature emerges regarding the natural history of COVID-19 in children, highlighting a generally mild course, as well as the efficacy of personal protection equipment (PPE) in mitigating COVID-19 spread in the medical environment, these fears are likely unfounded.[8–10]

On May 6, just at the "COVID-19 peak" in Boston, our patient coordinator received a call from a pediatrician in the community who had detected an abdominal mass on exam in a healthy 12-month old at his scheduled well-child care visit. Ultrasound revealed a large, multicystic mass within the right renal fossa with no normal-appearing right kidney appreciated. A follow-up pan computed tomography (CT) scan demonstrated a large (11.9 × 9.8 × 3.6 cm) right renal mass, splaying and thinning the right renal parenchyma, with internal regions of hypoattenuation thought to represent necrosis or hemorrhage. There was no definite vascular invasion. Imaging characteristics were most consistent with Wilms tumor, however, the differential diagnosis included a rhabdoid tumor, clear cell sarcoma of the kidney, or cystic nephroma. No nodal or distant metastases were identified by imaging. The patient underwent a right nephrectomy 4 days later at Boston Children's Hospital, with a diagnosis of stage II Wilms tumor made based on disease extent and histology. Treatment is expected to be curative in over 90% of cases with this presentation. This case underscores the indispensable role of the primary care provider not only in the diagnosis of an occult solid tumor, but on a timeline potentially crucial in preventing capsular rupture or tumor spread, either of which would have resulted in more intensive therapy and possibly a decreased chance of cure. How many children with stealth tumors or new cancer diagnoses remain at home, failing to benefit from the sensitive exam of their primary care providers? How many cancers have gone undiagnosed and what will the health status of children presenting with new diagnoses be in the coming weeks to months?

Solid tumor new-patient numbers at our institute not surprisingly, and presumed secondary to the COVID-19 quarantine, have dipped substantially and our colleagues nationally have noted similar trends.

We compared year-over-year trends in new-patient numbers to quantitate the observed difference. First, we examined data from the pre-COVID period to establish anticipated trends in growth—there was a 25% year-over-year increase in new-patient diagnoses comparing January-February in 2019 versus 2020. Comparing the March-to-May periods in 2019 versus 2020, there was a 56% decline in cases. Assessing a longer time period pre-COVID to further validate the findings confirmed a 59% decline in new cases comparing September 2019 to February 2020 (ie, a 6-month span pre-COVID) to March-May 2020. We examined whether this decline was secondary to a decrease in regional, national, or international referrals, but instead found that the decline was primarily in local patients. In examining a rebound in new cases with state reopening from June-July 2020, we discovered an increase in new cases with only a 19% residual decline compared with June-July 2019, reflecting gradual recovery. Undoubtedly, there is a contribution both from a decrease in in-person primary care visits, and also the reluctance of families to risk exposing children to the virus, especially on the heels of a recent report documenting a severe hyper-inflammatory postviral complication reported in pediatric patients.[11] What will be the toll of delayed solid tumor diagnoses, or pediatric cancer diagnoses in general, on the pediatric population? How will the COVID-19 quarantine inequitably impact underresourced communities, where the virus' high prevalence may augment family reluctance to seek primary care or in emerging economies with already limited treatment facilities for pediatric cancer care? More importantly, as communities begin to relax precautions and quarantine measures, will primary care clinics be able to manage the predicted uptick in visits? Will providers have allocated the precious time needed to evaluate patients on the level required to detect indolent or occult diseases?

To complicate matters, what challenges will oncology programs face as quarantine guidelines relax and patients present on a later timeline in the natural history of disease? The latter concern is of particular relevance to solid tumor patients for whom earlier diagnoses may impact disease stage and possibly outcomes. Adding to this stress, previously diagnosed and treated patients have likely had tumor surveillance scans delayed through this crisis, children with cancer predisposition syndromes have not undergone their routine surveillance, and survivors due for follow-up testing and care may be falling behind in detection and management of late toxicities of therapy.

Well-child care visits, at a minimum aligned with required vaccinations, should remain a priority both for primary care providers and families. The future trajectory of the COVID-19 crisis remains uncertain, but the epidemiology of pediatric cancer diagnoses remains a certainty. While rare, these are diagnoses that cannot be missed. Existing literature regarding the mild COVID-19 clinical course in children, with or without an oncologic diagnosis, coupled with the efficacy of PPE in preventing nosocomial spread should encourage families to seek care, and primary care providers to maintain standard practice hours particularly as we navigate an unpredictable future with the potential for a second wave of COVID-19 cases. As pediatric oncology providers, we remain indebted to our primary care colleagues and the active vigilance they provide the community. We must stand united in the difficult decisions surrounding practice-implementation we will undoubtedly face going forth.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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REFERENCES

1. Bouffet E, Challinor J, Sullivan M, Biondi A, Rodriguez-Galindo C, Pritchard-Jones K. Early advice on managing children with cancer during the COVID-19 pandemic and a call for sharing experiences. *Pediatr Blood Cancer*. 2020;67(7):e28327.
2. Balduzzi A, Brivio E, Rovelli A, et al. Lessons after the early management of the COVID-19 outbreak in a pediatric transplant and hemato-oncology center embedded within a COVID-19 dedicated hospital in Lombardia, Italy. Estote parati. *Bone Marrow Transplant*. 2020. https://doi.org/10.1038/s41409-020-0895-4
3. Fuerrari A, Zecca M, Rizzari C, et al. Children with cancer in the time of COVID-19: an 8-week report from the six pediatric onco-hematology centers in Lombardia, Italy. *Pediatr Blood Cancer*. 2020;67:e28410.
4. de Rojas T, Perez-Martinez A, Cela E, et al. COVID-19 infection in children and adolescents with cancer in Madrid. *Pediatr Blood Cancer*. 2020;67:e28397.
5. Boulad F, Kamboj M, Bouvier N, Mauguen A, Kung AL. COVID-19 in children with cancer in New York City. *JAMA Oncol*. 2020;6(9):1459-1460.
6. American Academy of Pediatrics. *Guidance on Providing Pediatric Well-Care During COVID-19*. Last updated 5/8/2020. American Academy of Pediatrics; 2020.
7. Santoli JMLM, DeSilva MB, Kharbanda EO, et al. Effects of the COVID-19 pandemic on routine pediatric vaccine ordering and administration - United States, 2020. *MMWR Morb Mortal Weekly Rep*. 2020;69(19):591-593
8. Mehta NS, Mytton OT, Mullins EWS, et al. SARS-CoV-2 (COVID-19): what do we know about children? A systematic review. *Clin Infect Dis*. 2020. https://doi.org/10.1093/cid/ciaa556
9. Castagnoli R, Votto M, Licari A, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. *JAMA Pediatr*. 2020;174(9):882-889.
10. Steensels D, Oris E, Coninx L, et al. Hospital-wide SARS-CoV-2 antibody screening in 3056 staff in a tertiary center in Belgium. *JAMA*. 2020;324(2):195-197.
11. Jones VG, Mills M, Suarez D, et al. COVID-19 and Kawasaki disease: novel virus and novel case. *Hosp Pediatr*. 2020;10(6):537-540.

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