

## Case of the Month

**'Case of the Month' from Memorial Sloan Kettering Cancer Center, New York, NY, USA: managing newly diagnosed metastatic testicular germ cell tumour in a COVID-19-positive patient**Nima Almassi , John P. Mulhall, Samuel A. Funt and Joel Sheinfeld

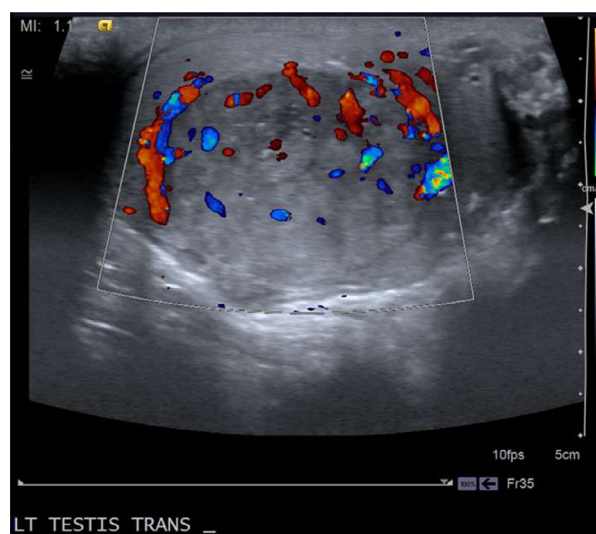
Memorial Sloan Kettering Cancer Center, New York, NY, USA

**Case Presentation**

A 17-year-old young man with history of a congenital solitary left testis presented to our clinic in late April 2020 with left testicular swelling and discomfort over the preceding few weeks. The patient denied unintentional weight loss or nipple tenderness but reported new, mild left-sided back discomfort. His medical history was notable for asthma and a congenitally absent right testis for which he underwent negative surgical exploration in childhood. Family history was negative for testicular cancer or cryptorchidism. Given the ongoing coronavirus disease 2019 (COVID-19) pandemic, which at the time of his initial presentation yielded over 2500 new cases and 300 deaths per day in New York City alone, the initial consultation was conducted by telemedicine and physical examination was not performed. A scrotal ultrasound was obtained demonstrating a 4.2 × 3.3 × 2.4 cm vascular hypoechoic neoplasm of the left testis (Fig. 1). Serum tumour markers were elevated with an  $\alpha$ -fetoprotein (AFP) of 63.4 ng/mL (reference range 0–6.1 ng/mL), hCG of 5,215.5 mIU/mL (reference range 0–2.2 mIU/mL), and lactate dehydrogenase (LDH) of 469 U/L (reference range 130–250 U/L), consistent with a diagnosis of non-seminomatous germ cell tumour (NSGCT). CT of the chest, abdomen, and pelvis demonstrated bulky para-aortic lymphadenopathy of 8 cm in largest dimension, without evidence of visceral metastasis (Fig. 2). Left radical orchidectomy with preoperative sperm banking was recommended. However, semen analysis demonstrated azoospermia on multiple samples, so *ex vivo* testicular sperm extraction (TESE) at the time of orchidectomy was planned.

Beginning in early April, our institution mandated preoperative COVID-19 screening for all patients within 48 h of surgery, with non-emergent cases for patients testing positive deferred for 21 days from an asymptomatic positive test or resolution of symptoms. This policy was enacted to minimise risk of disease transmission to hospital and surgical personnel, and to minimise the risk of perioperative morbidity, which was believed to be significantly elevated in

**Fig. 1** Scrotal ultrasound demonstrating a 4.2 × 3.3 × 2.4 cm vascular, hypoechoic neoplasm of the left testis. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

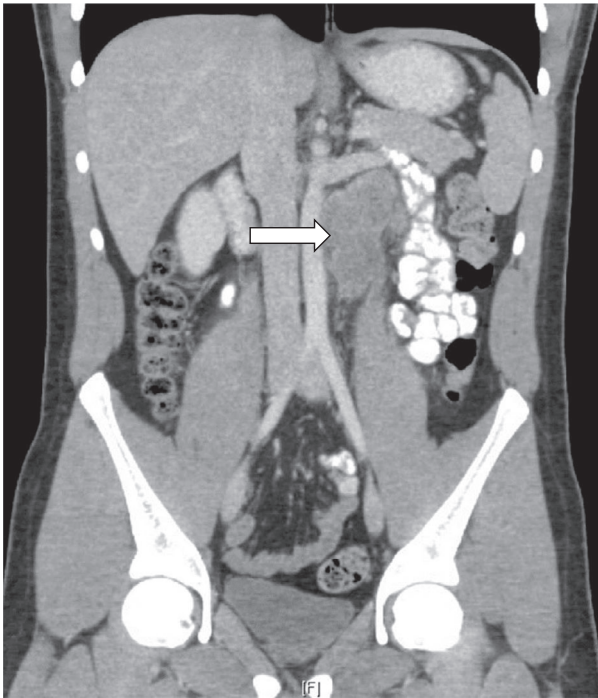


COVID-19-positive patients based on multiple surgical series [1,2]. In this case, the patient underwent preoperative screening and although asymptomatic, tested COVID-19 positive on polymerase chain reaction of a nasopharyngeal specimen resulting in surgical cancellation.

**Management Considerations**

Although asymptomatic, the patient's positive preoperative COVID-19 screening test presented a management dilemma with implications for surgical safety, systemic treatment burden, and future fertility. An early surgical series from Wuhan, China observed a high incidence of morbidity and mortality in 34 asymptomatic COVID-19-positive patients undergoing elective surgery, with 44% of patients requiring intensive care and 21% mortality at last follow-up [1]. These findings have since been corroborated in an international study of 1128 COVID-19-positive surgical patients. Among

**Fig. 2** Coronal images from abdominopelvic CT scan demonstrating bulky para-aortic lymphadenopathy measuring 8 cm in craniocaudal dimension (white arrow).



280 patients in this series who underwent elective surgery, 147 (53%) developed postoperative pulmonary complications and 53 (19%) died within 30 days of surgery [2]. In light of these observations, delaying all but emergent cases in COVID-19-positive patients appears prudent.

With the orchidectomy thus delayed, two management strategies were discussed with the patient and his parents (Table 1). Strategy #1 was to defer immediate treatment and await a negative COVID-19 screening test before then proceeding with radical orchidectomy and TESE, to be followed by induction chemotherapy. Such an approach would allow surgical sperm extraction before chemotherapy. Infertility is commonly observed in patients with testis cancer, with up to 35% of couples infertile at the time of testis cancer diagnosis and 50% of men demonstrating abnormal semen parameters [3]. Cisplatin-based chemotherapy induces azoospermia, and although up to 50% of men can recover spermatogenesis by 5 years of completing chemotherapy [3], such considerations are irrelevant to a patient with a solitary testis who will undergo orchidectomy and in whom the only chance for sperm retrieval is prior to treatment. In a pathological study of 214 patients who underwent radical orchidectomy, baseline azoospermia was not associated with lower sperm retrieval rates, with sperm identified in 58% of patients with azoospermia or cryptozoospermia [4]. An additional benefit of this management strategy was the

**Table 1** Comparison of the two management strategies considered in this case.

|                                    | Strategy #1   | Strategy #2   |
|------------------------------------|---|---|
| Description of management strategy | Delay treatment until patients tests COVID-19 negative, and then proceed with radical orchidectomy and TESE, followed by induction chemotherapy.    | Immediate induction chemotherapy, followed by post-chemotherapy surgery (RPLND and left radical orchidectomy) |
| Treatment delay?                   | Yes (until tests COVID-19 negative)   | No  |
| Fertility considerations           | Chance of sperm preservation with <i>ex vivo</i> TESE at time of radical orchidectomy   | Virtually no chance of harvesting viable sperm at post-chemotherapy orchidectomy                              |
| Surgical considerations            | Potential increased risk of perioperative morbidity with recent COVID-19 illness [1,2].<br>Surgical delay awaiting negative COVID-19 screening test | Defers surgery to the post-chemotherapy setting, potentially reducing risk of COVID-19 associated morbidity   |
| Chemotherapeutic considerations    | Potential for EP × 4 or BEP × 3 for IGCCCG good-risk disease depending on post-orchidectomy tumour markers  | Requires BEP × 4 for IGCCCG intermediate-risk disease   |

possibility to reduce the patient's chemotherapeutic treatment burden. The patient's pre-orchidectomy hCG of 5215.5 mIU/mL put him in the International Germ Cell Cancer Collaborative Group (IGCCCG) intermediate-risk category and would thus require four cycles of bleomycin-etoposide-cisplatin (BEP) if initiated on chemotherapy before orchidectomy. Proceeding first with orchidectomy would likely result in a drop in post-orchidectomy hCG to <5000 mIU/mL, thereby rendering the patient IGCCCG good risk and allowing treatment with four cycles of etoposide-cisplatin (EP) or three cycles of BEP.

Alternatively, with strategy #2 the patient would initiate induction chemotherapy immediately. This would avoid treatment delay, which would be an important consideration especially in a patient symptomatic of metastatic disease. For example, increasing severity of our patient's left-sided back pain may have required more rapid initiation of systemic therapy. In this case, treating with induction chemotherapy upfront would require four cycles of BEP based on IGCCCG intermediate-risk serum tumour markers, thereby subjecting the patient to the risk of bleomycin-induced pulmonary toxicity. Finally, deferring orchidectomy to the post-chemotherapy setting would essentially eliminate the possibility of identifying viable sperm in this azoospermic patient.

## Treatment Course

The patient and his parents were thoroughly counselled on the management options and the oncological, surgical, and

fertility implications of each option. The patient remained minimally symptomatic of his retroperitoneal disease, with only mild left-sided back discomfort, and elected to pursue strategy #1. Repeat COVID-19 screening was conducted 2 weeks later and was negative. The patient then underwent left radical orchidectomy, *ex vivo* TESE, and placement of a testicular prosthesis. He received a dose of intramuscular testosterone in recovery and was discharged home, with an uncomplicated postoperative course. Pathology demonstrated mixed NSGCT with predominance of embryonal carcinoma (70%) in addition to post-pubertal teratoma, yolk sac tumour, and choriocarcinoma. The tumour was confined to the testis and without lymphovascular invasion (pT1). Unfortunately, TESE did not yield viable sperm. Serum tumour markers were repeated 6 days after surgery and had fallen into the good-risk range, with an AFP of 28.4 ng/mL, hCG of 259.9 mIU/mL, and LDH of 353 U/L. Induction chemotherapy was initiated with the patient scheduled to receive four cycles of EP for IGCCCG good risk, clinical Stage IIC NSGCT. The presence of teratoma in the primary tumour and the large volume of retroperitoneal disease leave this patient at high risk of harbouring residual teratoma in the retroperitoneum after completing chemotherapy [5]. Therefore, post-chemotherapy retroperitoneal lymph node dissection (RPLND) is probable.

## Conclusion

The ongoing COVID-19 pandemic has introduced unique barriers to the timely treatment of patients with cancer. Multiple series have reported an increased risk of surgical morbidity and mortality amongst COVID-19-positive patients [1,2]. Although an alternate management strategy with deferred surgery was available in the case presented, it carried significant implications for systemic treatment burden and future fertility. Without an urgent indication to initiate systemic therapy immediately, we were able to wait until the patient tested COVID-19 negative before proceeding with radical orchidectomy and TESE, followed by induction chemotherapy for IGCCCG good-risk disease. The management considerations raised by this case highlight the

value of multidisciplinary care and the unique challenges that the COVID-19 pandemic has introduced for cancer care.

## Conflict of Interest

Nima Almassi and Joel Sheinfeld have no conflicts of interest to report. John P. Mulhall serves as a consultant for Vault Health. Samuel A. Funt has received research support from AstraZeneca and Genentech/Roche, has served in a consulting or advisory role for Decibel, AstraZeneca, and Immunai, and has stock or other ownership interests in Urogen, Allogene Therapeutics, Neogene Therapeutics, Vaxigene, Kronos Bio, and Vida Ventures.

## References

- 1 Lei S, Jiang F, Su W et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. *EClinicalMedicine* 2020; 21: 100331
- 2 Nepogodiev D, Glasbey JC, Li E et al. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Lancet* 2020; 396: P27–38
- 3 Lampe H, Horwich A, Norman A, Nicholls J, Dearnaley DP. Fertility after chemotherapy for testicular germ cell cancers. *J Clin Oncol* 1997; 15: 239–45
- 4 Shoshany O, Shtabholtz Y, Schreter E et al. Predictors of spermatogenesis in radical orchiectomy specimen and potential implications for patients with testicular cancer. *Fertil Steril* 2016; 106: 70–4
- 5 Beck SDW, Foster RS, Bihrlle R et al. Teratoma in the orchiectomy specimen and volume of metastasis are predictors of retroperitoneal teratoma in post-chemotherapy nonseminomatous testis cancer. *J Urol* 2002; 168: 1402–4

Correspondence: Joel Sheinfeld, Memorial Sloan Kettering Cancer Center, 353 East 68th Street, New York, NY 10065, USA.

e-mail: sheinfe@mskcc.org

Abbreviations: AFP,  $\alpha$ -fetoprotein; BEP, bleomycin-etoposide-cisplatin; COVID-19, coronavirus disease 2019; EP, etoposide-cisplatin; IGCCCG, International Germ Cell Cancer Collaborative Group; LDH, lactate dehydrogenase; NSGCT, non-seminomatous germ cell tumour; RPLND, retroperitoneal lymph node dissection; TESE, testicular sperm extraction.