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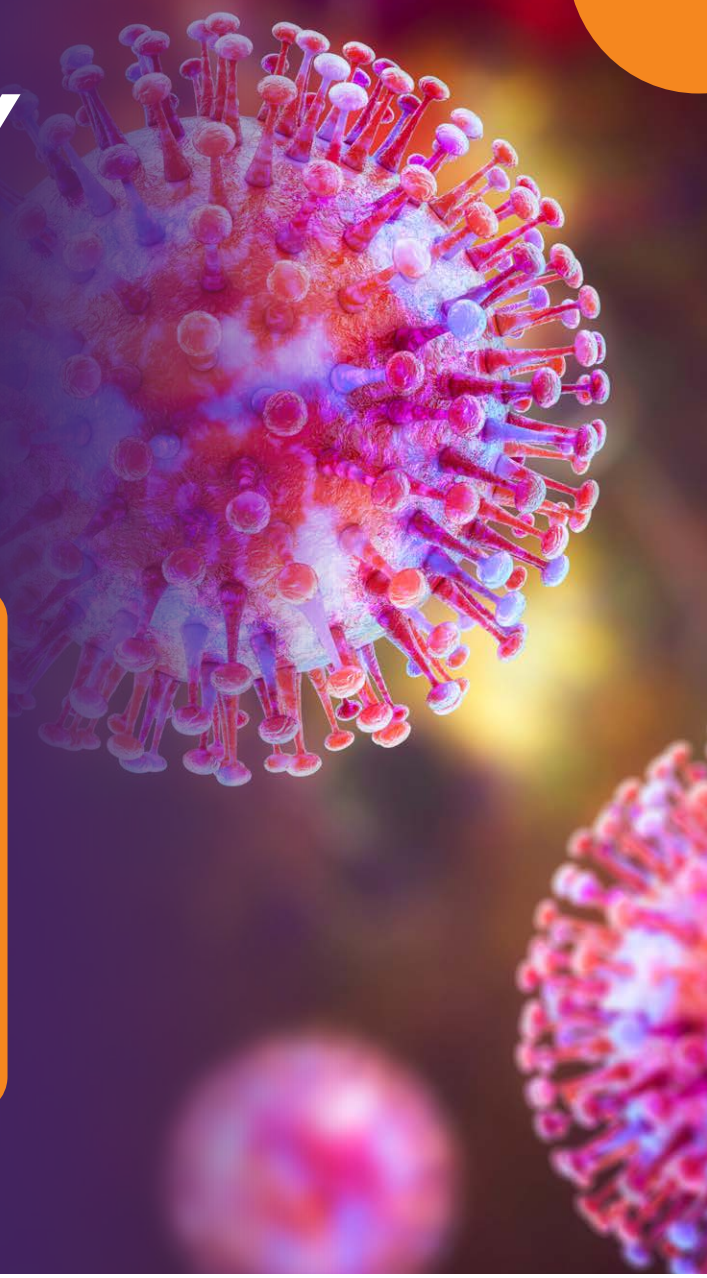

Featured articles:

Influenza, RSV and other seasonal respiratory viruses: Projections for 2022

By Dr Nomvuyo Mothobi

Throughout the 2020 and 2021 respiratory virus seasons, a significantly lower number of influenza and human respiratory syncytial virus (RSV) cases were reported in Australia than in prior years. This was probably attributable to COVID-19 control measures including closed international and state borders, state lockdowns, physical distancing and the use of masks.

With the opening of borders and easing of restrictions, together with waned population immunity, many are wondering whether we will see a large resurgence of respiratory virus cases over the winter of 2022.

An understanding is required of the best way to test for these viruses, together with SARS-CoV-2, in order to efficiently manage the health of patients and limit community spread.

The impact of the COVID-19 pandemic on the circulation of other respiratory viruses

The SARS-CoV-2 virus shares similar modes of transmission with other respiratory viruses including influenza and RSV, both of which can also be associated with severe respiratory illness and mortality, especially in certain high-risk groups.

The non-pharmaceutical interventions (NPIs) taken to control the spread of SARS-CoV-2, such as mask use and physical distancing, have likely had an impact on the reduction of the spread of other respiratory viruses as has been shown in various international studies.

Australia-wide, cases of laboratory-confirmed influenza were significantly lower than average in 2020 and 2021. There were 21,266 notifications in 2020 during the flu season, which is 8 times less than the 5-year average (163,015) (1).

In New South Wales during the usual epidemic months of April to June 2020, there was a 94.3% reduction in laboratory-detected RSV at a major paediatric facility with an associated 85.9% reduction in hospitalisation due to bronchiolitis and 89.1% reduction in admissions to intensive care (2).

There was also a decrease in influenza vaccine coverage in 2021 compared to 2020 in Australia as infection prevention priorities shifted to the global pandemic, with an approximately 40% decrease in the 6-month to 5-year-old age group (3).

Will we see a resurgence of influenza, RSV and other respiratory viruses in 2022?

With the easing of restrictions and opening of borders and the subsequent increase in activity, we may see an increase in the spread of other respiratory viruses.

In the absence of circulation of these viruses over the last two years, it can be predicted that there is likely to be waned protective immunity in the community particularly in immune-naïve children, resulting in an increase in the susceptible population, which could result in outbreaks of these infections.

"In the absence of circulation of these viruses over the last two years, it can be predicted that there is likely to be waned protective immunity in the community..."

The same paediatric centre in NSW identified a shift in the peak period for RSV cases to early summer in 2020 with an 83.19% increase in overall frequency in the 2 to 4-year-old age group, which was likely due to a reduction in COVID-19 NPIs with the easing of restrictions and an increased susceptible population (4).

In parts of the world, influenza outbreaks have been reported outside of the usual seasonal periods, which could be attributed to a reduction in adherence to NPIs with the relaxation of restrictions and high COVID-19 vaccine coverage as well as low influenza vaccine coverage (5).

Important considerations for respiratory virus testing this year

COVID-19 will remain an important diagnostic consideration, but it will be imperative to consider the possibility of other respiratory pathogens; especially influenza and RSV.

The early administration of antivirals for COVID-19 and influenza can significantly reduce the risk of severe infection and complications in high-risk patients and rapid diagnosis helps facilitate this.

Rapid diagnosis also allows infection prevention and control strategies to be promptly implemented to prevent further transmission and outbreaks of respiratory viruses, particularly in high-risk settings such as residential aged care facilities, schools and healthcare facilities.

Ordering PCR tests

- Multiplex PCR testing can assist with the rapid diagnosis of patients with respiratory symptoms.
- Request SARS-CoV-2 PCR and respiratory multiplex PCR on nasopharyngeal swabs or nose/throat swabs.
- Sending two swabs will assist the laboratory to provide timely results.
- Contact your local Clinical Labs microbiologist for additional testing advice.

References

1. The Department of Health: Public Datasets. 2021. The Department of Health [accessed 12 Feb 2022]. https://www1.health.gov.au/internet/main/publishing.nsf/Content/ohp-pub-datasets.htm
2. Britton, P. N. et al. 2020. COVID-19 public health measures and respiratory syncytial virus. *Lancet Child Adolesc Health*. 4, e42–e43.
3. ATAGI advice on seasonal influenza vaccines in 2021 – December 2021 update. 2021. The Department of Health [accessed 13 Feb 2022]. https://www.health.gov.au/resources/publications/atagi-advice-on-seasonal-influenza-vaccines-in-2021-december-2021-update
4. Saravanos, G. L. et al. 2022. RSV Epidemiology in Australia Before and During COVID-19. *Paediatrics*. 149 (2): e2021053537
5. Fujita, D. M. et al. 2022. COVID-19 and Influenza coinfection: The rise of Ômicron and H3N2 in Brazil – 2022. *Travel Med Infect Dis*. 46:102262

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Dr Nomvuyo Mothobi joined Australian Clinical Labs in Geelong having relocated from Sydney. She graduated from the University of Sydney and undertook basic physician training at St Vincent's Hospital in Sydney, after which she spent 2 years working in Zimbabwe where she gained extensive experience in HIV, TB and other opportunistic infections as well as clinical and operational research. She returned to Sydney to undertake dual training in infectious diseases and microbiology at St Vincent's and Royal Prince Alfred Hospitals. Following that she worked as a Staff Specialist at Prince of Wales Hospital. Dr Mothobi's areas of special interest include HIV, infections in transplant recipients and other immunocompromised hosts as well as molecular diagnostic methods and microbial genomics.

Recovery following COVID-19 infection: How investigative pathology tests can help

By Associate Professor Chris Barnes

The COVID-19 pandemic has resulted in more than 400 million cases and 5.5 million deaths worldwide. The pandemic continues to have major societal impacts putting unheralded pressure on healthcare services. Whilst the majority of COVID-19 infections lead to only mild clinical symptoms, prolonged clinical sequelae continue to occur in a significant proportion of infected patients. The current article explores evidence-based approaches to supporting patients recovering from COVID-19 infection.

Human response to viral infection

The COVID-19 disease is caused by infection with SARS-CoV-2 which is a virus belonging to the coronavirus family. The virus was identified in December 2019. Coronaviruses are a group of viruses that circulate among animals such as pigs, bats and camels. Occasionally the viruses "spill over" to humans which may be associated with the development of a more virulent form of infection.

The human body is constantly exposed to external threats and has developed a complex, multifaceted approach to respond to viral infections. Upon exposure to viral infections, the cells of the respiratory tract initiate an innate immune response which has both local and systemic effects and will ultimately lead to a more nuanced adaptive immunity and the production of antibodies directed against viral pathogens. Systemic effects are facilitated by stimulation of the range of cytokines and the interferon response mechanism.

This immune response is targeted against virus pathogens leading to effective and rapid elimination of the virus-infected cells. Mild local and systemic symptoms develop, and the patient quickly recovers. For unknown reasons, however, a small number of patients develop an exaggerated or prolonged immune response to the viral infection which may lead to local tissue damage affecting the upper airways and lungs (1). The consequence may be severe clinical symptoms including respiratory failure and death. Prolonged systemic symptoms from the systemic response to viral infections may also occur.

Studies have identified patients who may be at greater risk of prolonged clinical sequelae following COVID-19 infection. These include patients who had a more severe acute illness (including those requiring admission to intensive care for respiratory support) and patients with pre-existing comorbidities including obesity, pre-existing respiratory disease, diabetes, patients with other chronic health conditions such as kidney disease, and patients of older age.

Assisting recovery following COVID-19 infection

Most inflections involving COVID-19 result in only mild symptoms and prompt recovery. Even in the setting of mild symptoms, it is worth considering how best to assist patients to optimise achieving full recovery. Factors that have been shown to support patients with recovery following viral infection include not trivialising symptoms, avoiding overestimating functional capacity following viral infection and ignoring body signals.

In this setting, judicious ordering of routine pathology tests in patients presenting with prolonged symptoms such as fatigue may include assessment of full blood parameters and haematinics (iron stores and vitamin B12 / folate). This may be helpful in identifying potential nutritional deficiencies which may delay recovery and may be particularly prudent in females who are more at risk of iron deficiency.

More targeted approaches to pathology investigations may be helpful in patients presenting with additional "post-viral" symptoms (such as joint pain, chronic cough, muscle aches and headache). Educating patients with appropriate nutritional information, encouraging patients to prioritise rest and practice good sleep hygiene, and when appropriate commence a graduated exercise program, is important (2). Support in the form of patient education and targeted diagnostic tests can help patients with mild to moderate symptoms in achieving a rapid and full recovery following COVID-19 infection.

Specific post-COVID conditions and "long COVID"

A proportion of patients will develop significant and long-term clinical sequelae following COVID-19 infection. The WHO has provided a clinical case definition for "post-COVID-19 condition". This definition includes patients presenting with a range of symptoms including fatigue, shortness of breath and cognitive dysfunction that impact on everyday functioning with the symptoms extending beyond 12 weeks from initial symptoms and occurring within 3 months from a presumed or confirmed case of COVID-19 infection.

This disorder has been called "long COVID". The incidence of patients experiencing post-COVID-19 conditions (or long COVID) is not entirely clear but is thought to be between 10–35% with a higher proportion of patients with severe initial disease having prolonged symptoms (3). The biological basis of post-COVID-19 conditions remains unclear.

Patients identified as potentially being affected by post-COVID-19 conditions require a multi-disciplinary approach to management (4). Unfortunately, few evidence-based treatments are available.

Optimising the management of underlying health conditions including the management of diabetes, chronic respiratory illnesses and cardiovascular diseases is important. Investigation to identify any reversible health disorders may be helpful. Engagement with professional allied health teams including physiotherapists, occupational health teams and exercise physiologists should also be considered. With the number of patients with post-COVID-19 conditions likely to increase, the development of a clinical framework to support these patients and their treating clinicians will be necessary and should be a major focus for ongoing resourcing and research.

References

1. Garcia, Luis F. "Immune Response, Inflammation, and the Clinical Spectrum of COVID-19." *Frontiers in Immunology*, vol. 11, no. 2020.
2. Stormorken, Eva, et al. "Factors impacting the illness trajectory of post-infectious fatigue syndrome: a qualitative study of adults' experiences." *BMC Public Health*, vol. 17, no. 1, 2017, pp. 1471–2458.
3. Pavili, A. "Incidence, clinical spectrum, and challenges for primary healthcare professionals." *Arch Med Res*, vol. 52, no. 6, 2011, p. 575.
4. Royal Australian College of General Practitioners. Caring for patients with post-COVID-19 conditions. 2021, East Melbourne.

Clinical recommendations in assisting patient recovery post-COVID

- Timely ordering of pathology tests, including full blood count, iron, vitamin B12 and folate in patients presenting with prolonged post-COVID symptoms such as fatigue.
- Ordering of targeted pathology investigations in patients presenting with additional "post-viral" symptoms such as joint pain and muscle aches.
- Ensuring optimised management of patients living with chronic health conditions, including diabetes and cardiovascular diseases.
- Pathology investigations to diagnose any reversible health conditions.

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Associate Professor Chris Barnes is the National Director of Haematology and provides strategic direction nationally for haematology at Clinical Labs. He is a clinical and laboratory-trained haematologist who has been part of Melbourne Haematology and has worked with Clinical Labs (and previously Healthscope) for several years. A/Prof Barnes also works at the Royal Children's Hospital and is director of the Haemophilia Treatment Centre. He has experience in both management and leadership positions. A/Prof Barnes has an active clinical research interest and is also director of Melbourne Haematology (Clinical) and Melbourne Paediatric Specialists.

CASE STUDY

Radiation gastropathy associated atypia

A mimic of dysplasia and neoplasia.

By Dr Abha Malik and Dr Bryn Atmore

Introduction

Therapeutic radiation has been a long-known treatment for cancer, however, the side effects are the major limitation.

The gastrointestinal (GI) side effects are more common, particularly as the bowel is more vulnerable because of its anatomical location and rapidity of turnover of many GI epithelial cell types.

Severity of radiation damage depends also on patient factors–chemotherapy, radiotherapy regimen and organ mobility.

Radiation damage can be seen as mucosal ulceration, inflammatory infiltrate, epithelial atypia and fibrosis. These changes can be sometimes confused with viral inclusions or inflammatory bowel disease. Detailed history immunohistochemistry (IHC) can help in a confident diagnosis.

"Radiation damage can be seen as mucosal ulceration, inflammatory infiltrate, epithelial atypia and fibrosis."

Clinical history

Patient with a history of unknown primary, with documented bony metastasis, presented with gastric ulcer (which looked benign according to the clinician).

Specimen sent from gastric antrum and gastric ulcer to rule out malignancy.

Macroscopic findings

- Specimen labelled as gastric ulcer biopsy.
- Specimen consisted of six pieces of pale tissue measuring 3mm to 4mm in maximum dimension.

Microscopic findings

- Sections revealed gastric mucosa with foveolar type glands, and active chronic inflammation in lamina propria.
- In focal areas, the crypts and the glands show some reactive changes with cytoplasmic vacuolation, nuclear enlargement and nuclear irregularities with some nuclear pseudoinclusions. Few crypts show degeneration (Figs 2,3).
- Occasional nuclei show dense eosinophilic homogenisation of chromatin (Figs 3,4). Few bizarre nuclei with cytoplasmic vacuolization were noted. The nuclear to cytoplasmic ratio was low. These changes merge with normal gastric pits.
- Stromal fibroblasts also appeared atypical, and some vessels show thickening of walls.
- Atypical cells were positive for AE/AE3 and negative for cytomegalovirus (CMV) and herpes simplex virus (HSV) immunostaining (Figs 5,6,7).
- Case work-up was done and radiation oncologist confirmed that medial part of the stomach was caught between radiation field (Fig 1).
- Clinical history, histological findings and IHC correlated with the final diagnosis.

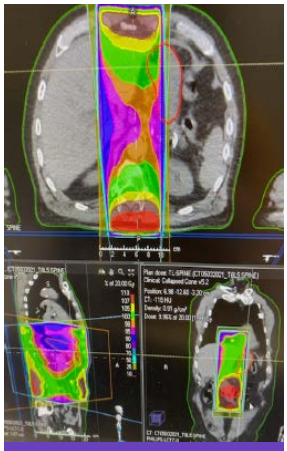


Figure 1. CT abdomen – stomach in radiation field.

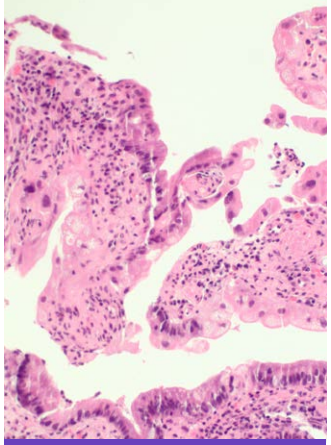


Figure 2. Ulceration of gastric mucosa, with crypt atrophy. Note low cytoplasmic ratios in the atypical cells and voluminous cytoplasm.

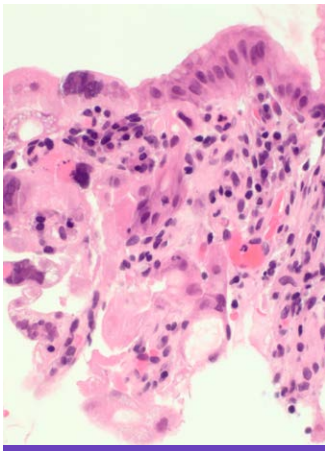


Figure 3. The surface epithelium and crypts show hyperchromasia, nuclear irregularity and pleomorphism.

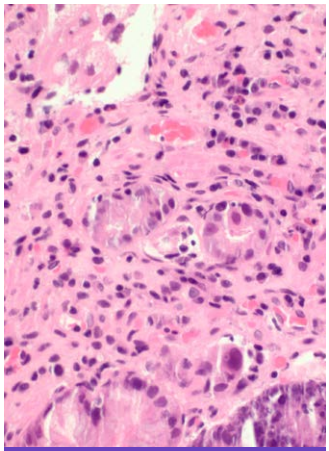
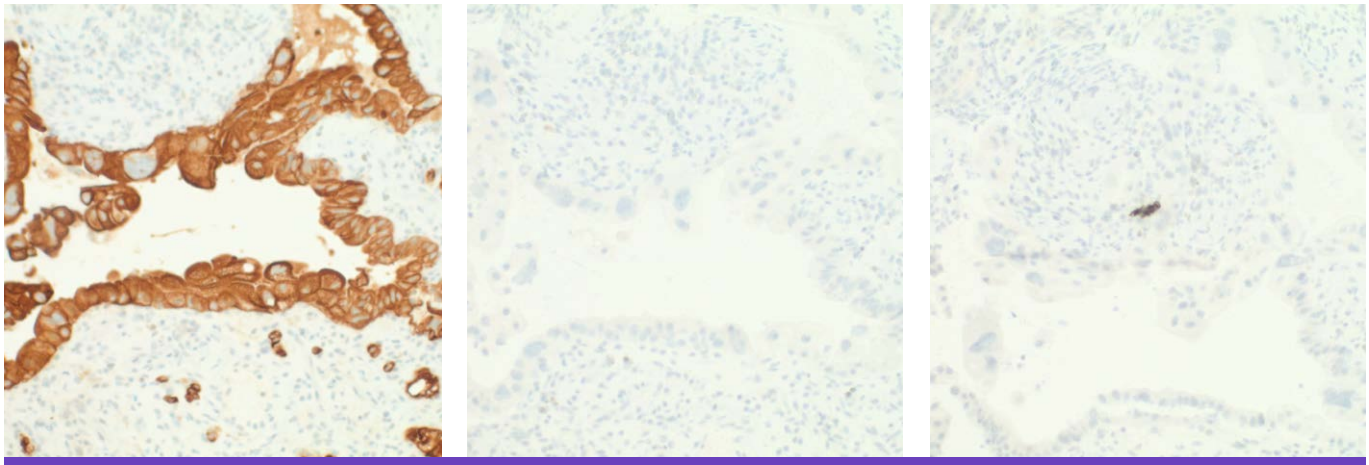


Figure 4. Atypical cells showing multinucleation resembling viral inclusions such as CMV or HSV.



Figures 5,6,7. Immunohistochemistry: Atypical cells were positive for AE/AE3 and negative for CMV, HSV immunostaining.

Discussion

This case highlights the importance of epithelial atypia secondary to radiotherapy, which may be mistaken for neoplastic or preneoplastic conditions and is a diagnostic pitfall.

Both chemotherapy and radiotherapy are increasingly utilised treatment modalities. Patients can present with various symptoms and findings on endoscopy etc. It's important to be aware of this complication, share relevant information with the diagnosticians to avoid misdiagnoses and over-treatment.

References

- Feakin, R.M. (2020). Radiation and the gastrointestinal tract, in R.M. Feakin (ed.), *Non-Neoplastic pathology of the gastrointestinal tract: A practical guide to biopsy diagnosis* (pp. 30–51). Cambridge: Cambridge UniversityPress
- Brien, T.P. Gastric Dysplasia-like epithelia atypia associated with chemoradiotherapy for oesophageal cancer: clinicopathologic and immunohistochemical study of 15 cases. *Mod Pathol.* 2001;14(5):389–396
- Weidner, N., Smith, J.G. Peptic ulceration with marked epithelia atypia following hepatic arterial infusion chemotherapy. A lesion initially misinterpreted as carcinoma. *Am J Surg Pathol*. 1983 Apr;7(3):261–8
- Andreyev, H.J. Gastrointestinal problems following pelvic radiotherapy: the past, the present and the future. *Clin Oncol* (RColl Radiol); 2007;19:790–799.
- Kennedy, G.D, Heise, C.P. Radiation colitis and proctitis. *Clin Colon Rectal Surg. 2007;20:64–72*

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