Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

basal layer of the epidermis, some of which were atypical (Fig. 2C,D). The papillary dermis was slightly oedematous with dilated small vessels associated with extravasated erythrocytes. In the superficial and reticular dermis, a moderate perivascular inflammatory infiltrate was observed, consisting mainly of lymphocytes. Neutrophils were visible mainly in the lumen of vessels, without appearance of leukocytoclastic vasculitis. The nuclei of some endothelial cells appeared swollen and turgid. We did not observe inclusion bodies or syncytial polynuclear giant cells, neither in epidermal keratinocytes nor in vascular endothelial cells.

A complementary immunohistochemical study revealed a prominent T lymphocytes infiltrate (CD3+), mostly T 'helper' CD4+ (65%) with some T 'cytotoxic' CD8+ (35%) (Fig. 2B). In addition, there was a discrete intraepidermal T lymphocytic exocytosis (CD3+ and CD4+), and very few B lymphocytes (CD20+) in the upper dermis.

These unusual epidermal histological changes (Fig. 2C,D) in the absence of significant interface dermo-epidermal inflammatory infiltrate or leukocytoclastic vasculitis may correspond to a viral cytopathogenic effect.

Since the first clinical reports of COVID-19 in China, this infection has been linked to several cutaneous signs: maculopapular rash, urticaria, chickenpox-like lesions,[1,2] pseudo chilblains,[3] dengue-like rash with petechiae,[4] livedo or necrosis.[5] Case reports of skin symptoms in COVID-19 often lack clinical images and/or histology. Unspecific histological findings have been reported so far, including a perivascular infiltrate of lymphocytes and dermal oedema,[6] or undetailed signs consistent with viral infection.[2]

In this letter, we report a pustular and erythematous rash, another example of the various skin presentations of COVID-19. This disease has already been linked to rashes mimicking drug related exanthema.[7] This rash could have been mistaken for skin drug reaction but the clinical improvement despite continuation of the treatment is not in favour of this hypothesis, nor is the histology. More importantly, we report histological images of possible cytopathogenic signs of SARS-CoV-2 infection in cutaneous tissue, suggesting a direct effect of the viral infection on skin cells. Herpes-like aspects have recently been observed in keratinocytes of an infected patient in Italy.[8] In addition, the presence of the angiotensin converting enzyme 2 (ACE2) and proteases already implicated in SARS-CoV-2 infection in the skin would allow the infestation of cutaneous tissue by the virus.[9–11] Obviously, the formal confirmation of such a hypothesis requires the detection of the virus or its particles in the infected epidermis using immunohistochemistry or PCR technique.

Conflicts of interest and sources of funding: The authors state that there are no conflicts of interest to disclose.

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DOI: https://doi.org/10.1016/j.pathol.2020.07.003

Is prostate infarction and acute urinary retention a possible complication of severe COVID-19 infection?

Sir,
Since the beginning of the COVID-19 pandemic in 2019, international efforts have been made to discover and describe the clinical characteristics, epidemiology, prevention and treatment of this disease caused by SARS-CoV-2 (severe acute respiratory syndrome Coronavirus 2).

The virus is involved with the damage of several organs, such as lungs, kidneys and brain, especially in critical patients. This is due to direct injury and, more importantly, by the induction of a severe proinflammatory state, labelled cytokine storm.[1–3] Interestingly, men have been more severely affected by the disease, especially the elderly.[4] This fact has not yet been clarified, but specific factors in the viral pathogenicity could shed light on it.

The infectivity of SARS-CoV-2 depends on the ligation of its viral spike (S) protein to Angiotensin-Converting Enzyme 2 (ACE2), associated with the activation of S protein by Type II Transmembrane Serine Protease (TMPRSS2), a gene regulated by androgen. ACE2 is found in more abundance in lungs, kidneys and intestines and has also been described in the prostate epithelial cells.[5] Although ACE2 and TMPRSS2 are expressed abundantly in prostate tissue, so far there are no records in the literature about COVID-19 prostate symptoms or specific histopathological findings.

Here we report a case of a patient with benign prostatic hyperplasia (BPH) who was in a critical condition due to COVID-19 infection and presented with acute urinary retention (AUR). We describe the clinical and pathological findings of this case.

A 71-year-old man (with a previous medical history of only hypertension) was seen at the hospital complaining of cough, back pain and dyspnoea which had started 7 days before. On admission he was in poor general condition, with oxygen saturation of 82%, requiring O_2 administration. He started treatment with ceftriaxone, azithromycin and oseltamivir. The reverse transcription polymerase chain reaction (RT-PCR) test of nasopharyngeal swab was positive for SARS-CoV-2.

The CT scan showed ground-glass pulmonary opacities typically seen in COVID-19 infection affecting less than 50% of the lung parenchyma. The laboratory tests showed D-dimer 447 ng/dL (reference 500 ng/dL), LDH 438 U/L (135–225 U/L), creatinine 1.55 mg/dL and C-reactive protein 235 mg/dL (normal <5 mg/dL). After 2 days of progressive respiratory deterioration he was transferred to the intensive care unit (ICU), needing mechanical ventilation.

He developed a distributive shock with the need for low doses of vasoactive drugs (noradrenaline), acute renal dysfunction with no need for hemodialysis, and atrial flutter that was promptly reverted with amiodarone. He was maintained in prophylactic anticoagulation with unfractionated heparin (enoxaparin 40 mg/day) during his entire hospitalisation. After 4 days in mechanical ventilation, he was extubated and remained in the ICU for an additional 5 days. When discharged from the ICU, 19 days after the beginning of the symptoms, the foley catheter was removed and he developed AUR. At that time, he was still requiring oxygen therapy with nasal catheter (FiO2 30%). The patient stated that he had moderate lower urinary tract symptoms for the last 3 years [International Prostate Symptom Score (IPSS) score 18 and Quality of Life (QoL) score 5], predominantly urgency, but he had never sought medical care, and had never had AUR before. Alpha-blocker therapy was initiated and after 5 days a trial without catheter was performed. The patient once again developed AUR with a residual urinary volume of 1100 mL and a new indwelling catheter was placed.

The urinalysis was normal, and blood and urine cultures were negative. Total prostate specific antigen (PSA) was 8.9 ng/mL, with a free to total ratio of 17% and a density of 0.04. He was submitted to a urinary tract and prostatic ultrasound that showed a large prostate (approximately 200 g), with anechoic images suggesting prostatic abscesses. No systemic signs of an acute prostatic abscess were seen at this point (normal blood count, and a PCR of 61 progressively decreasing). A pelvic computed tomography (CT) scan was performed showing two intraprostatic collections (5.0 and 10.0 mL) suggestive of a prostatic abscess. The magnetic resonance imaging (MRI) showed a 217 g prostate with two hyperintense areas in the T1 weighted imaging without peripheral enhancement after contrast infusion or diffusion restriction, suggesting a prostatic infarction (Fig. 1).

Being fully recovered from the pulmonary effect of COVID 33 days following the onset of the symptoms, he was submitted to a holmium laser enucleation of the prostate (HoLEP) to treat the BPH.

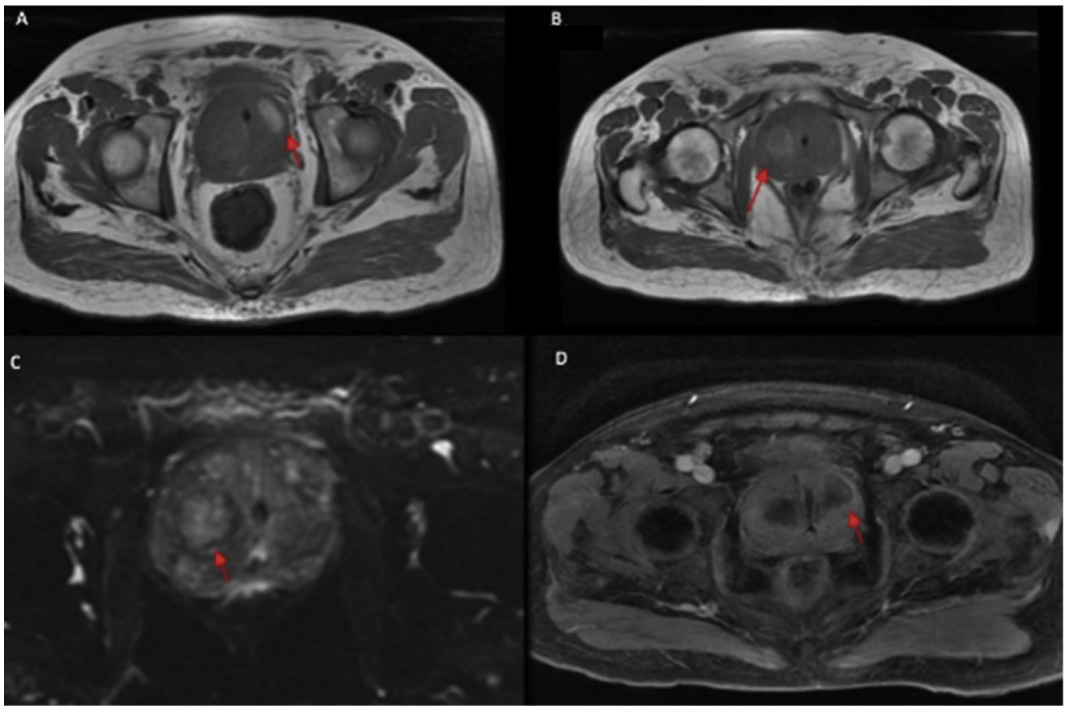

Fig. 1 (A,B) Prostate MRI T1 weighted phase showing the two hyperintense areas. (C) Prostate MRI showing no diffusion restriction. (D) Prostate MRI showing no peripheral enhancement at the T2 weighted phase after contrast infusion.

The procedure was performed with a spinal anaesthetic. The enucleation time took 90 minutes and there was no difficulty to perform the correct dissection. The *en bloc* low power technique with a 40 W (2J/20Hz) energy was used. There were no bleeding or other complications. The surgical specimen was removed through a 5 cm Pfannenstiel incision instead of morcellation to enable the best histopathology analysis possible, considering the need for a precise differential diagnosis.

The gross examination showed a large prostate, weighing 135.0 g, presenting mottled, reddish areas (Fig. 2). The histological examination showed thrombi in small vessels and extensive ischaemic prostatic infarction (Fig. 3). A fresh tissue fragment was reserved as soon as the specimen was resected and submitted to RT-PCR to search for the SARS-CoV-2 resulting negative.

The patient recovered well after surgery, was discharged on the third post-operative day and the catheter was removed on the fifth post-operative day. On day 10 after surgery, the patient was satisfied, describing a strong urinary stream, and mild urgency without urge incontinence. IPSS after surgery was 9 and QoL score was 2.

New clinical manifestations of COVID-19 infection have been described recently following the pandemic. For patients compromised by the cytokine storm after COVID infection, the procoagulant state seems to be a common and important manifestation, affecting many organs, evolving to insufficiency of multiple organs.[2,3,6] As far as we know, this is the first report of prostate involvement in the context of COVID infection. SARS-CoV-2 was already found in semen, but which organ is affected by the infection is not yet clear.[7]

COVID-19 critical evolution has been more common in men,[8] and some pathophysiological theories have emerged. Coronavirus infects cells by binding the viral S protein to the ACE2 receptor, which is found in lungs, kidneys, intestines and testicles.[8] The upregulation of TMPRSS by androgens is suggested to explain the increased male susceptibility to the infection. TMPRSS2 activates the S protein facilitating viral entry, and coexpression of ACE2 and TMPRSS in the prostate has already been shown in hillock and club cells (which are epithelial cells abundant in the prostatic urethra and collecting ducts, as well as the central zone of the prostate, surrounding the ejaculatory ducts[9]) that represent less than 1% of prostate epithelial cells, probably acting as a reservoir for SARS-CoV-2 and promoting direct damage to the prostate.[5]

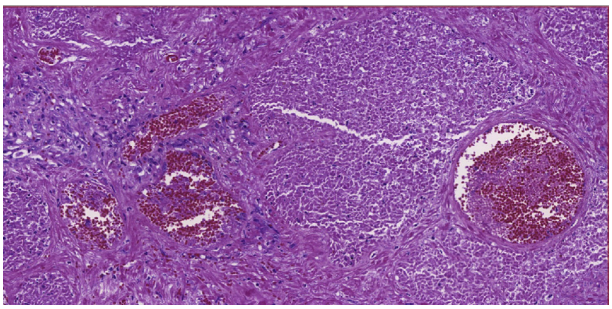

Fig. 3 Ischaemic necrosis of prostate and small vessel thrombosis.

The SARS-CoV-2 RT-PCR test was negative in the prostate tissue in our case, but we believe that the presence of the virus at the beginning of infection promoted the thrombogenic state in the organ, progressing to the ischaemic infarction. The surgery was performed 33 days after the onset of symptoms, at a time when there was no more virus in the airways and other tissues.

The systemic procoagulant and disseminated intravascular coagulation (DIC) state is well described in SARS-CoV-2 infection, affecting many organs and being one of the main causes of multiple organ dysfunction and death.[3]

The exact role for prostatic infarction in AUR is still not clear. Studies have shown no differences in AUR incidence, while others show up to 80% of AUR in patients with prostatic infarction versus only 27% in control patients.[10,11]

We understand that in the case reported here some confounder factors may explain the prostatic infarction development, such as the distributive shock, use of continuous sedative drugs and transitory atrial flutter.[10] However, even though it is common to see patients in ICU with severe haemodynamic shock and atrial arrhythmias we do not commonly see such a severe prostate infarction as seen in the case here described. Additionally, the exact role of general anaesthesia, cardiovascular diseases and

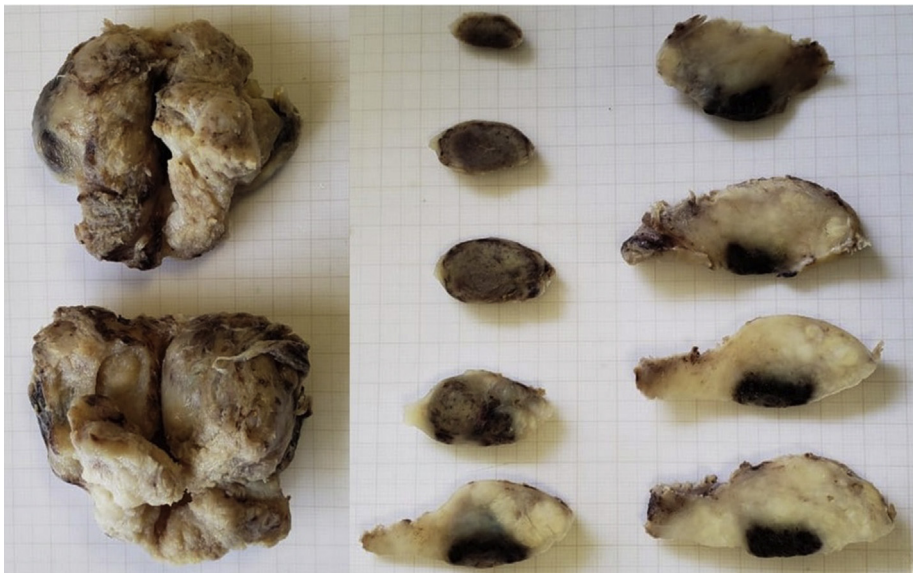

Fig. 2 Surgical specimen showing a large prostate with infarction areas.

prostate instrumentation in the development of prostate infarction remains controversial.[10]

Consequently, we believe that due to all the particularities associated with SARS-CoV-2 infection, the incidence of prostatic infarction resulting in AUR may increase, and urologists should be alert to this phenomenon.

Conflicts of interest and sources of funding: The authors state that there are no conflicts of interest to disclose.

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DOI: https://doi.org/10.1016/j.pathol.2020.09.001

Rapid deployment of pathology services to a remote Australian quarantine setting during the COVID-19 pandemic

Sir,

In December 2019, a new human coronavirus (SARS-CoV-2) with the potential to cause morbidity and mortality (COVID-19) was detected in China.[1] The virus has subsequently spread world-wide and a pandemic was declared by the World Health Organization (WHO) in early March 2020.[2] The rapid emergence of this virus has resulted in unprecedented public health responses from national governments aimed at containment of the outbreak. In early February 2020, like other nations,[3] the Australian government launched a mission to retrieve Australian citizens from Wuhan, China, caught up in the travel restrictions imposed in the Hubei province. The mission retrieved 278 Australian citizens to Christmas Island, Australia, to undergo quarantine for 14 days. Christmas Island is an Australian external territory situated in the Indian Ocean, 1500 km west of the Australian mainland. Evacuees were housed in a government facility with essential health care capability for the duration of the quarantine period. The evacuees remained on Christmas Island for a 14 day quarantine period, prior to return by air to the Australian mainland. A timeline of the events associated with planning and deployment of the pathology services to support the operation is summarised in Fig. 1.

The National Critical Care and Trauma Response Centre (NCCTRC) is the Australian Government's Health Emergency Response Capability and coordinates the preparedness and response including logistics, equipment and staff to health emergencies by Australian Medical Assistance Teams (AUSMAT). An AUSMAT, consisting of doctors, nurses, paramedics and logisticians with expertise in public health, primary health care, acute care, infectious diseases and microbiology, was deployed to Christmas Island to provide medical support to the quarantined individuals. A second team travelled to Wuhan to accompany the Australian citizens returning to Australia. NCCTRC is a Commonwealth Department of Health funded organisation sitting within the Northern Territory Department of Health. AUSMAT deployments are funded by the Commonwealth Government through emergency management funding arrangements depending on the type of response. The AUSMAT mobile laboratory capability includes the Biofire FilmArray 1.5 and Biofire FilmArray Torch multiplex Polymerase Chain Reaction systems (BioMérieux, USA) for diagnosing conventional respiratory pathogens. This was supplemented with the deployment by Australian Defence Force (Royal Australian Air Force) of a complete laboratory-based PCR set up, the High-Plex 24 System (AusDiagnostics, Australia), including automated nucleic acid extraction system, a robot with thermocycler for first stage PCR, a real-time PCR thermocycler for second stage amplification/product detection and reagents. Haemotological (Hemocue, Sweden) and biochemical (EPOC Blood Analysis System; Siemens Healthcare, Germany) testing are additional elements of the AUSMAT mobile laboratory capability.

Testing of suspected cases of COVID-19 was based on available Australian case definitions at the time of quarantine. Individuals with clinical evidence of fever or acute respiratory infection (e.g. cough or shortness of breath) regardless of fever were sampled by collection of combined nasopharyngeal and throat swabs. Initial screening for a range of respiratory pathogens was conducted using the Biofire FilmArray Respiratory (RP) Panel (BioMérieux). Negative samples from patients with ongoing symptoms were then subject to testing by a multiplex PCR panel