



Sir Ganga Ram Hospital

newsletter

vol 25 no 4

visit us at www.sgrh.com

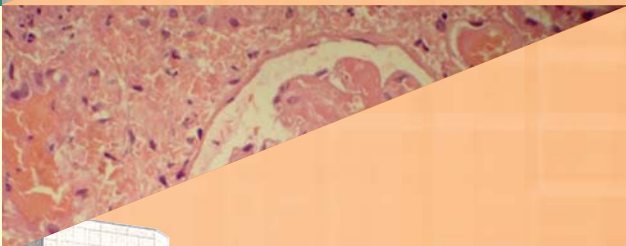
October–December 2021



Post Covid-19 complications:
Ophthalmic manifestations
and more
... page 2



Department in Focus:
Institute of Anaesthesiology,
Pain and Perioperative Medicine
... page 5



Case Report:
Atypical HUS triggered
by Covid-19
... page 8



Post Covid-19 complications: Ophthalmic manifestations and more

The full spectrum of diseases and complications associated with the Covid pandemic is yet to be unravelled. Various studies have suggested that synergistically administered life-saving drugs (corticosteroids and IL-6 inhibitors) for management of Covid-19 and uncontrolled diabetes trigger long-lasting immunomodulation which leads to loss of mucosal immunity, overexpression of GRP 78 and suppression of innate immune response. There is an activation of coagulation cascades and prothrombotic states. A combination of these factors is responsible for post-Covid-19 manifestations and often permanent sequelae to different organs with a multitude of presentations.

However, it was the ophthalmic and rhinological manifestations that held the centre stage with the 'Epidemic within the Pandemic' of rhino-orbito-cerebral mucormycosis (ROCM) or the so-called 'black fungus', which is essentially a misnomer. ROCM, however, is not the only manifestation in the ophthalmic region.

Covid-19 may have ophthalmic manifestations as the presenting feature or may involve the eye at a later stage, weeks after the recovery. Several ophthalmic manifestations have been described in the literature. These include conjunctival and ocular surface manifestations, vascular occlusions in the retina and neurological involvement affecting the eyes (Table 1). The orbital disease especially mucormycosis as a part of the ROCM has been the most common and significant involvement.

Rhino-orbito-cerebral mucormycosis (ROCM)

With the second wave of SARS-CoV-2, India has seen ROCM, otherwise a rare fungal infection, emerged as another life-threatening condition. Mucormycosis is a rapidly progressive and destructive fungal infection with higher mortality rates noted in patients with delayed diagnosis and therapeutic intervention. Due to this, patients with ROCM warrant a multidisciplinary approach for early diagnosis and immediate medical as well as surgical management.

Before the recent epidemic, the incidence of ROCM has been very low. A study at the SGRH by the Department of Ophthalmology reported 40 cases of this fatal fungal infection in the past 10 years in the pre-Covid era.



Fig. 1. Clinical presentation – peri-orbital swelling, ptosis, proptosis, chemosis and total ophthalmoplegia in the left eye

Table 1. Ophthalmic manifestations and complications of Covid-19

Anterior segment manifestations	Posterior segment manifestations	Neuro-ophthalmic manifestations
Follicular conjunctivitis	Central retinal vein occlusion (CRVO)	Papillophlebitis
Viral keratoconjunctivitis	Central retinal artery occlusion (CRAO)	Optic neuritis
Conjunctivitis in children	Acute macular neuroretinopathy (AMN)	Adie's tonic pupil
Episcleritis	Acute retinal necrosis and vitritis (ARN)	Neurogenic ptosis
Eyelid margin telangiectasia	Serpiginous choroiditis	Cerebrovascular accidents with loss of vision
Orbital manifestations		
Dacryoadenitis		
Retro-orbital pain		
Orbital cellulitis and sinusitis		
Mucormycosis		

Clinical manifestations

Rhinological involvement is often the first manifestation of the disease. Clinically, an early disease may present as nasal blockage, unilateral mild facial pain and headache with ocular motility restriction and diplopia. Complete ophthalmoplegia, proptosis, chemosis, loss of vision and severe facial swelling (unilateral or bilateral) at presentation, is an indication of an extensive spread of the disease and poor prognostic factors such as intracranial extension have to be looked for (Fig. 1).

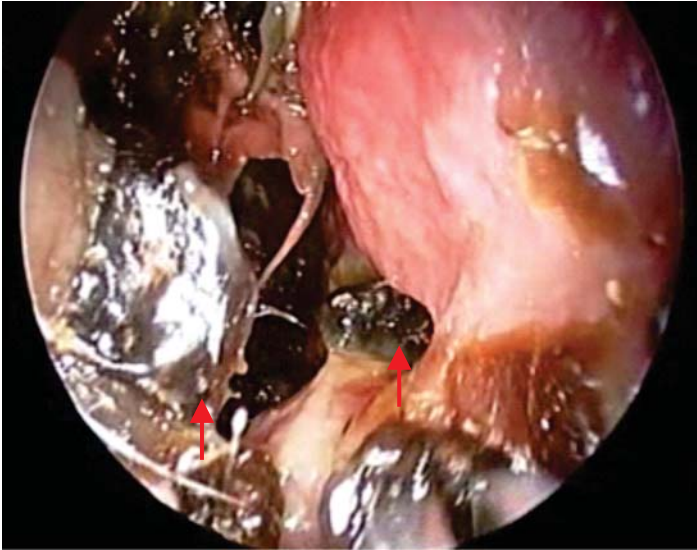


Fig. 2. Diagnostic nasal endoscopy showing nasal mucosal eschars (Image courtesy: Dr Manish Munjal, Dr Shweta Gogia)

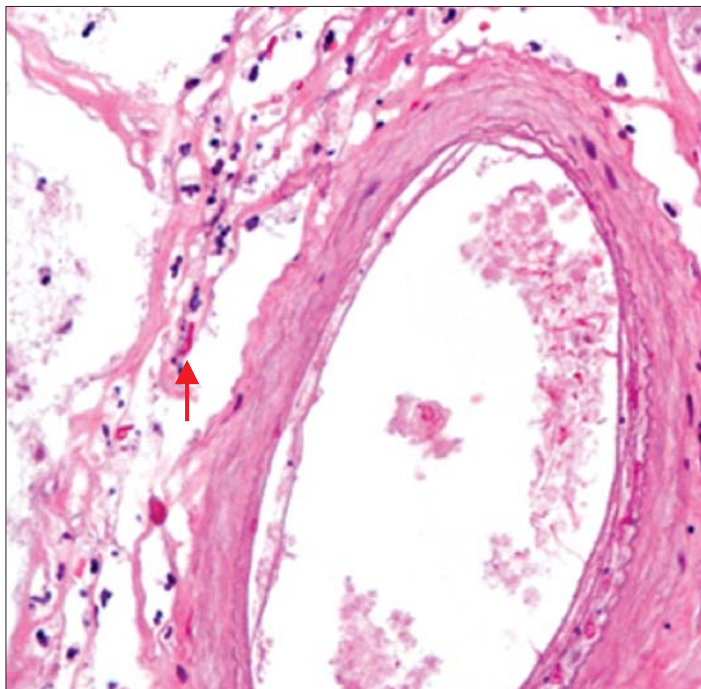


Fig. 4. H&E, 400x: Angioinvasion and perineural invasion. Image of optic nerve with central artery wall and surrounding neural tissue being invaded by broad irregular pleomorphic hyphae of *Mucor* (Image courtesy: Dr Shashi Dhawan, Dr Aruparna Sengupta)

Management

In 2019, the European Confederation of Medical Mycology (ECMM) described the global guidelines for diagnosis and management of mucormycosis. The diagnosis of mucormycosis includes diagnostic nasal endoscopy with nasal mucosal swab/biopsy for KOH and culture, histopathological identification and imaging for an understanding of the extension of the disease in paranasal sinuses, orbit and brain (Figs 2–5). Histopathologically and microbiologically proven disease mandates immediate medical management with a combination antifungal therapy (amphotericin B [AmB] and

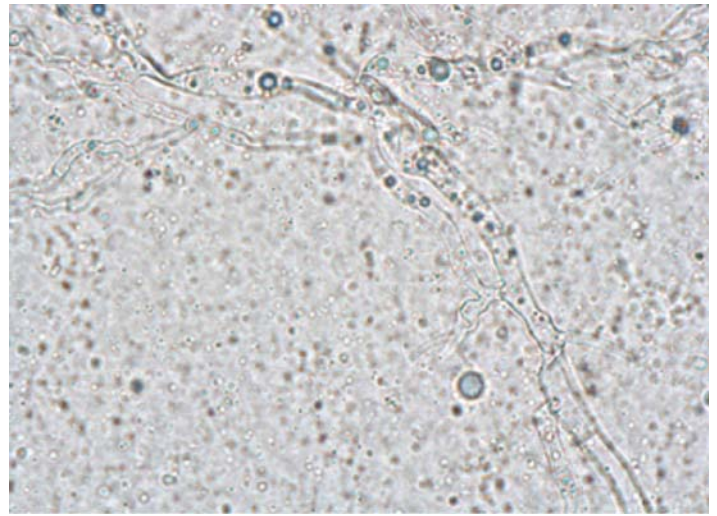


Fig. 3. KOH preparation (40x) showing broad, aseptate branching fungal hyphae (Image courtesy: Dr Chand Wattal, Dr Jaswinder Kaur)

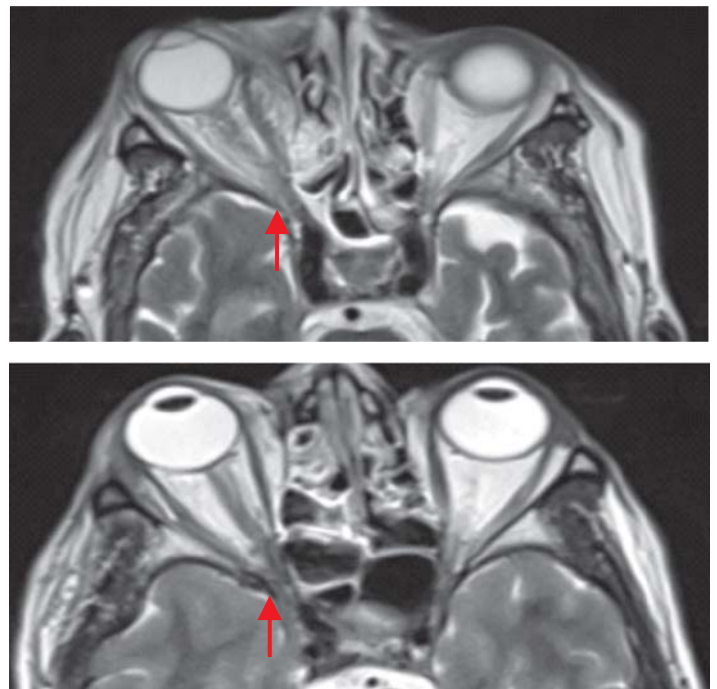


Fig. 5. MRI showing orbital apex involvement and cavernous sinus extension (Image courtesy: Dr Seema Sud, Dr Salil Bhargav)



SIGNS AND SYMPTOMS FOR COVID ASSOCIATED MUCORMYCOSIS

IF YOU SEE ANY OF THESE SIGNS & SYMPTOMS



- HEADACHE
- FACIAL PAIN
- FACIAL SWELLING
- FACIAL SKIN DISCOLORATION



- PALE COLOR OF PALATE
- BLACKENING OF PALATE
- DENTAL PAIN
- LOOSENING OF TEETH



- STUFFY NOSE
- BLOODY NASAL DISCHARGE
- BROWNISH DISCHARGE FROM NOSE



- BLURRING OF VISION
- DOUBLE VISION
- RESTRICTED EYE MOVEMENTS
- DROOPING OF EYELID
- BULGING OF EYE

IMMEDIATELY CONSULT YOUR TREATING OTORHINOLARYNGOLOGIST / OPHTHALMOLOGIST

Fig. 6. Signs and symptoms for Covid-associated mucormycosis

posaconazole) along with pan sinus surgery, intraorbital AmB or orbital exenteration depending on the radiological extent of the disease for removal of dead tissue and decrease the fungal load. Early diagnosis is the key to the prevention of severe morbidity and mortality and detailed guidelines for monitoring of Covid patients for early detection were prepared and followed at the SGRH.

The SGRH experience

During the first Covid-19 wave in India, the incidence of patients affected with the black fungus was comparatively lower than the numbers in the second wave. The SGRH treated 31 patients of ROCM, predominantly males in the fifth and sixth decade, during the first wave. Four patients lost their lives as a result of the extensive spread of the disease in the brain/body, the mortality being much lower than that known for the condition.

In the second Covid-19 wave, the disease became rampant across the country with over 40,000 cases reported and it was declared an epidemic by the Government of India. We have treated 233 patients of ROCM to date. Of these, 161 patients had long-standing diabetes and 38 patients had a recent history of high blood

sugar levels after Covid-19. The mean age of the patients was 50 years. A very large proportion (80%) of these patients had received steroids for the treatment of mucormycosis. Nasal and sinus surgery or exenteration (removal of the eye with all orbital contents) was required in a large number of patients (148 and 24, respectively). A total of 187 patients have been discharged, having recovered or shown good progress. Loss of life (~14%), which was mostly noted in active cases of Covid-19 and often due to causes unrelated to mucormycosis, has been extremely low by international standards, which shows a very high level of meticulous care at our hospital. A multi-department prospective study on Covid-associated ROCM is currently underway at the SGRH.

Public education about the disease is extremely important for early diagnosis and management (Fig. 6). This prevents serious disease and helps save lives. However, the number of cases of Covid-19 who develop mucormycosis is probably less than 1 in 500 and does not warrant the kind of panic that was generated during the second wave of the pandemic.

Compiled by
 A.K. Grover, Manish Munjal, Shaloo Bageja, Anurag Mittal

Institute of Anaesthesiology, Pain and Perioperative Medicine

Introduction

The Institute of Anaesthesiology, Pain and Perioperative Medicine has successfully completed over six decades of existence at Sir Ganga Ram Hospital. By virtue of incorporating significant technological, human-resource, functional and clinical updates in our daily practice our institute has consistently maintained its position as a 'state-of-the-art' essential clinical services provider. Clinical anaesthesia services, academics, research, pain and palliative clinic and charitable activities are integral, central facets of our institute.

Anaesthesia services

We provide round-the-clock anaesthesia services to 24 operation theatres in the SSRB OT complex. Outside the complex we cover an obstetrics theatre, intervention radiology and neurointerventional catheterization labs, vascular hybrid lab, lithotripsy, CT scan and MRI and 2 minor OTs.

The institute offers anaesthesia services for over 15 surgical subspecialties, which include paediatric (Fig. 1), transplant (liver and kidney), thoracic and neuroanaesthesia to name a few. Since March 2012, we are providing anaesthesia for advanced robotic surgeries (Fig. 2) and have till date performed over 2500 procedures. Our round-the-clock, consultant-based anaesthesia services manage elective/emergency surgical patients nearly 25,000 patients annually. The institute also has a postoperative and an organ transplantation ICU.

Acute and chronic pain services

We have a dedicated Acute Pain Service (APS) which includes labour analgesia. Our robust 'Pain Relief Unit' deals with acute postoperative pain as well as pain management for chronic and cancer pain. The institute takes pride in providing specialized and state-of-the-art pain relief services. We perform highly skilled pain

relief procedures which include C-arm guided transforaminal injections for low backache (Fig. 3), radiofrequency ablation, ultrasound-aided nerve-blocks, alcohol/neurolysis and ozone-nucleolysis. The work done by the 'Pain Management' team has been well recognized by the national fraternity.

State-of-the-art monitoring modalities

The institute looks forward to newer/emerging techniques that lead to improvement in patient management. We have advanced technology/aids to bolster routine clinical anaesthesia including patient safety monitors (Fig. 4); specific haemodynamic monitors for fluid administration and optimization during critical/long surgery (minimal invasive cardiac-output monitors) (Fig. 5), anaesthesia-depth monitoring (Bispectral Index) and motor and sensory nerve evoked potential monitoring during complex spine surgeries. We have also embraced the ultrasound technology in our clinical practice. Ultrasound is routinely used for administering regional nerve blocks (Fig. 6) and also for perioperative patient monitoring such as echocardiography, optic nerve sheath diameter (ONSD) and diagnostic lung ultrasound.

Palliative care services

We have introduced 'Palliative Care Services' to terminally ill and cancer patients through a dedicated team of doctors and nurses.

Academic activities

The institute has 41 consultants, 4 senior residents and 13 postgraduate students (DNB) (Fig. 7). We run a 'Pain Fellowship' programme under the aegis of GRIPMER. Similar fellowships in other subspecialties, paediatric and transplant are also running successfully. For the past 5 years, we have been running a successful international thoracic anaesthesia fellowship programme sponsored by the 'World Federation of Societies of



Fig. 1. Paediatric anaesthesia



Fig. 2. Robotic surgery



Fig. 3. C-arm guided nerve block



Fig. 4. State-of-the-art anaesthesia workstation



Fig. 5. Minimal invasive cardiac monitoring



Fig. 6. Ultrasound-guided nerve block



Fig. 7. Consultants and Residents of the Institute of Anaesthesiology, Pain and Perioperative Medicine

Anaesthesiologists (WFSA)'.
 One important cornerstone of our institute is an emphasis on focused clinical research. Our consultants are involved in various research projects ranging from basic to clinical anaesthesia sciences with numerous publications in reputed national and international journals. The institute is also involved in collaborative research with PGIMER, Chandigarh on 'automated anaesthesia delivery systems'.

We also conduct a regular annual audit of our anaesthesia services to enhance our patient care.
 An annual 'Anaesthesia Update' has been running successfully for more than 15 years. In the coming years, we aim to continue to embrace new technologies and update our systems and protocols so that we continue to provide compassionate patient care.

Compiled by Jayashree Sood, Archna Koul, Nitin Sethi

Contributed by Jayashree Sood, Archna Koul, Nitin Sethi

Endovascular Live (EVL) 2021

Humanity has faced one of the toughest times in the past one year. With a lot of unavoidable negativity around, it was very important to find ways of creating positive vibes. The best way is to create positivity through knowledge sharing. It was this thought which made resolve of the Team Institute of Vascular and Endovascular Sciences (IVES) stronger and thus the First Hybrid Conference of this magnitude, i.e. Endovascular Live (EVL) 2021 was organized under the able leadership of Dr V.S. Bedi. The first announcement for arranging meeting of this magnitude was done on 8 June 2021. Seats for the Fellows Course had to be doubled and registration was closed within a week. Registration for physical attendance got oversubscribed and closed on 30 June.

EVL 2021 became a great success story of mutual learning as 52 complex cases were showcased in a span of two days (13–14 August) from 10 centres of excellence from India and the USA.

More than 130 interventionists participated in the physical meeting held at The Imperial, Janpath, New Delhi – a place associated with the journey of Indian Independence. More than 1100 consultants participated on the virtual platform, thus making EVL 2021 a true Indian International Conference on Endovascular Intervention.

Feedback from participants has been really encouraging. The Team IVES thanks all participating centres for showing exemplary live cases with exceptional learning values. Great enthusiasm shown by all participants encourages us to set new standards in learning and thus achieve world standards for Vascular and Endovascular Care.

*Contributed by
Nikhil Sharma*

Department of Vascular & Endovascular Surgery



Dr Anupam Sachdeva

Sir Ganga Ram Hospital (SGRH) is an institution which delivers high-quality patient care and also develops patterns of teaching for postgraduate students in all specialties. Over the past four decades, SGRH has demonstrated high standards of medical education. This has been done to meet not only the standards set by the National Board of Examinations (NBE) in medical sciences but also to improve patient care. The DNB programme was started at the SGRH in 1984 in five disciplines:

1. General Medicine
2. Surgery
3. Paediatrics
4. Orthopaedics
5. Obstetrics and Gynaecology

Subsequently, the FNB was started in 2002 in various branches. Today, SGRH caters to DNB programmes in 42 disciplines, 16 in Broad specialties, 20 Super-specialties, 6 Post-doctoral fellowships. Over the years, the standard of training at SGRH has been recognized as a benchmark by the NBE. Before the admissions were centrally controlled on the basis of NEET exams, SGRH used to admit candidates in our DNB programme on the basis of a written examination. The written examination was done as a virtual OSCE projected on the screen with 600–800 candidates sitting in a big auditorium giving answers to the questions projected on a screen. The answer sheets were collected from the candidates and brought to the hospital where a team of assessors was given the key to check the answer sheets. The result was declared the same day on the internet and then the shortlisted candidates were asked to appear for an interview. The marks obtained in the theory (OSCE) and the interview were as per the norms of NBE and directions of the high court. SGRH had a huge experience in conducting virtual OSCEs much before others envisaged them. The Covid pandemic brought in major difficulties and challenges, which were:

1. Inability of the students to travel from their city to other cities for the examination.
2. Reluctance of the faculty for going to another city for conducting the examination.
3. The need to conduct the examination in a single day properly to

evaluate and assess the candidate in all aspects of a particular subject.

4. The need for reducing the number of candidates per centre from a total of 24–25 to 10–12 to avoid crowding and facilitating their evaluation.

With this in view, the NBE also instituted virtual OSCEs and virtual cases in all the medical disciplines. Along with this, the candidate was expected to conduct ward rounds for their evaluation. This meant that the NBE selected various institutions across the country which have the wherewithal to deliver the goods. Previously, OSCE was being conducted across the country in only 2–3 branches such as paediatrics, ENT, etc. In 2021, SGRH was selected as a centre for conducting the NBE examinations in 22 medical disciplines. It was observed that the team at SGRH constituted by the Department of Academics, Department of IT and exam coordinators in these specialties conducted themselves immaculately during the examinations and had the least glitches and questions. In fact, during the month of August and mid-September, almost every day we had some examination or were in the process of preparing for the examination the following day.

This shows the professional approach of the team of academics and the various departments involved. This ability of SGRH to deliver the goods in academics has been well recognized and I delivered a 20-minutes lecture on Teacher's Day (5 September 2021) during the Association of National Board Accredited Institutions North Zone (ANBAI) Conclave at Marriott Hotel, Hyderabad. This conclave was attended by the Vice-President Hon'ble Shri Venkaiah Naidu Ji, President governing body, National Board of Examinations in Medical Sciences and the Executive Director of National Board of Examinations in Medical Sciences. The efforts put in by SGRH to improve the academic work was appreciated by everybody. We spend nearly Rs 32 crore on academics per annum including the salaries of the DNB students. At this point of time, we have a total of 257 students, which include DNB Broad specialties Diploma Holders 110, DNB Super-specialties 135, FNB students 12. During this past one-and-a-half years of the pandemic, we have converted huge challenges into great opportunities.

SGRH had a huge experience in conducting virtual OSCEs much before others envisaged them.

*Contributed by Anupam Sachdeva
Director Paediatric Haematology Oncology and
Bone Marrow Transplantation
Institute For Child Health*

Case Report

Atypical HUS triggered by Covid-19

Abstract

We present a case of an atypical haemolytic uremic syndrome (aHUS) precipitated by Covid-19 disease. A 26-year-old man was diagnosed with Covid-19 disease and acute kidney injury. His kidney biopsy was suggestive of thrombotic microangiopathy. Five sessions of plasmapheresis were done but were discontinued in view of non-recovery of kidney function. He was then referred for a kidney transplant. On genetic analysis, he was found to have mutations in the complement system (CFHR1 and 3), which suggested this was a case of aHUS precipitated by Covid-19 disease. In view of the high risk of recurrence of the primary disease in live-related kidney donor transplantation, he was advised for simultaneous liver and kidney transplant.

Introduction

Acute kidney injury (AKI) is a common complication of Covid-19 disease with incidence varying from 0.5 to 80% with increased incidence in hospitalized patients.¹ AKI can be severe in the form of thrombotic microangiopathy and severe acute tubular necrosis. Most commonly kidney injury occurs due to haemodynamic abnormality in severe Covid; however, direct invasion and injury by the virus, cytokine storm, abnormal coagulation causing thrombotic injury and necrosis, etc. have also been reported.² Endothelial damage seen in cases of Covid-19 disease is one of the important factors associated with the thrombotic state, microvascular damage and necrosis.³ Endothelial damage in these patients can also be secondary to complement dysfunction such as atypical haemolytic uremic syndrome precipitated by Covid-19 disease.⁴ aHUS is associated with complement system dysregulation either due to mutations in the complement system or because of autoantibodies causing endothelial damage, intravascular thrombosis and tissue injury. It can be precipitated by pregnancy, infections or malignancy.⁵ We report a case of aHUS precipitated by Covid-19 disease.

The Case

A 26-year-old man was admitted with fever, myalgia and sore throat. RTPCR from a nasopharyngeal swab confirmed Covid-19 infection. Clinically, he had mild Covid disease without any need for supplemental oxygen. His laboratory parameters included normal creatinine with mildly elevated inflammatory markers (Table 1). He was managed conservatively with antipyretics and multivitamins. From day 7 of illness, he started complaining of decreased urine output. His creatinine was found to be increased (4 mg/dl). Urine microscopy was suggestive of 5–6 RBCs/HPF, 2+ protein, and RBC

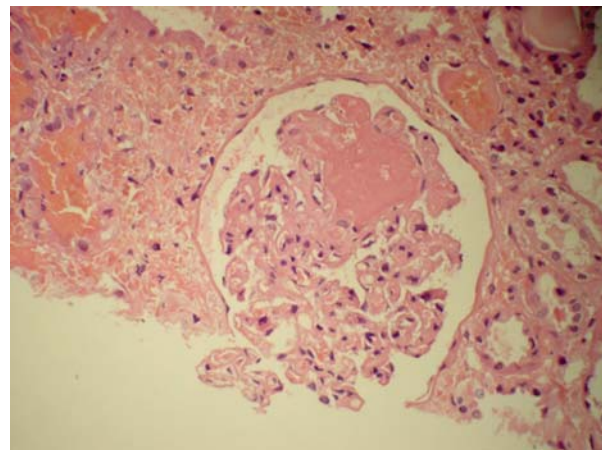


Fig. 1. Photomicrograph showing a glomerulus with fibrin thrombi and mesangiolysis (H&E stain, original magnification $\times 200$)

casts. His complete blood count was suggestive of bicytopenia (anaemia and thrombocytopenia) (Table 1). Peripheral smear showed normocytic normochromic anemia and reduced platelets numbers with schistocyte index > 4 . Ultrasound abdomen showed normal-sized kidneys. Six units of platelets were transfused before kidney biopsy in view of thrombocytopenia. Biopsy was suggestive of acute tubular necrosis with thrombotic microangiopathy (TMA) (Fig. 1). He was initiated on haemodialysis in view of persistent oliguria. His haemoglobin and platelet counts were stabilized after five sessions of plasma exchange; however, he remained oliguric. Genetic testing was performed which revealed homozygous deletion of the region encompassing upstream region, exons 1, 2, 3, 6 and intron 4 of CFHR3 and intron 1, 3 and exons 5, and 6 of CFHR1 genes. Anti-complement factor H antibody was negative. Thus, he was diagnosed as a case of atypical HUS secondary to mutations in CFHR 1 and 3. Eculizumab is not available in India and could not be arranged due to financial constraint, so, he is currently waitlisted for simultaneous liver-kidney transplantation.

Discussion

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can cause disease ranging from mild upper respiratory tract infection to critical illness-causing multi-organ damage. Incidence of AKI varies from 0.5% to 80% with increased incidence in hospitalized patients.¹ The aetiology of AKI is multifactorial. Prerenal causes include hypovolemia and, sepsis while renal causes include direct viral injury, endothelial damage, complement activation, cytokine storm and hypercoagulation. All these factors can result in various histological features such as acute tubular necrosis, collapsing glomerulopathy, or thrombotic microangiopathy.⁴

Table 1. Laboratory characteristics of the patient at admission, after 1 week and after 2 months

Investigation	At admission	After 7 days	After 2 months
Haemoglobin (g/dl)	13	7	9.2
Total leukocyte count (cells per μ l)	3400	6000	5400
Platelets ($\times 10^3$ cells per μ l)	288	88	175
Total bilirubin (mg/dl)	0.8	2.2	1.0
Direct bilirubin (mg/dl)	0.3	0.6	0.3
SGOT (U/L)	21	14	12
SGPT (U/L)	14	39	18
ALP (U/L)	56	76	54
LDH (U/L)	177	680	120
Total protein (g/dl)	6.3	6.64	6.2
Albumin (g/dl)	3.2	2.27	2.8
INR	0.9	1.2	0.9
Creatinine (mg/dl)	0.9	4.0	5.8
Serum HCO ₃ ⁻ (mEq/L)	23	18	20
C3 (mg/L) (970–1576)	–	1304	–
C4 (mg/L) (162–445)	–	178	–
CRP (mg/dl) (<6)	17	14	5
Ferritin (ng/ml) (4.63–204)	758	589	544
D-dimer (μ g/ml) (<0.25)	0.2	0.5	0.3
IL 6 (pg/ml) (<6.40)	14	16	2
Viral serology: Anti-HAV Anti-HEV HBsAg Anti-HCV		Negative Negative Negative Negative	
ANA ANCA		Negative Negative	
Urine routine microscopy		pH 6.7 RBCs/HPF 5–6 Protein 2+ RBC casts (+)	pH 6.5 RBCs/HPF 2–3 WBCs 3–4 Protein 1+ Glucose (–)
24-hour urine protein		0.8	0.7

Acute tubular injury is the most common cause of AKI in patients with Covid-19 disease.⁶ It accounts for more than 60% of cases of AKI from a study in the USA.⁷ However, Covid-19 can affect all compartments of kidney parenchyma including glomerulus, tubules and vessels.

Glomerular diseases consist of collapsing glomerulopathy, crescentic glomerulonephritis, thrombotic microangiopathy, podocytopathies, etc. Amongst glomerular disease, collapsing glomerulopathy is the most common type seen mostly in patients with high-risk APOL1 genotypes.¹ Incidence of TMA is very rare and was found to be around 2.12% in a study done by Ferlicot *et al.* analysing kidney biopsies of patients having Covid with AKI.⁶ Endothelial dysfunction with subsequent microvascular injury-causing thrombotic microangiopathy is an important mechanism of organ failure including kidneys in Covid-19 disease patients. SARS-CoV-2 uses angiotensin converting enzyme 2 (ACE2) receptor to infect the host. ACE2 receptors are expressed in lung, heart, kidney, and intestines. They are also expressed on endothelial cells. On binding to ACE2 receptors, SARS-CoV-2 causes endothelitis with subsequent vessel injury and organ damage.⁸ Patients with inherited defects such as polymorphisms in ACE2 gene,⁹ APOL1 genotype,¹⁰ or complement dysfunction such as atypical HUS are at higher risk for AKI.

Few case reports are present in the literature showing the association of TMA with Covid-19 disease. Kulkarni *et al.*¹¹ reported a case of TMA secondary to Covid-19 disease in the background of IgA nephropathy with no renal recovery. TMA secondary to Covid-19 disease was also reported by Jhaveri *et al.*¹² where the patient ultimately died.

Atypical HUS is an inherited disorder characterized by a defect in the complement system causing alternate complement pathway activation, endothelial damage, and thrombotic microangiopathy.¹³ Complement system mutations associated with aHUS include loss of function mutations in complement factor H (CFH) (most common), complement factor H-related (CFHR) 1-3, membrane cofactor protein (MCP) (most benign amongst all), Complement factor I (CFI) and gain of function mutations in

complement factor B (CFB) and C3. CFHR 1–3 mutations are generally associated with autoantibody (anti-factor H) causing TMA thus making them responsive to plasmapheresis.¹⁴ Our patient had CHFR 1–3 mutation without autoantibody against factor H, explaining the probable reason for poor response to plasma exchange.

aHUS can be triggered by various factors such as upper respiratory tract infections, pregnancy.⁵ In our case, Covid-19 disease was the triggering factor. A similar case report was published by Ville *et al.* which reported relapse of aHUS after contracting Covid-19 infection.¹⁵ Also, Mat *et al.* described a case of aHUS associated with Covid-19 disease with C3 gene mutation.¹⁶

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may precipitate aHUS by the following mechanism. As mentioned above, the SARS-CoV-2 virus causes endothelial dysfunction which stimulates complement activation causing tissue injury. This complement activation may be amplified in patients with an inherited defect in complement regulation such as aHUS patients causing tissue injury including TMA and kidney failure.¹⁵

Treatment of aHUS consists of plasma exchange with fresh frozen plasma, terminal complement blockade such as eculizumab or liver transplant.¹⁷ Patients with aHUS have a variable rate of recurrence post kidney transplant depending on the mutation. The outcome of kidney transplants with mutations in CFHR1 and CFHR3 is not known. However, except in patients with low risk of recurrence (isolated MCP mutation or those with anti-CFH antibodies that are cleared from blood), prophylactic measures such as eculizumab are used along with kidney transplant to prevent recurrence.¹⁸ In the case series reported by Sami Alasfar, the authors proceeded with kidney transplant with eculizumab prophylaxis in a patient with a mutation in CFHR1 and CHR3 to prevent recurrence.¹⁹ In conclusion, atypical HUS can be triggered in susceptible individuals even in mild cases of Covid-19 infection.

Compliance with ethical standards

Conflict of interest: The authors have declared that no Conflict of interest exists. **Ethical approval:** This article does not contain any studies with human participants or animals performed by any of the authors. **Informed Consent:** Informed consent was obtained from all individual participants included in the study.

References

- Ng JH, Bijol V, Sparks MA, Sise ME, Izzedine H, Jhaveri KD. Pathophysiology and pathology of acute kidney injury in patients with COVID-19. *Adv Chronic Kidney Dis* 2020;**27**:365–76.
- Su H, Yang M, Wan C, Yi LX, Tang F, Zhu HY, *et al.* Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. *Kidney Int* 2020;**98**:219–27. doi: 10.1016/j.kint.2020.04.003.
- Noris M, Benigni A, Remuzzi G. The case of complement activation in COVID-

- 19 multiorgan impact. *Kidney Int* 2020;**98**:314–22.
- Nadim MK, Forni LG, Mehta RL, Connor MJ Jr, Liu KD, Ostermann M, *et al.* COVID-19-associated acute kidney injury: Consensus report of the 25th Acute Disease Quality Initiative (ADQI) Workgroup. *Nat Rev Nephrol* 2020;**16**:747–64. doi: 10.1038/s41581-020-00356-5.
- Jokiranta TS. HUS and atypical HUS. *Blood*. 2017;**129**:2847–56. doi: 10.1182/blood-2016-11-709865.
- Ferlicot S, Jamme M, Gaillard F, Oniszczuk J, Couturier A, May O, *et al.*; AP-HP/Universities/Inserm COVID-19 research collaboration. The spectrum of kidney biopsies in hospitalized patients with COVID-19, acute kidney injury, and/or proteinuria. *Nephrol Dial Transplant* 2021:gfab042. doi: 10.1093/ndt/gfab042.
- Mohamed MMB, Lukitsch I, Torres-Ortiz AE, Walker JB, Varghese V, Hernandez-Arroyo CF, *et al.* Acute kidney injury associated with coronavirus disease 2019 in urban New Orleans. *Kidney360* 2020;**1(7)**:614–22.
- Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, *et al.* Endothelial cell infection and endotheliitis in COVID-19. *Lancet* 2020;**395**:1417–18. doi: 10.1016/S0140-6736(20)30937-5.
- Delanghe JR, Speeckaert MM, De Buyzere ML. The host's angiotensin-converting enzyme polymorphism may explain epidemiological findings in COVID-19 infections. *Clin Chim Acta* 2020;**505**:192–3.
- Velez JCQ, Caza T, Larsen CP. COVAN is the new HIVAN: The re-emergence of collapsing glomerulopathy with COVID-19. *Nat Rev Nephrol* 2020;**16**:565–7. doi: 10.1038/s41581-020-0332-3.
- Kulkarni A, Nasa P, Polumuru S, Singh A. Thrombotic microangiopathy causing acute kidney injury in a COVID-19 patient. *Indian J Nephrol* 2021. Available from: <http://www.indianjephrol.org/preprintarticle.asp?id=312251&type=0>.
- Jhaveri KD, Meir LR, Flores Chang BS, Parikh R, Wanchoo R, Barilla-LaBarca ML, *et al.* Thrombotic microangiopathy in a patient with COVID-19. *Kidney Int* 2020;**98**:509–12. doi: 10.1016/j.kint.2020.05.025.
- Afshar-Kharghan V. Atypical hemolytic uremic syndrome. *Hematology Am Soc Hematol Educ Program* 2016;**2016**:217–25.
- Chaudhary P, Hegur M, Sarkissian S, Smith RJ, Weitz IC. Atypical haemolytic-uraemic syndrome due to heterozygous mutations of CFH/CFHR1-3 and complement factor H 479. *Blood Transfus* 2014;**12**:111–3. doi: 10.2450/2013.0107-13.
- Ville S, Le Bot S, Chapelet-Debout A, Blancho G, Fremeaux-Bacchi V, Deltombe C, *et al.* Atypical HUS relapse triggered by COVID-19. *Kidney Int*. 2021;**99**:267–8. doi: 10.1016/j.kint.2020.10.030.
- Mat O, Ghisdal L, Massart A, Aydin S, Goubella A, Blankoff N, *et al.* Kidney thrombotic microangiopathy after COVID-19 associated with C3 gene mutation. *Kidney Int Rep* 2021;**6**:1732–7.
- Loirat C, Fakhouri F, Ariceta G, Besbas N, Bitzan M, Bjerre A, *et al.*; HUS International. An international consensus approach to the management of atypical hemolytic uremic syndrome in children. *Pediatr Nephrol* 2016;**31**:15–39. doi: 10.1007/s00467-015-3076-8.
- Portoles J, Huerta A, Arjona E, Gavela E, Agüera M, Jiménez C, *et al.*; Matrix Investigators. Characteristics, management and outcomes of atypical haemolytic uraemic syndrome in kidney transplant patients: A retrospective national study. *Clin Kidney J* 2020;**14**:1173–80.
- Alasfar S, Alachkar N. Atypical hemolytic uremic syndrome post-kidney transplantation: Two case reports and review of the literature. *Front Med (Lausanne)* 2014;**1**:52. doi: 10.3389/fmed.2014.00052.

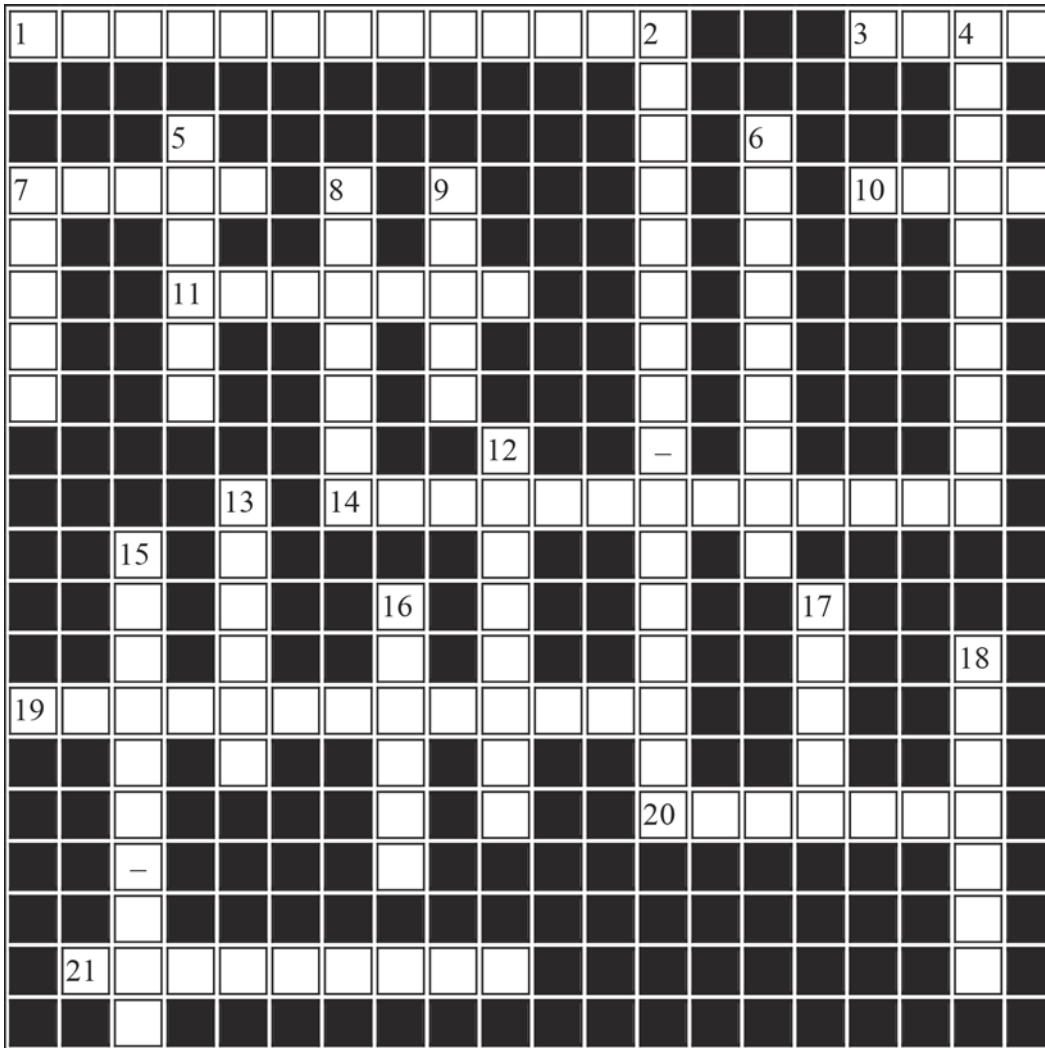
Compiled by

Vaibhav Tiwari, Gaurav Bhandari, Anurag Gupta, Vinant Bhargava
Manish Malik, Ashwini Gupta, Anil Kumar Bhalla, D.S. Rana

Department of Nephrology

Pallav Gupta, Department of Pathology

Newsletter Crossword



Across

1. Dream-like state caused by prolonged sleep deprivation (13)
3. After effect of trouble is lasting and healing (4)
7. Before it is complete, it prevents a baby developing problems later on (5)
10. Onset of labour is imminent in an impressive display (4)
11. Absence of thirst even in presence of body water depletion (7)
14. Hereditary disorder of sight due to a lack of cone vision. Patient is colour blind (13)
19. Important contraindication to surgical reconstruction of bone (13)
20. Species of mushrooms, some could be poisonous (7)
21. Tough white fibrous tissue, e.g. that surrounds testis (9)

Down

2. Sounds are heard but convey no meaning (8-7)
4. Excessive and persistent fear of heights (10)
5. Series of tests or research studies in court hearing (6)
6. Away movement leads to kidnapping (9)
7. Syndrome of uncontrollable paroxysm of sneezing (5)
8. Sac or duct-like enlargement of a canal (7)
9. Anxiety (5)
12. A level of surpassing achievement at vaginal orifice during childbirth (8)
13. Measurement or a quantity that has both size and direction spreading disease (6)
15. Its bite causes sleeping disturbances in Africa (6-3)
16. Landmark where coronal suture is intersected perpendicularly by sagittal suture (6)
17. Ulnar nerve is prone to compressive injury in this canal (5)
18. After having agreed to marry, infants head or buttock settles into the pelvis during birth (7)

Created by P.K. Pruthi, Director, Institute of Child Health

NEW ENTRANTS

Dr Asish Kumar Sahoo *Critical Care & Emergency Medicine Associate Consultant 19.07.2021*

Dr Nikhil Vilas Chaudhari *Vascular & Endovascular Surgery Associate Consultant 17.08.2021*

Dr Ravi Chauhan *Orthopaedics Associate Consultant (Ad hoc) 11.08.2021*

Dr Deepika Gupta *Surgical Oncology Associate Consultant (Ad hoc) 17.08.2021*

PROMOTIONS

Dr Ashutosh Taneja *Critical Care & Emergency Medicine Senior Consultant 17.08.2021*

Dr Bhim Singh Nanda *Plastic Surgery Senior Consultant 17.08.2021*

Dr Richa Singh *Paediatric Neurosurgery Consultant 17.08.2021*

Dr Rahul Kumar *Critical Care & Emergency Medicine Consultant 17.08.2021*

CROSSWORD ANSWERS

ACROSS

1. Oneirophrenia 3. Scar 7. Abort 10. Show 11. Adipsia 14. Achromatopsia 19. Osteomyelitis 20. Amanita
21. Albuginea

DOWN

2. Auditory-aphasia 4. Acrophobia 5. Trials 6. Abduction 7. Achoo 8. Ampulla 9. Agita 12. Crowning 13. Vector
15. Tsetse-fly 16. Bregma 17. Guyon 18. Engaged

We welcome your comments. Please send us your feedback at sgrhnewsletter@sgrh.com

Founder Patron: Late Shri Dharma Vira

Patron: Dr D.S. Rana

Editor: Dr C. Wattal Co-editor: Dr Vijay Arora

*Editorial Board: Dr A.K. Bhalla, Dr P.K. Pruthi, Dr Archana Koul, Dr Nitin Sethi, Dr Rajat Mohan,
Dr Satnam Singh Chhabra, Dr Neeraj Jain, Dr Anubhav Gupta*

Editorial and Production Consultants: BYWORD

Printed at: Indraprastha Press (CBT)

Design: Netra Shyam

Sir Ganga Ram Hospital, Sir Ganga Ram Hospital Marg, Rajinder Nagar, New Delhi 110060

e-mail: gangaram@sgrh.com Fax: 011-25861002 EPABX: 25750000