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CoVID and Co-morbidity: A Pediatric Case series on the 'Incompatible Duplet'

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ABSTRACT: SARS-CoVID pandemic started with unknown disease process and progression. It continues to cause morbidities and mortalities in different age groups at varying rates. The research world is still unfolding the pathology and treatment aspects of the disease. Paediatric population has different spectrum of the disease as compared to adults but are complicated by the co-morbidities and co-infections similarly. We in our case report present two such paediatric cases in adolescent age groups with co-morbidities, the complicated course and the challenges in the hospital due to COVID.

Key words: CoVID, Comorbidity, Tuberculosis, Cerebral Palsy, complications

I. INTRODUCTION:

The CoVID-19 pandemic brought a chaos in a not so organised world (the same disease can have varied presentations in different groups of human race!) by posing challenges initially in understanding the pathophysiology of the disease followed by figuring out the management guidelines. The disease process is further complicated by the presence of co-morbidities by either direct interactions, immune system modulation or by restricted choice of treatment in view of the underlying condition. Here we are reporting two such Pediatric cases with comorbidities**,** complicated further by CoVID infection emphasising the need of discovering the pathways of recovery.

Case 1: 10 year old female child presented with history of cough since 3 months , worsened since 1 month, fast breathing since 2 weeks worsened since last 2 days. It was associated with left sided chest pain. There was no history of fever or decreased appetite. For the above complaints, she was investigated and treated in other hospitals and received oral antibiotics and homeopathic treatment (details not available). COVID by RT PCR was done in view of the pandemic which came positive. Initial investigations showed leucocytosis with neutrophilic predominance. ESR and Ferritin were normal however CRP (74 mg/L) and D-Dimers (3917 ng/ml) were elevated. Chest X Ray showed bilateral consolidation with left sided pleural effusion. At presentation she was mildly tachypneic with minimal sub costal and inter-costal retractions and required 4 litres of Oxygen by face mask. She had mild hepatosplenomegaly. Diagnostic and therapeutic pleural tapping was done which showed straw coloured fluid, lymphocytic predominant (450 cells) with elevated ADA levels. Gene Xpert on pleural fluid sample was negative. Pleural fluid smear was done which ruled out the presence of malignant cells. Pleural fluid LDH and Serum LDH were normal. Pleural fluid LDH to serum LDH ratio was 0.82. Mantoux test was positive. ANA profile was negative. Her respiratory distress settled after pleural tapping though she continued to require 2 litres of Oxygen by nasal prongs (Saturations in room air was 88-92% & 95-97 % with 2 litres of Oxygen). SF ratios were maintained above 330 consistently. Diagnosis of Presumptive pleural Tuberculosis with COVID pneumonia was made. Anti-tubercular treatment was started with steroids (Prednisolone 2mg/kg). Enoxaparin was started in view of high D-Dimer levels. Empirically antibiotics (Ceftriaxone) were started due to elevated inflammatory counts and inflammatory markers. Throat swab Culture grew MRSA. Linezolid was added as per sensitivity pattern.

Fig. 1 Pleural Fluid Sample

Her COVID RT PCR was repeated after 10 days which came as negative. Repeat Chest X rays showed better lung fields in the left lobe of lung.

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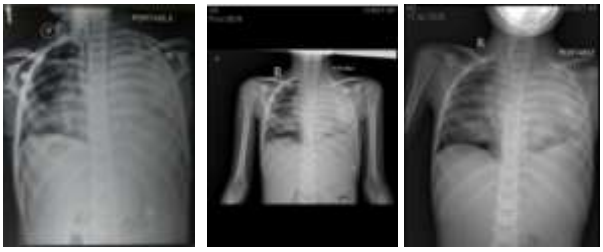

Fig 2: Serial Chest X Rays showing improvement in the lung fields

Due to persistent Oxygen requirement, HRCT chest with contrast was done which showed significant mediastinal, bilateral perihilar and abdominal lymphadenopathy. Multifocal infective consolidations with ground glass halo involving both lungs with left lobe extensive involvement and Moderate left pleural effusion.

Fig 3: HRCT Lungs with contrast

She showed transient improvement in D-Dimers and CRP but there was worsening again. Antibiotics were upgraded (Ceftriaxone was changed to Meropenem) and antifungals (Fluconazole) were added in view of suspected sepsis after repeating Culture. Peripheral Blood C/S grew Staphylococcus hemolyticus. Linezolid was changed to Vancomycin. In view of hepatosplenomegaly, Lymphoma was considered as a possibility. Peripheral smear showed neutrophilic leucocytosis. Bone Marrow aspiration was done which showed myeloid hyperplasia and biopsy was normal as well (No malignant cells). Bone Marrow culture was negative

HIV done was negative. 2D Echo was done which was normal. Pulmonologist opinion was taken and BAL and lung biopsy were planned. On day 21 of admission she had increased respiratory distress & Oxygen requirement. Chest X Ray, blood gas showed worsening when she was electively intubated. Post Intubation during Mechanical ventilation she had two cardiac arrests. She did not survive the second cardiac arrest in spite of all the resuscitative measures.

Case 2: 11 year old female child, a known case of spastic quadriplegia, Global developmental delay , GMFC level V and seizure disorder with Epilepsia partialis continua on multiple anti-epileptic drugs presented with fever of 2 days, seizures 2-3 episodes and hurried breathing since previous night for which nebulisations were given at home. She presented with severe respiratory distress and grunting. She was intubated and mechanically ventilated. COVID by RT-PCR was tested which was positive. Initial investigations showed neutrophilic leucocytosis (Total counts- 28,400, Neutrophils/Lymphocytes: 65%/20%), elevated CRP (44.6mg/L) & D-Dimer (9534.08ng/ml), normal Ferritin and ESR. Liver function and renal function tests were normal. Remedesivir was started and antibiotics were added empirically (Ceftriaxone) Blood C/S and Urine C/S were sent which were sterile. Her Chest X Ray showed bilateral inhomogeneous opacities more in right Para cardiac and right lower zones. LMW and steroids (Methyl Prednisolone (2mg/kg) were started.

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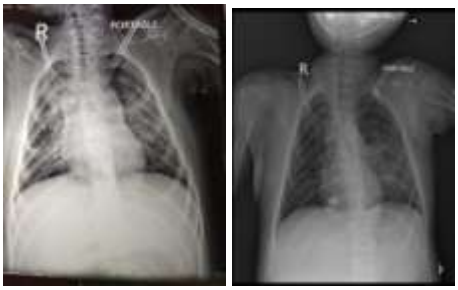

Fig 4: Serial Chest X Rays showing improvement.

She started having multiple episodes of convulsions on day 2 of admission when the anti-epileptics were optimized. Midazolam infusion was started (up-to 14mcg/kg/min). Seizures got controlled and Midazolam was tapered and stopped over next 36 hours. She required Vasopressor (Nor-epinephrine up-to 0.2 mcg/kg/min) during Midazolam infusion which was subsequently tapered and stopped over next 24 hours. She had increased pressure requirements on ventilator, increased ET tube secretions and worsening CRP however Ferritin remained normal and D-Dimers improved. Antibiotics were upgraded (Meropenem and Vancomycin) and antifungal (Fluconazole) was added empirically after sending repeat blood C/S and ET tube secretions C/S. Her ventilator parameters improved, secretions decreased and CRP improved as well. Serial Blood gases and Chest X Rays showed improvement and electrolytes were normal. She was extubated to Non-Invasive Ventilation on Pressure Control mode with subsequent decreased requirements on day 5 of admission.

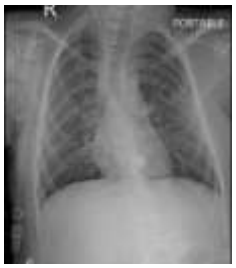

Fig 5 : Chest X Ray on Non Invasive Ventilation

On day 7 of admission, she had a cardiac arrest on Non Invasive Ventilation. Pneumothorax was ruled out. She could not be revived despite all resuscitative measures.

II. DISCUSSION:

Multiple studies in adults have shown that the presence of comorbidities complicates the course of CoVID infection. Chronic diseases share several standard features with infectious disorders, such as the proinflammatory state, and the attenuation of the innate immune response(1). Recently, Guo et al. (2019) retrospectively analysed the clinical data of patients with viral pneumonia and found that the absolute count levels of CD3+T cells, CD3+CD8+ T cells and CD3+CD4+ T cells in the deceased group were significantly lower than those in the survival group, suggesting that the levels of various inflammatory factors in the deceased group were higher than those in the survival group.(2)

Most of the current studies of CoVID19 pathophysiology have described the disease as a hard hit on host immune factors. Lymphopenia, exhausted lymphocytes specially T-cells, Cytokine response, Acute respiratory Distress Syndrome attributed to virus host interaction and interferon Dysregulation.(3)

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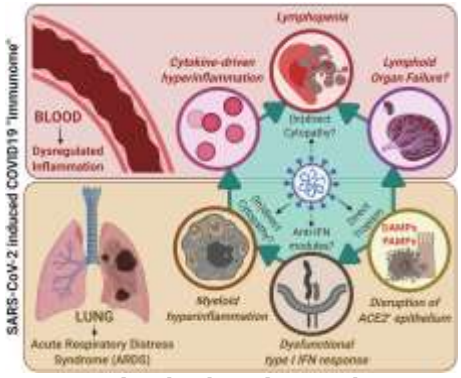

Fig 4: CoVID-19 Lung associated pathophysiology with systemic immunopathology(3)

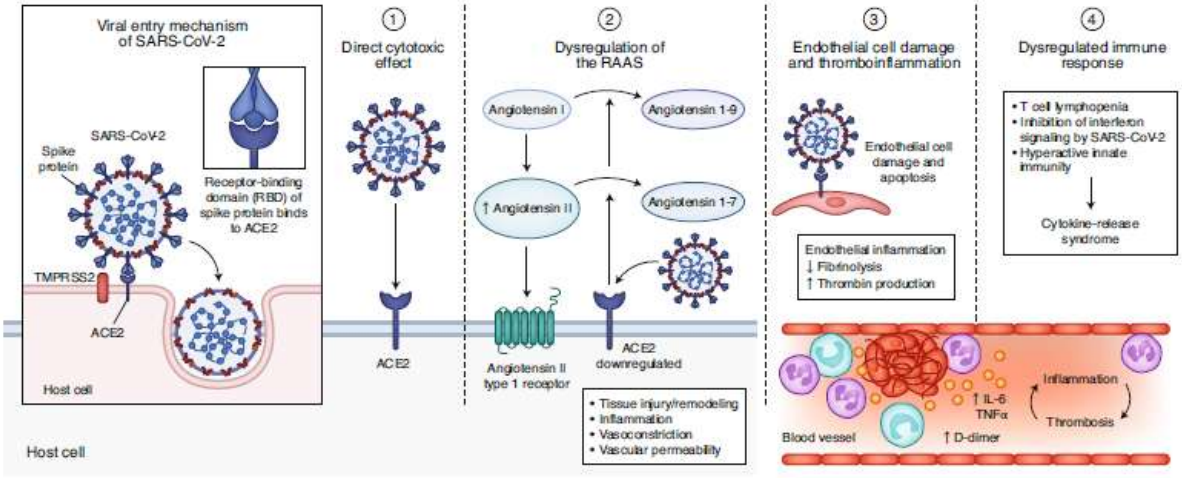

Fig 5: Pathophysiology of CoVID-19 (1)-direct virus-mediated cell damage; (2) Dysregulation of the RAAS as a consequence of downregulation of ACE2 related to viral entry, which leads to decreased cleavage of angiotensin I and angiotensin II; (3) endothelial cell damage and thromboinflammation; and (4) Dysregulation of the immune response and hyper inflammation caused by inhibition of interferon signalling by the virus, T cell lymphodepletion, and the production of proinflammatory cytokines, particularly IL-6 and TNFα. (5)

The chronic infections and other co-morbidities are well known to depress or modulate the innate and acquired immunity and further enhance the pathological effects of infections. Mycobacterium tuberculosis is known to cause lung function impairment and tissue remodelling via immune moderators.

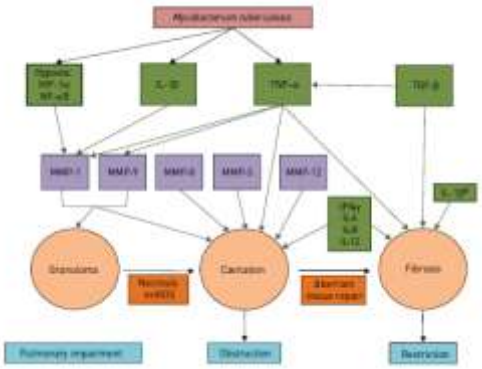

Fig 5: Lung function impairment and tissue remodelling pathogenesis in Tuberculosis via immune mediators (4)

A recent imaging study revealed that TB lesions in humans are severely hypoxic. Reproducing hypoxia in in vitro culture conditions resulted in up regulation of MMP-1 in MTB-infected cells via hypoxia-inducible factor and nuclear factor (NF)-κB activation (6). This damaged and hypoxic lung and altered immune response can form a nidus and further aggravate the fatal effects of CoVID SARS infection.

Though cerebral palsy does not directly affect the immune system, the comorbidities associated with it increase the susceptibility to infections and their severity e.g. poor nutrition, reduced or lack of mobility leading to low metabolic rates and circulation affecting end organ efficient functioning, recurrent lung infections and aspiration pneumonias, associated disorders like seizures, gastro-oesophageal reflux, sleep disorders and multiple medications for the same.(7,8)

It can be concluded that CoVID as a pandemic has posed a lot of challenges in understanding the disease process and its treatment. The research world including the scientists and the medical fraternity are trying to solve the puzzle and bringing up the results. However, a lot has to be unfolded still and before we find a perfect solution!

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