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## SPONTANEOUS SPINAL SUB-DURAL HEMATOMA: A RARE COMPLICATION IN SEVERE COVID-19 DISEASE

Jyoti Goyal<sup>1\*</sup>, Vipul Mishra<sup>2</sup>, Mradul Sharma<sup>3</sup> and Ajay Bullagan<sup>4</sup>

<sup>1</sup>HOD Internal Medicine;

<sup>2</sup>HOD Pulmonology critical care;

<sup>3</sup>HOD Neurosurgery;

<sup>4</sup>HOD Radiology - Pushpanjali Hospital & Research Centre Pvt. Ltd

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### ABSTRACT

This case is a rare case in terms of development of a serious and unpredictable complication: spinal subdural hematoma and paraparesis, in a patient of severe COVID 19 disease. Patient was being treated with prophylactic dose of anticoagulant therapy as standard care for moderate COVID 19 disease. This complication posed a challenging therapeutic decision for clinicians to decide on the timing of surgical intervention, inability to use anticoagulation despite the high risk of thromboembolic complications in this disease, and on the use of immune-modulators in cytokine release syndrome, as it causes increase in risk of secondary bacterial sepsis in such bedbound paraparetic patients.

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## INTRODUCTION

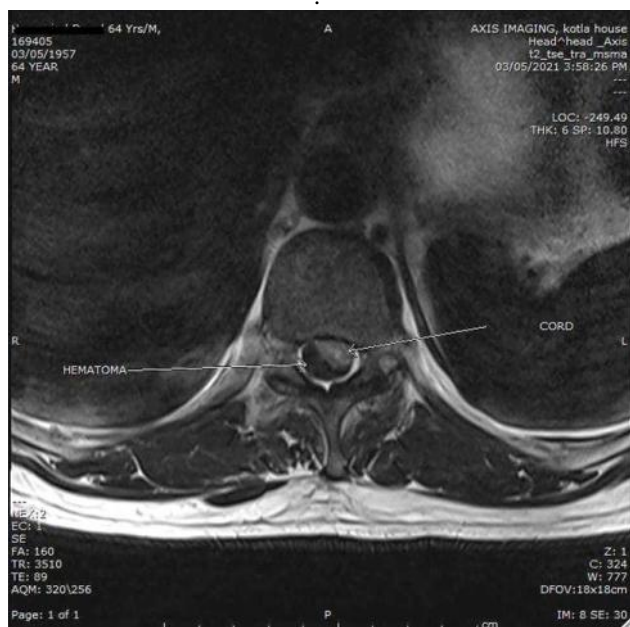
A 64-year-old male presented to us with complaints of fever for 5 days with upper respiratory tract symptoms. Five days after onset of symptoms he started developing breathlessness. Patient came to hospital emergency where his spo2 was 90% on room air. After initial stabilization he was evaluated for suspected COVID-19 in context of his symptomatology in ongoing covid pandemic. His covid antigen test was positive. HRCT chest was done to assess the severity of lung involvement. HRCT findings were typical of Covid lung changes and CT severity index was 18/25. Patient was admitted in ICU and was put on NRBM (Non rebreathing mask) with 10 lit of oxygen per minute. Spo2 was 93-94% with oxygen support and respiratory rate was 24-28 breaths per minute.

He was started on injection Remdesivir, IV steroids, anticoagulants in prophylactic dose along with other supportive care as per the institutional protocol. Significant lab parameters at the time of admission were: CRP18.5, D dimer 0.38, TLC was 4900/mm<sup>3</sup> with 34% lymphocytes and normal kidney and liver function tests. On day 3 of admission, he developed sudden onset of severe backache, lower limb weakness, and loss of bladder control. Immediately neurology advise was sought and MRI spine was done. MRI spine showed intradural hematoma from D7/D8 level to L3 posteriorly with significant cord oedema and hematoma in erector spinae muscle. Anticoagulants were stopped immediately. The patient was evaluated with multidisciplinary team including a neurologist and a neurosurgeon. Surgery was deferred in view of very high risk because of Covid lung disease, hypoxemic respiratory Failure, and high oxygen requirement. Hence it was decided to continue conservative medical management. Patient was treated with high dose steroids for 3 days to decrease the swelling around spinal cord. Steroids were tapered fast after 3 days and he was put on maintenance dose of methylprednisolone 40 mg twice daily.

\*Corresponding author: Jyoti Goyal,  
HOD Internal Medicine.



**Figure 1. T2 weighted sagittal image shows intradural hyperintense signal with fullness of thecal sac**



**Figure 2. T2 weighted axial image reveals hypointense hemorrhage in the intradural space causing cord compression**

His back pain improved dramatically though power remained 1/5 in both lower limbs. On day 7 of admission his oxygen requirement and work of breathing increased along with increased CRP (122.6) and IL6 (98.29). His procalcitonin at this point of time was normal. After explaining the risks and benefit of immunomodulator therapy, patient was offered Adalimumab to control cytokine release syndrome (CRS) Patient received 4 injections of Adalimumab 40 mg each in 4 different quadrants of abdomen subcutaneously. Adalimumab was chosen over tocilizumab because of nonavailability of the latter and some case reports saying high risk of spinal abscess with its use.

## DISCUSSION

Spontaneous spinal epidural hematoma without history of trauma, coagulopathy or spinal instrumentation is a very rare disease.

Incidence of spontaneous spinal hematoma is 0.1 per 100000 patients per year (1). Spontaneous spinal epidural hematoma is associated with significant morbidity, because it can cause disabling neurological deficits, and approximately 50% of patients do not recover fully (2). Most important risk factor for spinal hematoma are increasing age, coagulopathy, thrombocytopenia, liver disease and use of anticoagulants. Most important cause of spontaneous spinal hematoma is use of anticoagulants and clotting disorder (3). There may have been multiple risk factors that may have been associated with development of this very rare complication encountered in treatment of Covid 19. These may have been Elderly male, increased risk of thrombosis as well as bleeding (in some) in Covid patients, and concomitant use of anticoagulant therapy although no etiological conclusion can be made. However, the therapeutic decision to use anticoagulants in moderate to severe COVID-19 disease cannot be modified without any anticipation of this risk of spinal hematoma. Though covid 19 is associated with increased risk of thrombosis but in one large multicentric study done in COVID-19 disease, 4.8% of overall bleeding risk was reported in all hospitalized patients and hence it is important to assess the risk benefit ratio of its use. Interestingly high TPA (Tissue plasminogen activator) levels were found in covid patients with high bleeding risk. Further studies are needed for the use of TPA levels to identify covid patients, who are at high risk of bleeding (4).

MRI spine is the diagnostic modality of choice for any spinal emergency as it is quick, non-invasive, gives the extent of pathology, delineates underlying lesion and gives information on cord oedema. Emergency surgical decompression is the treatment of choice and should be done as soon as possible within 24 hours of insult (5). However, here we report a rare case of spontaneous subdural hematoma developing in patient being treated conservatively for moderate to severe COVID-19 disease. In such a case, very careful consideration should be made on the timing of surgical intervention due to increased risk of perioperative mortality and morbidity. Optimal timing of surgical intervention in such patients with COVID-19 and hypoxic respiratory failure is unknown. In a largest case series of conservatively treated spontaneous spinal epidural hematoma showed that conservative management is possible when neurological deterioration is not seen (6). COVID-19 disease is associated with increased immunothrombosis and risk of DVT and PE which further gets increased in cases of paraparesis along with bedridden status. Treating these patients without use of anticoagulants and antiplatelets is challenging specially with high D dimers and increasing oxygen requirements. Use of immunomodulator (Tocilizumab) in selected cases of cytokine storm in COVID-19 is being practiced as standard medical management (7). Use of immunomodulator in this case was a difficult decision because of multiple reasons. Paraparetic patients are very prone to get secondary infections and use of immunomodulators may be double edged sword and can increase the risk of secondary sepsis. Secondly a case series of three patients depicting development of spinal cord dysfunction after use of tocilizumab. Two out of these three cases developed spinal abscesses after the use of tocilizumab, which was supposed to be a serious complication of this drug (8). Therefore, we had a detailed discussion with our in hospital covid team along with patients' representatives. We decided not to use Tocilizumab in this case because of the difficult availability, high risk of secondary sepsis and the case series documenting risk of spinal abscesses.

Table 1. Laboratory Parameter

Test Done	On Day of Admission	Day 4	Day 7	Day 10	Day 15	On Day of Discharge	Reference Range
Haemoglobin (in g/dL)	13.1	12.4	13.2	12.3	15.2	12	13.00 – 17.00
TLC (in thou/mm <sup>3</sup> )	4.9	16.24	9.98	11.6	11.82	9.71	4.00 – 10.00
Neutrophils (in %)	62.4	23.49	19.62	11.05	11.09	7.98	2.00 – 7.00
Lymphocytes (in %)	34.3	15.4	9.9	3.3	1.9	10.2	1.00 – 3.00
Platelet Count (in thou/mm <sup>3</sup> )	62	58	75	130	183	95	150.00 – 410.00
Creat (in mg/dL)	1.39	2.4	1.36	1.1	1.2	93	0.67 – 1.17
Urea (in mg/dL)	40	80	68	68	85	60	17.00 – 43.00
Sodium (in mEq/L)	133	137	136	134	137	140	136.00 – 146.00
Potassium (in mEq/L)	4.5	4.58	4.3	4.36	3.57	4.19	3.50 – 5.10
SGOT (in U/L)	54	58	56	55	44	64	<50
SGPT (in U/L)	73	105	127	144	136	93	<50
CRP (in mg/L)	18.5	58.28	122.64	41.32	24.55	5.37	<5.00
D. Dimmer (in mg/L FEU)	0.38	2.07	4.63	7.58	4.96	4.35	<0.50
PCT (in ng/mL)	0.107	0.418	0.11	5.7	2.3	0.05	<0.5
IL6 (in pg/mL)	3.75	–	98.29	–	6.92	6.04	<7.0

After careful evaluation of risk benefit ratio, we decided to use Adalimumab to control cytokine release syndrome (CRS). Adalimumab has got >20 years of experience of its use and has demonstrated good safety profile in high-risk cases. Though adequately powered randomized controlled trial are needed to prove its safety and efficacy in COVID-19 disease but many observational studies and data has shown its mortality and morbidity benefit<sup>(9, 10)</sup>. As these patients are at high risk of development of complications and sepsis, hence a close vigilance and timely identification and intervention is required to prevent and treat this complication. Specific respiratory muscle training (inspiratory muscle training) and cough assist devices are useful to prevent secondary infections and pneumonia and reduces the risk of respiratory complications in patients with spinal cord involvement and COVID-19<sup>(11)</sup>. Patient was discharged on 20th day of hospital admission with detailed home care advice with 1-2 lt/minute of oxygen therapy at home, with advice on Spo<sub>2</sub> monitoring. At the time of discharge these patients and their caregivers need lot of education and support to help and prevent their patients getting further complications associated with paraplegia like urine and chest infections, bedsores, DVT and PE<sup>(12)</sup>.

#### Learning Points/Take Home Messages 3-5 Bullet Points

- This complication needs quick evaluation and diagnosis so as to take important therapeutic decision to hold anticoagulant.
- Conservative management of spinal hematoma in case when risks of surgery outweigh benefit may be tried as in our case.
- Judicious and careful use of immunomodulator: Adalimumab
- Early identification and management of secondary sepsis
- Continuity of care at home and rehabilitation and regular follow up assessments.

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