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POSSIBILITY OF INTESTINAL TRANSPLANT AFTER COVID19 : 1ST CASE OF VENOUS BOWEL ISCHAEMIA FOLLOWING ASTRA ZENAECA VACCINE

Surgery

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ABSTRACT

A 56-year-old lady presented to the hospital with worsening headache, strain in left eye+nausea 2 wks post vaccination (Astra Zeneca Covid Vaccine 1st dose).MR Venogram showed no evidence of cerebral venous thrombosis. So, HIT test was requested & steroids started on admission. 2 days later some abdominal discomfort started followed by malaena. USS+CT scan abdomen revealed thrombosis involving the portal vein & its tributaries. These findings plus positive HIT test result and rising lactate (5.6) indicated venous rather than arterial thrombosis which meant that there was no place for thrombectomy or IV thrombolysis. A diagnostic laparoscopy was done to check for the bowel viability keeping in mind the possible need for bowel resection. Unfortunately, the entire small bowel was found to be non-viable due to the venous bowel ischaemia. No option of reconstruction was available.The procedure was abandoned & patient sent to the ITU. Later inotropic support was withdrawn to let the patient die with dignity.Complete small bowel resection and postoperative TPN support may have saved the patient's life for some time. But indefinite TPN post complete small bowel resection till the availability of a bowel transplant donor, was an option that was impracticable in the current already overburdened district hospitals.

KEYWORDS

VATT /VITT (Vaccine associated thrombotic/induced thrombocytopenia), TPN(Total parenteral nutrition) COVID-19 Astra Zenaeca adverse effects

BACKGROUND:

Bowel ischaemia means less blood supply to the intestines due to less mesenteric blood flow (1). The overall incidence is low (0.09 to 0.2%) but mortality rate is high [2]. Acute bowel ischaemia is usually acute mesenteric ischaemia (AMI) which means a sudden interruption of the blood supply to a segment of the small intestine [3] due to mesenteric arterial embolism (50%), mesenteric arterial thrombosis (15-25%), mesenteric venous thrombosis (MVT) (5-15%) [4, 5] and superior mesenteric artery (SMA) vasoconstriction in 20% cases [6,7,8,9].

Regarding the venous bowel ischaemia caused by MVT, it is usually an extension of Portal vein thrombosis (PVT) alongwith splenic vein thrombosis. This is classified as the portal venous system thrombosis [10,11]. The most common presentation is abdo minal pain and CT scan abdomen is diagnostic as seen in the current case. Outcomes are mainly determined by underlying prothrombo tic state, recurrence of the throm bosis and developing short bowel syndrome (12). In regards to severe COVID-19 cases which present with interstitial pneumonia progressing to acute respiratory distress syndrome, sepsis and multi-organ failure [13, 14]; current evidence suggests that hypercoagulable state is the cause of increased mortality [15,16,17]. The evidence came from the data regarding global thrombotic events which is entered into the World Health Organization (WHO) Global Database for Individual Case Safety Repo rts (VigiBase). Analysis of such COVID-19 vaccine related data entered between Dec ember 13, 2020 and March 16, 2021, was performed by Smadja et al. This covered a population of almost 362 million vaccinated individuals across the world. The study focused on Pfizer-BioNtech (BNT162b2), Moderna (mRNA-1273), and Oxford Astra Zeneca (ChAdOx1 nCov-19) vaccine related thrombotic events. 62 cases of cerebral venous sinus thrombosis and 24 cases of splanchnic vein thrombo sis including 18 fatal thrombotic events, have been reported in the EudraVigilance drug safety database among 25 million vaccinated individuals as of March 22, 2021. Now the number has risen to 169 cases of cerebral venous sinus thrombosis and 53 cases of splanchnic vein thrombosis among 34 million recipients of Astra Zenaeca vaccine. Recently analysis of blood samples from 11 patients with post-vaccination (with Astra Zenaeca) thrombotic events yielded evidence of immune thrombotic thrombocyto penia mediated by platelet-activating antibodies against platelet factor 4. None of these patients had received heparin [18]. Similar evidence was found from analysis of samples from 5 patients in Norway, who presented with venous thrombosis and thro mbocytopenia 7 to 10 days after receiving st dose of Astra Zenaeca vaccine. Another similar 23 cases were reported from the U.K following Covid19 Astra Zenaeca vaccine. This potentially life endangering clinical entity has been termed "vaccine-induced immune thrombotic thrombocytopenia (VITT)".

Overall mortality is approximately 40% either from ischaemic brain injury or from superimposed haemorrhage (19). Here I report the case of death due to complete small bowel venous ischaemia as a result of MVT & VITT following Astra Zenaeca Covid-19 dose 1. We know that for patients with irreversible intestinal failure, isolated intestinal transplantation holds particular promise (20) but this was not available in the current case.

Case Description-
(6/4/21 to 11/4/21 in hospital):

A 56-year-old otherwise healthy lady presented to the hospital A/E nearly 2 weeks post vaccination (Astra Zenaeca Covid Vaccine 1st dose). She complained of worsening headache alongwith strain in her left eye since vaccination and now nausea. Initial suspicion was cavernous venous thrombosis & therefore MR Venogram was done but it came back negative. The patient had no visual disturbances. MRI head suggested possible demyelination. Further CT head revealed focal hypodensity in right frontal region a likely lacunar infarct (see images). Regarding blood investigations (see tables & graphs for trends) on admission, the platelet count was 11 and LFT mildly deranged. Therefore, HIT test was requested (? ITP /? VATS) & patient admitted under haematology team. Her past medical history was primary hypertension, spondylolisthesis of lumbosacral region and a kind of Raynauds syndrome. She had been found negative during bowel cancer screening in February 2020. On 26/3/21 she had received her 1st dose of SARS COV 2 after which she developed the symptoms. On admission the patient was started on iv methyl prednisolone & TED stockings were given. Two days post admission she said "tummy ache" and relatively loose bowel motion.USS abdomen was requested query portal vein thrombosis while Methyl prednisolone dose was reduced & Fondaparinex started. Same night she had backache that got relieved by codeine.

Next morning, she developed 3 episodes of malaena. CT scan abdomen showed thrombosis of portal vein extending to its tributaries. VBG lactate was 5.6 & therefore the on-call general surgical team was involved. A discussion between general surgeons, vascular surgeons, gastro-enterologists, radiologists, ITU specialists & haemologists followed. The conclusion was that it was a case of venous & not arterial bowel ischaemia. Therefore, there was no place for thrombectomy or IV thrombolysis. The patient was informed about all investigation results and possible options. Finally, she agreed to be taken to theatre for diagnostic laparoscopy & proceed. She had been informed beforehand that in case non-viable bowel is found the procedure would be abandoned. When the procedure was started with Hassons technique for the first port (umblical), haemmorhagic fluid spurted out like a fountain. We managed to get the pressure of 12 mm and inserted the camera. A necrotic dusky dead small bowel was found from DJ flexure to ileo-caecal junction. Not even a bit of small bowel was viable. No option of reconstruction was available. Umblical port was therefore closed & the procedure stopped. The patient taken to ITU on nor-adrenaline and metaraminol infusions. Family was informed that there was nothing left to offer that could stop her from dying. So they came to spend some time with the patient on inotropic support which

was later withdrawn to let her die with dignity.

DISCUSSION

As per current guidelines prophylactic anticoagulation with low-molecular-weight heparin should be administered to COVID-19 patients although this is contraindicated for patients with heparin-induced thrombocytopenia (HIT). Delayed recognition of HIT in COVID-19 patients can contribute to the poor outcome in such patients (20). In the present case the thrombosis had extended into the tributaries of the portal vein to such an extent that the entire small bowel had died. Complete small bowel resection and immediate TPN was not considered.

Literature review shows that the patients receiving TPN are always at risk of complications like central access vein thrombosis & infections, osteoporosis, cholecystitis and liver damage (21). However, TPN does provide a chance of long productive life to patients without the use of their intestines. Their long-term survival depends on the cause of intestinal failure. Three-year survival ranges from 65 to 80 percent.

The remaining 20 to 35 percent fare poorly and intestinal transplant is required as a life-saving procedure (22). Such intestine transplant candidate patients need to be assigned to a transplant coordinator who then links the patient with intestinal transplant care team that comprises of Transplant surgeons, Gastroenterologists, Nutritionists, Pain management specialists, Pharmacists, Psychiatrists, Social workers and Credit analysts. The patient needs a series of tests and scans to find out risks and benefits from surgery. These include CT scans of the head, chest, and abdomen, Endoscopy, Blood test, Stress test, Heart catheterization and Pulmonary function testing. After the evaluation, if found eligible for an intestinal transplant, the patient is placed on place intestinal transplant waiting list. Since intestinal transplant is fairly uncommon, the wait list is short. But, the criteria for donor organs are specific (23).

Summary

A middle-aged lady had her first dose of COVID 19 vaccine & over the next few day. she started developing progressive headache, nausea, vomiting & abdominal pain. After multiple investigations and medical management, ultimately, she was taken to theatre only to find a dead bowel. The only option for survival was to take out her entire small bowel and put the patient on lifelong TPN while awaiting a bowel transplant; an impossible choice to make in a busy emergency theatre.

CONCLUSION

To save a patient's life, TPN may be considered in all bowel resections whether partial or complete. In the present case the unavailability of the option of reconstruction in a DGH was enough to avoid complete bowel resection & the patient was left to die. How right this is ethically can be debated but how easily the option of intestinal transplant can be chosen is a big question in itself. With already never-ending hospital waiting lists in place for life threatening conditions, putting another patient for a remotely possible intestinal transplant somewhere sometime was not a practicable option.

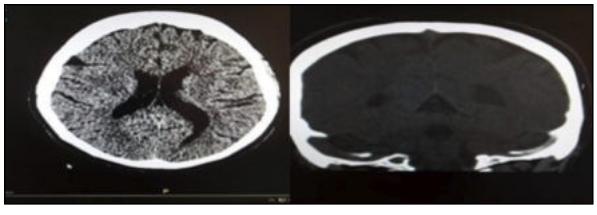

Figure1-*Neuro Imaging During The Patients Hospital Admission*

TABLE 1

Haematology	*Normal range*	*6/4/21 10:50am*	*6/4/21 14:15pm*	*07/5/21*	*8/5/21*	*9/5/21*	*10/5/21*
Hb		*149*	*150*				
WCC		*6.7*	*8.2*	*8.2*	*15.4*	*17.7*	*16.5*
neutrophils		*3.37*	*4.19*	*6.43*	*12.38*	*13.51*	*12.87*
Monocytes		*0.83*	*1.13*	*0.27*	*1.63*	*2.67*	*1.81*
CRP		*22*		*12*	*8.4*		*11*
Platelets		*11*	*12*	*24*	*30*	*68*	*80*
Red cell count		*4.82*	*4.83*	*3.91*	*4.2*	*3.95*	*4.04*
ESR		*7*			*36*		
LFT							
Bili		*5*		*7*	*7*	*9*	*12*
AST		*86*		*53*	*76*	*61*	*55*
ALT		*91*		*77*	*94*	*92*	*92*
ALP		*90*		*85*	*90*	*83*	*82*
GGT		*194*		*196*	*221*	*197*	*203*

	Normal range	**6/4/21 10:50 am**	**6/4/21 12:15 noon**	**07/5/21**	**8/5/21**	**9/5/21**	**10/5/21**
Clotting profile							
INR		1.1	1.1		1.3	1.4	1.4
aPTT		32.7	32.6		27.9	46	27.4
Aptt ratio		1.1	1.1		0.9	1.3	1.3
PT		14.8	14.9		17.2	18	14.9
Clauss fibrinogen			1.20		0.40	1.10	1.00
Heparin Induced thrombocytopenia				positive			
d-dimer for DIC			13078			14145	
phosphate		1.02					
calcium		2.58		2.52	2.51		
Adjusted calcium		2.60		2.62	2.57		
LDH		269					
TOTAL Protein							
Albumin		39		33	36		
Globulin		43		64	60		

SERUM ELECTROPHORESIS - NORMAL except IgG which was high (39.92)

LIPID PROFILE - NORMAL

KIDNEY Function

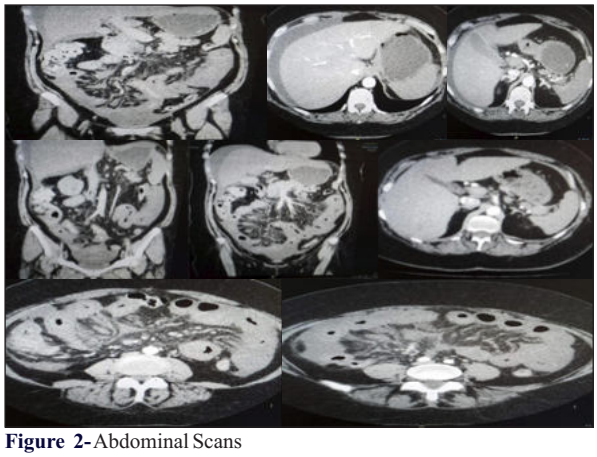

Figure 2-Abdominal Scans

Figure 3- *Pictures Of The Non Viable Small Bowel Seen During Laparoscopy*

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