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.

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Extending the clinical spectrum of thrombotic thrombocytopenic syndrome attributable to adenovirus-based vaccines for Covid-19

The report by Yocum et al. [1] adds a new dimension to the syndrome of vaccine-induced thrombotic thrombocytopenia(VITT) attributable to Ad26.COV2·S vaccination [2,3].

In their report Yocum et al. report a case [1] which differed from the other two VITT cases [2,3] in having acute kidney injury as the manifestation of the prothrombotic state, arguably as a result of thrombotic occlusion of renal microvasculature [4]. Furthermore, at 62, their patient was older [1] than the patients in the other two reports [2,3], and the 37 days interval between vaccination and symptom onset [1] was longer than the vaccine-to-symptom onset interval documented in the other two reports [2,3].

The symptomatology was also distinctive, the main feature being an acute-onset confusional state characterised by combative behaviour which included ripping things off the wall and tearing her room apart. The patient had also been vomiting and her room was covered in emesis, and there was also feces on the floor. All this, in spite of the fact that, prior to going upstairs to her room, she had been in a state of good mental and physical health, and had eaten dinner with her family. Physical examination revealed scattered petechiae but did not reveal any focal neurological signs.

In the context of thrombotic thrombocytopenia the association of acute confusional symptoms and acute onset renal failure reported by Yocum et al. could, arguably have been attributable to sudden-onset thrombotic occlusion of cerebral microvasculature and sudden onset thrombotic occlusion of renal microvasculature, both phenomena well recognised in thrombotic thrombocytopenic purpure [4]. By contrast, in See et al., and in Muir et al., thrombotic occlusion was extrarenal in location, involving the cerebral venous sinuses, middle cerebral artery, portal venous system, internal jugular vein, and lower limb deep veins, respectively [2,3]. Notwithstanding the cerebrovascular involvement the only manifestation of cognitive impairment was “cognitive fogginess” in only one patient [2]. Accordingly, there appear to be fundamental differences in the pattern of vascular involvement, namely, microvascular thrombotic occlusion in Yocum et al. [1] versus large vessel thrombotic occlusion in the other two cases [2,3].

Synonyms for VITT include “Vaccine-Induced Prothrombotic Immune Thrombocytopenia”(VIPIT), and Thrombotic Thrombocytopenic Syndrome(TTS) [5]. Tom Shimabukure and his team defined a “definite” case of TTS as one characterised by the following:-

(i) Platelet count <150,000/μl with confirmatory peripheral smear showing reduced platelets with no evidence of clumping that could indicate a falsely low platelet count.

(ii) Presence of thrombosis/thromboembolism confirmed by one or more of the following, namely, imaging studies, surgical procedures, and pathologic examination [6].

The Expert Haematology Panel of the United Kingdom defined a “definite case” of VITT as one characterised by platelet count <150,000/μl, and very raised D dimer levels, the latter above the level expected for venous thromboembolism. That panel also noted that, in many cases, antibodies to platelet factor 4 have been identified in the absence of exposure to heparin treatment [7].

The ChAdOx1-nCoV 19 is another adenovirus-based vaccine for which data on VITT have been published in the medical literature. There are data on 58 cases(45 females) of whom 48 were aged <60 [8-22]. The twin derangements of thrombocytopenia and raised D-dimer levels were documented in 51 cases. In the 7 other cases only one of either of the two derangements was documented. Thrombotic manifestations were present in 57 cases. The only patient who lacked clinically overt thrombotic manifestations was a 71 year old woman who, nevertheless, had a D dimer level of 20,000 μg/L [9]. The spectrum of thrombotic occlusion comprised cerebral venous sinus thrombosis (CVST)(36 cases), and, also, thrombosis involving the middle cerebral artery, the coronary arteries, portal venous system, the internal jugular veins, and the lower limb veins, respectively. One patient was exceptional in having documentation of thrombotic occlusion at microvascular level(involving the brain and kidneys), but this documentation was only made at autopsy [10]. Only one patient(aged 34) presented with mental agitation, and that patient had CSVT and intracranial hemorrhage [8]. The longest interval between vaccination and onset of symptoms of VITT was 24 days [9]. The latter was in a 49 year old woman in whom pulmonary embolism was the only documented manifestation of VITT [9].

In short, the report by Yocum extends the clinical spectrum of the thrombotic thrombocytopenic syndrome attributable to adenovirus-based Covid-19 vaccines to include symptoms that can best be explained by assuming that thrombotic occlusion had taken place at microvascular level. This pattern of thrombotic occlusion has also been documented in one example of VITT attributable to ChAdOx1-nCoV-19 vaccination [10].

Declaration of Competing Interest

I have no funding and no conflict of interest.

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