

UN CAS DE THROMBOLYSE INTRAVEINEUSE D'UN INFARCTUS CEREBRAL EN UNITE COVID19 : UN CHALLENGE THERAPEUTIQUE

A CASE OF STROKE THROMBOLYSIS IN COVID 19 UNIT: A THERAPEUTIC CHALLENGE

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Résumé

Introduction : La pandémie de COVID-19 a posé de nouveaux défis dans la gestion de l'AVC ischémique (AVCI) à la phase aiguë. Nous rapportons un premier cas national d'une thrombolyse intraveineuse (TIV) d'un AVCI en unité Covid 19 en dégageant les challenges diagnostique et thérapeutique.

Observation : Il s'agit d'une femme âgée de 60 ans, qui a été hospitalisée au centre COVID-19 de Sfax pour prise en charge d'une détresse respiratoire. Au cours de son hospitalisation (soit trois semaines après le début des symptômes respiratoires), elle a présenté brutalement une lourdeur de l'hémicorps gauche. Une alerte thrombolyse a été lancée après deux heures du début des symptômes. Le NIHSS était à 13. Un scanner cérébral fait à trois heures et demi a montré des signes précoces d'ischémie cérébrale. La TIV a été initiée à quatre heures du début de la symptomatologie sans amélioration notable (NIHSS = 12 en post thrombolyse).

Conclusion : La TIV de l'AVCI chez les patients atteints de COVID-19 pose un défi aux personnels de la santé. Des efforts doivent être faits au niveau extra et intra-hospitalier pour améliorer les délais et la réponse au traitement.

Mots - Clés : Accident vasculaire cérébral ischémique ; Phase aiguë ; Thrombolyse ; COVID-19

Abstract

Introduction: The COVID 19 pandemic has certainly posed new challenges in the acute management of ischemic stroke (IS), and the benefit risk ratio of intravenous thrombolysis (IVT) in patients testing positive for COVID 19 is not yet well established.

Case report: A 60-year-old woman was admitted at the COVID 19 center of Sfax for further management of COVID-19-related respiratory distress syndrome. During hospitalization (three weeks since the onset of respiratory symptoms), she developed sudden onset of hemiplegia (NIHSS=13). Thrombolysis alert has been triggered and a CT Scan was performed two and three hours and a half from the onset of the symptoms respectively. IVT was initiated four hours from the onset of the symptoms. There was no remarkable clinical improvement after IVT (NIHSS=12).

Conclusion: IVT among stroke patients with COVID-19 remains a challenge to health care professionals. Efforts need to be made at the extra and the intra-hospital level to improve delays and treatment response.

Key-words: Ischemic stroke; Acute phase; Thrombolysis; COVID-19

ملخص

مقدمة: لقد فرضت جائحة كوفيد-19 تحديات جديدة في إدارة السكتة الدماغية الإقفارية في المرحلة الحادة. سنقدم أول حالة وطنية لانحلال الخثرة في الوريد في وحدة كوفيد 19، مع تسليط الضوء على التحديات التشخيصية والعلاجية الحالة: هذه سيدة تبلغ من العمر 60 عامًا، تم نقلها إلى مركز كوفيد-19 بصفاقس لإدارة ضائقة تنفسية. أثناء مكوثها في المستشفى (أي بعد ثلاثة أسابيع من بدء أعراض الجهاز التنفسي) ظهر فجأة ثقل في النصف الأيسر من الجسم. تم إطلاق تنبيه إذابة الجلطات بعد ساعتين من ظهور الأعراض. أظهر مسح الدماغ الذي تم إجراؤه في 3.5 ساعة علامات مبكرة على نقص التروية الدماغية. بدأت إذابة الجلطة بعد أربع ساعات من ظهور الأعراض. لم يكن هناك تحسن سريري ملحوظ بعد إذابة الجلطة الخلاصة: إذابة الجلطة الدماغية لدى مرضى كوفيد-19 يشكل تحديًا لموظفي الرعاية الصحية يجب بذل الجهود على المستوى الخارجي وداخل المستشفى لتحسين أوقات العلاج والاستجابة له

كلمات المفاتيح : السكتة الدماغية الإقفارية ; المرحلة الحادة ; انحلال الخثرة ; كوفيد-19

INTRODUCTION

Intravenous thrombolysis (IVT) with the use of recombinant tissue plasminogen activator (rt-PA/Alteplase) is an effective and universally recommended method of treatment in the acute ischaemic stroke within 4.5 h of symptom onset. There is no contraindication in the administration of IV Alteplase in patients with communicable diseases [1].

In COVID-19 hospitalized patients, acute stroke has been observed in 1% to 2.5% of cases with high in hospital mortality rate [2]. Although COVID-19 pandemic has produced an enormous collateral damage over stroke systems of care leading to a drop of mild strokes admissions and late arrival of severe strokes, only incidental cases of large vessel occlusion in young adults infected by SARS-CoV-2 have been reported without a clear causative relationship [3].

Administering IVT in COVID-19 positive patients poses a challenge to the healthcare professionals. A link between COVID-19 and stroke and its outcome when given IV Alteplase has yet to be reported.

OBSERVATION

A 60-year old female, with a past history of diabetes and hypertension, presented to the emergency department with cough and cold symptoms of one-week duration associated with shortness of breath and fever. She was confirmed COVID-19 positive by reverse transcription polymerase chain reaction. She was then admitted in the medical COVID-19-unit care. High-resolution computed tomography of the chest showed more than 50% of areas of ground glass densities with focal areas of consolidation predominantly in both perihilar and peripheral regions of the lungs (figure1).

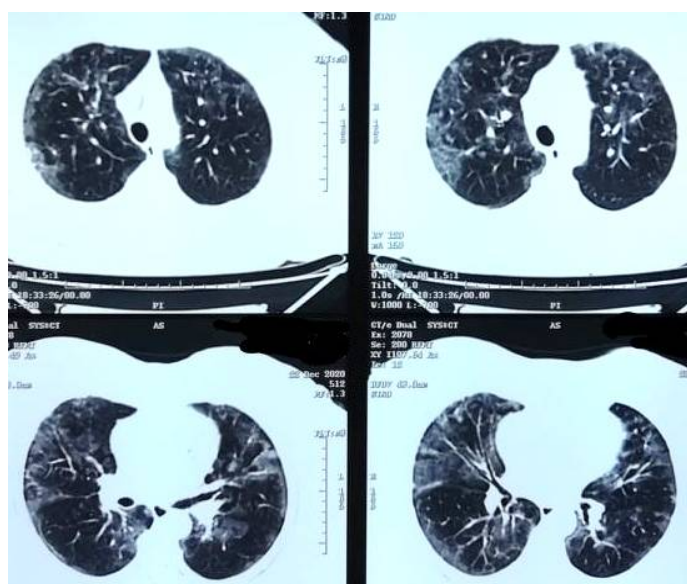


Figure 1: Areas of ground glass densities with focal areas of consolidation in both perihilar and peripheral regions of the lungs.

During hospitalization (three weeks since the onset of respiratory symptoms), she developed sudden onset of left hemiplegia and severe dysarthria (National Institutes of Health Stroke Scale (NIHSS) =13). Thrombolysis alert has been triggered and a brain CT Scan without intravenous

contrast was performed two and three hours and a half from the onset of the symptoms respectively. Brain CT scan showed an early sign of middle cerebral artery (MCA) infarction consisting of hyperdense right MCA and indicating thrombus within the vessel (figure 2).

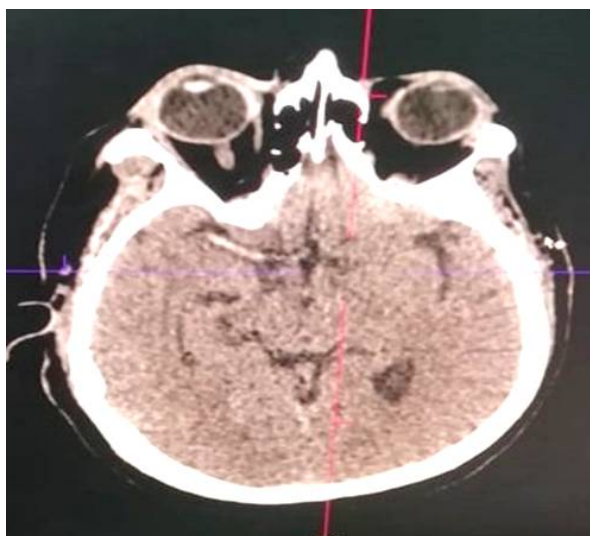


Figure 2: Brain CT scan shows hyperdense right middle cerebral artery

The Alberta stroke programme early CT score was 8. Her biological workup showed increased level of D-dimer, C-Reactive Protein and Fibrinogen (1144 ug/ml, 60 mg/L and 4,5 g/L respectively). IVT with Alteplase was initiated four hours from the onset of the symptoms. There was no remarkable clinical improvement after IVT (NIHSS=12) nor hemorrhagic transformation on control brain CT scan.

DISCUSSION

The COVID-19 infection caused by the SARS-CoV-2 virus has been in a state of pandemic declared by the World Health Organization since March 2020. The most frequent presentation of the disease is viral pneumonia with fever and dry cough. Some patients quickly progress to acute respiratory distress, which may lead to death, most frequently due to respiratory and multiorgan failure [4].

Neurological symptoms have frequently been described in association with the disease, but these have been mostly nonspecific alterations. It is well established that COVID-19 frequently presents with a state of altered coagulability, with increased risk of pulmonary embolism and other thrombotic events such as stroke [5]. Patients present with altered levels of procoagulant factors and inflammatory biomarkers such as D-dimer, C-Reactive Protein and Fibrinogen. These biological parameters have been shown to increase stroke severity and disability which were consistent with findings in our patient [6].

Currently, there are no reports elucidating the direct relationship of COVID-19 and its influence on stroke outcome. Possible mechanisms that may explain acute ischemic events in COVID-19 patients include cardiovascular compromise in the setting of infection, reduced oxygenation in the setting of acute respiratory distress syndrome, and systemic inflammation causing thrombosis [4]. COVID-19 infection negatively modifies acute stroke procedures and, due to its pro-coagulative effect, may potentially impact on IVT outcome. However, due to decline in the volume of stroke hospitalizations and IVT treatments in previous waves of the disease, only a few reports associated the impact of SARS-CoV-2 infection on the outcome of stroke patients treated with IVT. According to the literature, SARS-CoV-2 infection prolongs length of stay in hospital after IVT, but does not influence in-hospital outcome. It was not associated with an increased risk of disability, mortality, and hemorrhagic transformation compared to those without COVID-19 [7,8].

Our patient had proximal occlusion of the right MCA which would decrease the rate of arterial recanalization. Moreover, IVT was initiated 4 hours from the onset of the symptoms which is an increased treatment delay reducing the benefits of thrombolysis in patients with acute IS.

Indeed, management of stroke among COVID-19 positive patients is a struggle in most countries due to hindrance from rapid response of the stroke team. This is likely from extrinsic factors such as inadequate Personal Protective Equipment as well as lack of imaging modalities solely dedicated for

COVID-19 patients to avoid rapid viral transmission like in our case. These occur on top of the already existing problem of shortage of healthcare professionals as they are inadvertently exposed and hence, quarantined. Further studies will help explore other possibilities of a causal relationship in order to define guidelines in the management of stroke among COVID-19 positive cases. But until now, IV rt-PA is still the gold standard treatment for acute IS associated to COVID-19 infection [9].

CONCLUSION

The management of COVID-19 patients who suffer from stroke poses a challenge to healthcare professionals. Currently, IV Alteplase should continue to be considered as the standard of care in IS patients with confirmed COVID-19 who are eligible for thrombolysis. Efforts need to be made at the extra-hospital and intra-hospital level to improve delays and treatment response.

REFERENCES

- [1] Berge, E., Whiteley, W., Audebert, H., De Marchis, G. M., Fonseca, A. C., Padiglioni, C et al. European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke. *European stroke journal*, 2021, vol. 6, no 1, p. I-LXII.
- [2] Elkind, Mitchell SV, Robert A. Harrington, and Ivor J. Benjamin. The role of the American Heart Association in the global COVID-19 pandemic. *Circulation*, 2020, vol. 141, no 15, p. e743-e745.
- [3] Requena, M., Olivé-Gadea, M., Muchada, M., Garcia-Tornel, A., Deck, M., Juega, J. et al. COVID-19 and stroke: incidence and etiological description in a high-volume center. *Journal of Stroke and Cerebrovascular Diseases*, 2020, vol. 29, no 11, p. 105225.
- [4] Naval-Baudin, P., Rodriguez Caamano, I., Rubio Maicas, C., Pons-Escoda, A., Fernandez Vinas, M. M., Nuñez, A et al. COVID-19 and ischemic stroke: clinical and neuroimaging findings. *Journal of Neuroimaging*, 2021, vol. 31, no 1, p. 62-66.
- [5] Asakura, H., Ogawa, H. COVID-19-associated coagulopathy and disseminated intravascular coagulation. *International journal of hematology*, 2021, vol. 113, no 1, p. 45-57.
- [6] Ibañez, C., Perdomo, J., Calvo, A., Ferrando, C., Reverter, J. C., Tassies, D., & Blasi, A. High D dimers and low global fibrinolysis coexist in COVID19 patients: what is going on in there? *Journal of thrombosis and thrombolysis*, 2021, vol. 51, no 2, p. 308-312.
- [7] Sobolewski, P., Antecki, J., Broła, W., Fudala, M., Bieniaszewski, L., & Kozera, G. Systemic thrombolysis in ischaemic stroke patients with COVID-19. *Acta Neurologica Scandinavica*, 2022, vol. 145, no 1, p. 47-52.
- [8] Sasanejad, P., Hezarkhani, L. A., Arsang-Jang, S., Tsivgoulis, G., Ghoreishi, A., Kristian, B. et al. Safety and outcomes of intravenous thrombolytic therapy in ischemic stroke patients with COVID-19: CASCADE initiative. *Journal of stroke and cerebrovascular diseases*, 2021, vol. 30, no 12, p. 106121.
- [9] Sasanejad, P., Hezarkhani, L. A., Arsang-Jang, S., Tsivgoulis, G., Ghoreishi, A., Kristian, B. et al. Safety and outcomes of intravenous thrombolytic therapy in ischemic stroke patients with COVID-19: CASCADE initiative. *Journal of stroke and cerebrovascular diseases*, 2021, vol. 30, no 12, p. 106121.