e-SMART
SMART MEETING ANESTHESIA RESUSCITATION INTENSIVE CARE
31° SMART - VIRTUAL MEETING
November 13-15, 2020

VIRAL REACTIVATION IN COVID19 PATIENTS ADMITTED TO ICU: AN OBSERVATIONAL RETROSPECTIVE STUDY

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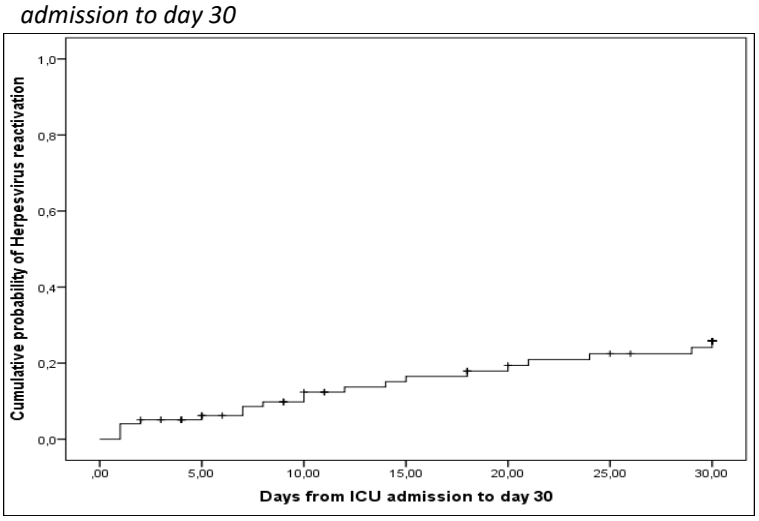
Background: ICU patients with severe COVID19 pneumonia have a dysregulated immune response. These patients may develop an immune anergy after the proinflammatory phase and this may raise the occurrence of reinfections. Whereas bacterial co-infections have been frequently documented, viral reactivation were probably underestimated.

Methods: On February 28th was introduced in our ICU a screening to detect CMV reactivation in COVID19 patients, and on April 8th we started to detect systematically the other Herpesviruses reactivation. The incidence was assessed in consecutive adult COVID19 patients admitted to our ICU with moderate to severe ARDS. These patients were tested for Herpesviruses, including HSV-1, HSV-2, EBV, CMV, VZV, HHV-6 and HHV-8.

Table 1: characteristics and treatment of viral reactivation

	CMV Screened: 101	HSV Screened:26	EBV Screened:26
Blood reactivation	14 (3,9)	7 (26,9)	5 (19,2)
Clinical reactivation	3 (3,0)	5 (19,2)	1 (20,0)
Prophylaxis	**Gancyclovir** 2 (2,0)	**Acyclovir** 5 (19,2)	**Acyclovir** 5 (19,2)
Treatment	7 (50)	4 (57,1)	1 (20,0)

Figure 1: Cumulative probability of viral reactivation fron ICU admission to day 30



Results: Fourteen patients out of 101 resulted positive for CMV viremia (13,9%), after a median of 12 days (IQR 9-22 days) from ICU admission. Seven patients (50%) were treated with Gancyclovir. Mortality at 30 days was 50% in patients with reactivation of CMV and 26,4% in patients without CMV reactivation (p=0,073). Among 26 patients screened for other Herpesviruses other than CMV, 12 patients (46,2%) had a reactivation, with 7 patients reactivating HSV1 (26,9%), and 5 patients EBV (19,2%). The time for reactivation was a median of 15 days (IQR 6,5-22,5) from ICU admission. Between these patients, 5 were treated with Acyclovir (41,6%). Mortality at 30 days was 25% in the group of patients with viral reactivation, and 46% in patients with no reactivation (p=0,271). In the multivariable logistic regression evaluating risk factors for 30-day mortality CMV reactivation was not significantly associated (OR 2,60 - 95% CI [0,64-10,58], p=0,183).

Conclusions: Considering recent reports, viral reactivations in COVID19 critically ill patients might be underestimated. Introducing in ICU protocols systematic screenings to detect viral reactivations may guide specific treatment and improve patient's outcome.

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PROFILASSI/TERAPIA VIRUS ERPETICI IN PAZIENTI CON INFEZIONE DA SARS-COV 2

2. Valutazione settimanale di CMV-DNA.
   - Se CMV-DNA>10,000 UI/ml-20,000 UI/ml trattamento con ganciclovir 5mg/kg x2/die ev con valutazione bisettimanale di CMV-DNA. Il trattamento sarà da proseguire per almeno 14 giorni, fino a due riscontri di CMV-DNA negativo. Possibile switch a valganciclovir 900 mg x2/die per os nel paziente stabile.
   - Se CMV-DNA <10,000 UI/ml valutazione bisettimanale di CMV-DNA
   - In caso di riattivazione citomegalica valutare riduzione immunosoppressione (es. steroidi)
   - Se si imposta tp con ganciclovir sospendere acyclovir in profilassi
   - La dose di ganciclovir va ridotta a seconda di eGFR

3. Valutazione settimanale di HSV1 e 2 plasma. In caso di riscontro di riattivazione di HSV su plasma:
   - Se >10,000 copie/ml impostare tp con acyclovir 5-12,5mg/kg IV x3/die a seconda della clinica correlata
   - Se <10,000 copie/ml impostare profilassi con acyclovir 400 mg x2/die per os o 5 mg/kg x2/die ev
   - In entrambi i casi valutare riduzione immunosoppressione (es. steroidi)
   - In entrambi i casi valutare a seconda della clinica se indicati esami di secondo livello quali rachicentesi o BAL per valutare presenza di encefalite/polmonite da HSV1. Una qualunque positività su liquor cefalo-rachidiano sarà da considerarsi significativa; su BAL invece il cut-off per HSV1 è 10^5 UI/ml