

Lecture consigliate da Anna M. Tortorano (gennaio 2018)

L'importante attività influenzale della presente stagione con 472 casi gravi ricoverati in terapia intensiva, 72 dei quali deceduti (Italia, periodo settembre 2017 - settimana 5/2018) porta di attualità il rischio di aspergillosi in questa categoria di pazienti, anche se immunocompetenti. A tale proposito segnalo tre articoli

Invasive pulmonary aspergillosis is a frequent complication of critically ill H1N1 patients: a retrospective study. Wauters J, Baar I, Meersseman P, Meersseman W, Dams K, De Paep R, Lagrou K, Wilmer A, Jorens P, Hermans G. *Intensive Care Med.* 2012 Nov;38(11):1761-8.

PURPOSE: Despite their controversial role, corticosteroids (CS) are frequently administered to patients with H1N1 virus infection with severe respiratory failure secondary to viral pneumonia. We hypothesized that invasive pulmonary aspergillosis (IPA) is a frequent complication in critically ill patients with H1N1 virus infection and that CS may contribute to this complication.

METHODS: We retrospectively selected all adult patients with confirmed H1N1 virus infection admitted to the intensive care unit (ICU) of two tertiary care hospitals from September 2009 to March 2011. Differences in baseline factors, risk factors, and outcome parameters were studied between patients with and without IPA.

RESULTS: Of 40 critically ill patients with confirmed H1N1, 9 (23 %) developed IPA 3 days after ICU admission. Five patients had proven and four had probable IPA. Significantly more IPA patients received CS within 7 days before ICU admission (78 versus 23 %, $p = 0.002$). IPA patients also received significantly higher doses of CS before ICU admission [hydrocortisone equivalent 800 (360-2,635) versus 0 (0-0) mg, $p = 0.005$]. On multivariate analysis, use of CS before ICU admission was independently associated with IPA [odds ratio (OR) 14.4 (2.0-101.6), $p = 0.007$].

CONCLUSIONS: IPA was diagnosed in 23 % of critically ill patients with H1N1 virus infection after a median of 3 days after ICU admission. Our data suggest that use of CS 7 days before ICU admission is an independent risk factor for fungal superinfection. These findings may have consequences for clinical practice as they point out the need for increased awareness of IPA, especially in those critically ill H1N1 patients already receiving CS.

Invasive Aspergillosis Associated With Severe Influenza Infections. Crum-Cianflone NF. *Open Forum Infect Dis.* 2016 Aug 10;3(3):ofw171

BACKGROUND. Invasive aspergillosis may occur in the setting of severe influenza infections due to viral-induced respiratory epithelium disruption and impaired immune effects, but data are limited. **METHODS.** A retrospective study was conducted among severe influenza cases requiring medical intensive care unit (ICU) admission at an academic center during the 2015-2016 season. Data collected included respiratory cultures, medical conditions and immunosuppressants, laboratory and radiographic data, and outcomes. A systematic literature review of published cases in the English language of aspergillosis complicating influenza was conducted. **RESULTS.** Six (75%) of 8 ICU influenza cases had *Aspergillus* isolated; 5 were classified as invasive disease. No ICU patient testing negative for influenza infection developed aspergillosis during the study period. Among cases with invasive aspergillosis, influenza infection was type A (H1N1) ($n = 2$) and influenza B ($n = 3$). Published and current cases yielded $n = 57$ (European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group criteria: 37% proven, 25% probable, and 39% possible cases). An increasing number of cases were reported since 2010. Sixty-five percent of cases lacked classic underlying conditions at admission for aspergillosis, 86% had lymphopenia, and 46% died. **CONCLUSIONS.** Aspergillosis may occur in the setting of severe influenza infections even among immunocompetent hosts. Risks may include influenza A (H1N1) or B infections and viral-induced lymphopenia, although further studies are needed. Prompt diagnosis and antifungal therapy are recommended given high mortality rates.

Influenza-Associated Aspergillosis in Critically Ill Patients. van de Veerdonk FL, Kolwijck E, Lestrade PP, Hodiament CJ, Rijnders BJ, van Paassen J, Haas PJ, Oliveira Dos Santos C, Kampinga GA, Bergmans DC, van Dijk K, de Haan AF, van Dissel J, van der Hoeven HG, Verweij PE; Dutch Mycoses Study Group. *Am J Respir Crit Care Med.* 2017; 196 (4): 524-527.

In uno studio retrospettivo multicentrico con il coinvolgimento di 8 centri olandesi (dicembre 2015-aprile 2016) vengono riportati 23 casi di aspergillosi acuta invasiva tra 144 pazienti con influenza grave ricoverati in terapia intensiva. Il galattomannano è risultato positivo su BAL in 17/18 pazienti (94%) e *Aspergillus* è stato isolato da BAL in 14 pazienti (78%) ed è risultato resistente agli azoli in 4 casi (29%). L' elevata mortalità (61%, nonostante la terapia antivirale) è stata attribuita a diagnosi tardiva e ritardato inizio della terapia antifungina.