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EDITORIAL

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Open the doors of the ICU to patients with malignancies and neurological complications

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Admission of patients with malignancies to intensive care units (ICUs) remains a controversial issue. Although remarkable advances have been made in early diagnosis, in supportive care and in the treatment of cancer patients [1, 2], whether cancer patients should be admitted to the ICU is still a matter of debate. The mortality rate from septic shock in immunocompetent patients is reported to be as high as 55%, and oncological patients may have even greater morbidity and mortality [3]. As the number of ICU beds remains limited, questions related to the ethics of admitting such patients to the ICU are rapidly raised [4]. The literature is also conflicting: one study reported very high mortality rates for cancer patients requiring mechanical ventilation [5], but other studies have reported identical outcomes for patients with and without cancer [1, 6, 7]. These differences may be due to advances in patient management (for example, use of non-invasive mechanical ventilation) and earlier recognition of chemotherapy toxicity [1, 6, 7]. In view of the conflicting data, an "ICU trial" has been proposed, consisting of 4 days of full-code treatment for cancer patients admitted to the ICU, followed, on day 5, by a reappraisal of the level of care [8].

In this issue of Intensive Care Medicine, Legriel et al. [9] report their experience of 100 patients with malignancies who were admitted to the ICU for central neurological complications over a 7-year period. Seventy-four percent of these patients had haematological malignancies. Moreover, this was a cohort of severely ill cancer patients—60% required invasive mechanical ventilation for a median duration of 4 days, 15% needed vasopressors and 6% renal replacement therapy. The major reasons for admission were coma (56%), seizures (48%), focal signs (35%), encephalopathy (31%) and/or meningeal symptoms (7%). Interestingly, seizure activity was inaugural in 11 (91%) of the 12 patients with seizures and 27 (75%) of the 36 patients with status epilepticus. Standard diagnostic tests provided the diagnosis in 83% of patients, with only 4 patients needing a neurosurgical biopsy (3 cases of B-cell and 1 of T-cell lymphoma). The main etiologies of the neurological complications were drug-related brain toxicity (28%), malignant brain infiltration (21%) and cerebrovascular abnormality (20%). The mortality rate of an unselected population admitted to a neuro-ICU has been reported as 18% [10], but mortality in cancer patients with hematological and solid tumors admitted to general ICUs can reach 54–60% [11]. Nevertheless, although these patients had severe disease (cancer and neurological complications), ICU and hospital mortality rates were 28 and 45%, respectively.

This study [9] has some major limitations. First, the retrospective design limits the data that are available for analysis. Second, and probably more importantly, it is difficult to extrapolate these results to other ICUs.

This study was performed in a hospital where more than half the beds are reserved for patients with malignancies, and 30% of the ICU admissions are patients with a malignancy. The attending doctors are, therefore, more likely to be aware of cancer-related neurological complications and drug-related neurological toxicity than physicians in a more general ICU. These encouraging data, therefore, need to be confirmed in other general ICUs.

The diagnostic approach used by the authors was very simple [9] and could be improved relatively easily, which may decrease the mortality rate. Fifty-six percent of the patients were admitted for coma and 48% for seizures; for the majority, this epileptic phenomenon was inaugural. Coma and epilepsy were explored by intermittent EEG, performed according to the clinical setting. No data are provided regarding the duration or frequency of these EEGs, except that they were "intermittent." Although continuous EEG monitoring can easily be performed for prolonged periods of time, it is not widely available, mostly due to the cost of the technology and the lack of experienced neurologists able to read these EEGs. Among general patients admitted to neuro-ICUs, 11–55% have been reported to have electrographic seizures [12]. Using continuous EEG monitoring, Jordan et al. [13] noted that, among 124 patients admitted to the neuro-ICU, 34% had seizures, which were non-convulsive status epilepticus in 76% of cases. In 570 patients undergoing continuous EEG monitoring for detection of subclinical seizures or an unexplained decreased level of consciousness, 19% had seizures, most of which were non-convulsive; 88% were detected during the first 24 h, but the rest needed more than 24 h of monitoring to be detected [14]. After control of convulsive status epilepticus, 48% of patients continued to show electrographic seizures on continuous EEG monitoring, and 14% had non-convulsive status epilepticus [15]. Even when treated with intravenous drugs (such as propofol, midazolam or barbiturates), 12–51% of patients in refractory status epilepticus still had subclinical breakthrough electrographic seizures, and 43–63% had withdrawal seizures at the end of the pharmacological coma [16]. In medical ICU patients mostly admitted for sepsis, 10% had electrographic seizures, and 17% had periodic epileptiform discharges [17]; 67% of the seizures had no detectable clinical correlate and were detected only by continuous EEG monitoring. Mc Hugh et al. [18] analyzed the rate of electrographic seizure detection in the ICU using intermittent EEG and reported electrographic seizures in only 2% of their routine EEGs, which was far less than expected. This last study illustrates the fact that intermittent "routine" EEG is insufficient for detection of non-convulsive seizures and can lead to unacceptable delays in providing adequate treatment.

Video recording synchronized with continuous EEGs is very helpful, enabling subtle clinical correlates to be identified. It can also help detect artifacts, which are numerous in the ICU setting, e.g., respiratory physiotherapy can mimic rhythmic delta activity on the EEG and can be misinterpreted as a seizure. With video surveillance, the EEG reader can also see when the patient is being stimulated, which can lead to major changes in the EEG pattern.

Seizures can increase metabolic demands in injured cerebral zones, which may lead to increased damage. Early recognition of electrographic seizures and status epilepticus is important to limit this effect. Moreover, the prognosis of status epilepticus is highly dependent on the administration of early, effective treatment. The general rule "time is brain" also applies to oncological patients.

In conclusion, this retrospective study reported that the ICU and hospital mortality rates of patients with mostly haematological tumours admitted for neurological complications reached 28 and 45%, respectively. The main causes of the neurological alterations were seizures and toxicity-induced treatment. Rapid diagnosis, including continuous EEG monitoring, may reduce mortality rates. These data should encourage the intensivist to admit these patients to the ICU, enabling them to receive optimal care.

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