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WHAT'S NEW IN INTENSIVE CARE

Critical care in hematologic emergencies

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Life expectancy in patients with hematological malignancies (HM) has improved markedly in recent years owing to advances in therapy and supportive care [1]. As a result, more patients are both at risk of acute complications and have greater potential for recovery, leading to increasing intensive care unit (ICU) admissions. The care of critically ill hematologic patients is not confined to large academic centers but represents a global challenge, underscoring the need for intensivists across all practice settings to be familiar with the emergencies that precipitate critical illness and their management. Treating these patients requires a complex, coordinated, multiprofessional effort. In many cases, initial stabilization must take place in the first-contact ICU before transfer to a specialized center, if needed. In this article, we outline the general principles of ICU management and highlight specific approaches to these unique complications.

General management

Within the first year after diagnosis, approximately 14% of patients with HM require ICU admission, with rates varying between 7 and 22% depending on the underlying disease. Overall ICU mortality is around 20% [2]. Although acute myeloid leukemia (AML) carries the highest risk for ICU admission, aggressive non-Hodgkin lymphomas and multiple myeloma account for a greater absolute number of cases due to their higher prevalence. The leading reason for ICU admission is acute respiratory failure (ARF) (50%), followed by acute kidney injury (38%) and sepsis (30%) [2].

Several principles in the general management of hematological emergencies can be lifesaving. These include early admission, etiologic diagnosis, early treatment and expert advice, which can be summarized under the mnemonic "**E4**" (Fig. 1A). Timely ICU admission has consistently been associated with improved outcomes [3], as these patients are prone to rapid deterioration and benefit from prompt intensive care.

Life-threatening conditions in HM patients can arise from multiple etiologies. Figure 1B summarizes the major hematologic emergencies. Despite their heterogeneity, a structured approach can facilitate timely diagnosis and management. We have, therefore, grouped these complications into five major categories and propose the acronym "CAUSE", where each letter corresponds to a clinically meaningful domain. C stands for *Cancer progression*, which can cause organ dysfunction due to infiltration, compression, or obstruction; A stands for *Associated to cancer*, including indirect cancer-related complications, such as paraneoplastic syndromes, autoimmune phenomena, endothelial dysfunction, cytokine-mediated syndromes, hyperviscosity and coagulation disorders (e.g., thrombosis or disseminated intravascular coagulation); U stands from *Unrelated to cancer*, referring to complications arising from comorbidities or unrelated acute conditions (e.g., myocardial infarction and trauma); S stands for *Sepsis and infections*, reflecting the high susceptibility of this immunosuppressed population to infections by both typical and opportunistic pathogens; and E accounts for *Effect of therapy*, encompassing toxicities associated with chemotherapy, immunotherapy, or radiotherapy leading to organ dysfunction.

Applying this approach may strengthen clinical reasoning and facilitate earlier interventions with a direct impact on outcomes. Accurate etiologic diagnosis is crucial, as concrete treatment strategies are commonly condition-specific. This principle is well-established in ARF, but likely extends across other clinical scenarios. Notably, in ARF, 15% of cases have no determined etiology, which is associated with poorer outcomes [4]. A structured diagnostic approach is preferred over isolated tests,

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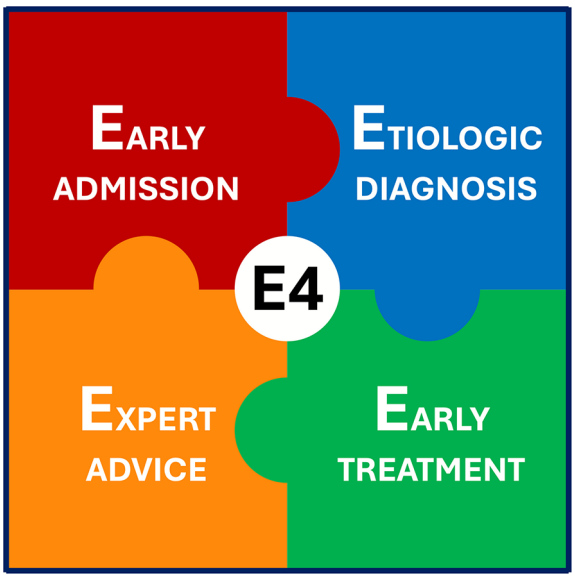

A

Fig. 1 To support timely diagnostic reasoning and highlight key principles in the general management of critically ill patients with hematologic malignancies, the mnemonics **E4** and **CAUSE** provide clinicians with a structured approach to rapidly identify and manage the full spectrum of acute complications in these patients. **Fig. A. E4** summarizes four key actions in general management. **Fig. B. CAUSE** outlines the five major etiologic categories leading to ICU admission in this population. For each category, the figure also summarizes the different entities it includes, along with examples, underlying condition, main clinical features, and specific therapeutic approaches. [a]It should include supportive treatment as required. [b]These complications may also appear or worsen as a consequence of treatment for the hematologic malignancy. [c]Consider treatment interruption or modification. *AIHA* autoimmune hemolytic anemia, *AKI* acute kidney injury, *AML* acute myeloid leukemia, *APL* acute promyelocytic leukemia, *aPTT* activated partial thromboplastin time, *ARF* acute respiratory failure, *ATRA/ATO* all-trans retinoic acid/arsenic trioxide, *BsAs* bispecific antibodies, *CAR* chimeric antigen receptor, *CHF* chronic heart failure, *CNS* central nervous system, *COPD* chronic obstructive pulmonary disease, *CRS* cytokine release syndrome, *DIC* diffuse intravascular coagulation, *DVT* deep vein thrombosis, *G-CSF* granulocyte colony-stimulating factor, *HLH* hemophagocytic lymphohistiocytosis, *HM* hematological malignancy, *HSCT* hematopoietic stem cell transplantation, *ICANS* immune effector cell-associated neurotoxicity syndrome, *Ig* immunoglobulin, *LDH* lactate dehydrogenase, *MDS* myelodysplastic syndromes, *MM* multiple myeloma, *PE* pulmonary embolism, *PEx* plasma exchange, *PT* prothrombin time, *RDT* radiotherapy, *RRT* renal replacement therapy, *SOS* sinusoidal obstructive syndrome, *SVC* superior vena cava, *TLS* tumor lysis syndrome, *TMA* thrombotic microangiopathy

integrating clinical assessment with targeted efficient investigations to enable personalized care.

Bedside evaluation should begin with medical history, physical examination, basic laboratory tests, and imaging. The DIRECT approach has been suggested in this setting: D for duration of symptoms, I for the type of immunosuppression, R for radiographic pattern, E for clinical experience, and T for Computed Tomography imaging [5].

While designated for ARF, this strategy may be adapted to other scenarios such as sepsis or AKI with minimal adjustments. The integration of symptom chronology, type of immunosuppression, and radiologic or laboratory patterns can guide focused investigations in these contexts as well. Following the CAUSE framework, cancer-related and associated complications (C and A), as well as some infectious complications (S), often appear at diagnosis or during refractory/relapsed disease, whereas treatment-related complications and most infections (S and E) typically arise after therapy has been initiated.

Early and appropriate treatment is essential, encompassing both supportive and etiologic interventions. Supportive care in HM patients follows general critical care principles, although evidence is limited due to their frequent exclusion from large clinical trials. Several studies have evaluated oxygenation and ventilatory strategies in immunocompromised patients, most of whom have HM. These suggest that while intubation should be avoided when possible, it should not be delayed, and the approach must be individualized, as no single strategy (conventional oxygen, high-flow nasal oxygen or non-invasive mechanical ventilation) has proven superior overall [6–8]. Management of septic shock in HM patients should follow established guidelines for the general population [9].

Specific management

Etiologic treatment (Fig. 1) involves two broad scenarios. In some cases, the complication itself has a specific treatment. For example, severe infections associated with the HM or its treatment require appropriate antimicrobial therapy. Opportunistic infections are possible, so careful review of risk factors and diagnostic work-up is essential [10]. Immune-mediated complications and endothelial syndromes such as autoimmune hemolytic anemia in B-cell lymphomas, cytokine release syndrome or immune effector cell-associated neurotoxicity syndrome in chimeric antigen receptor T-cell recipients, and implant syndrome in autologous transplant patients often respond to corticosteroids and other targeted therapies [11]. Some conditions, such as hyperviscosity syndrome in monoclonal gammopathies (e.g., Waldenström macroglobulinemia), may benefit from plasma exchange [12].

In other situations, treating the underlying malignancy is necessary, particularly in complications falling under the C and A categories of the CAUSE framework. This is especially relevant when the complication occurs at the

Category[c]	Emergency	Examples / Causes	Underlying condition	Clinical Features	Initial Treatment [a]
Cancer progression	Obstruction	SVC syndrome; ureteral, bronchial or tracheal obstruction; massive pleural effusion; cardiac tamponade	Lymphoma, MM	Facial swelling, dyspnea, central cyanosis; Obstructive AKI, atelectasis and ARF; Obstructive shock	Corticosteroids, stent, RDT; percutaneous drainage; surgery; HM treatment
	Compression	Spinal cord compression	Lymphoma, MM	Back pain, motor/sensory deficit	Corticosteroids, RDT, surgery; HM treatment
	Organ infiltration	Bone marrow, lung, kidney, liver, CNS, mucosa	AML, MDS, T-cell malignancies	Cytopenia, ARF, AKI, liver failure, neurological symptoms	HM treatment
Associated to cancer	Hyperviscosity	Serum (monoclonal Ig peak), Whole blood (leukostasis or polycythemia)	Waldenström, MM, Leukostasis in AML	Mucosal bleeding, visual disturbance, neurological symptoms	PEx, cytoreduction; HM treatment
	Tumor Lysis Syndrome (TLS) [b]	Spontaneous	High-grade lymphoma, Hyperleukocytic leukemia	High LDH, hyperkalemia, hyperphosphatemia, hypocalcemia, hyperuricemia, AKI	Hydration, rasburicase, alopurinol, electrolyte control, RRT; HM treatment
	Electrolyte disturbances [b]	Hypercalcemia, hypocalcemia, hyperkalemia	MM (hypercalcemia); TLS in AML or lymphoma (hypocalcemia, hyperkalemia)	Confusion, weakness, arrythmias	Hydration, bisphosphonates, RRT, TLS treatment; HM treatment
	Thrombosis [b]	DVT, PE	Most HM	Edema, ARF, chest pain	Anticoagulation; HM treatment
	Coagulation disorders [b]	DIC, fibrinolysis	AML, especially APL; HLH; CAR T-cells	Bleeding, thrombosis, thrombocytopenia, prolonged PT/aPTT	Blood products; HM treatment
	Autoimmune disorder	AIHA	B-cell malignancy	Hemolysis, fever	Corticosteroids; HM treatment
	Inflammatory disorder	HLH	Lymphoma	Pancytopenia, hyperferritinemia, hypertriglyceridemia, visceromegaly, fever	Corticosteroids, Immunosuppressive drugs, Etoposide, Emapalumab; HM treatment
	Endothelial dysfunction [b]	TMA; Peri-engraftment syndrome; SOS	HSCT recipient	MAHA, organ dysfunction; capillary leak syndrome; hepatomegaly, hyperbilirubinemia, weight gain, ascites	Terminal complement inhibitors; Corticosteroids; Defibrotide
Unrelated to cancer	Complications from comorbidities; non-oncologic events	Myocardial infarction, trauma, ...	Any HM	Depending on the cause	Depending on the cause
Sepsis and infections	Typical and opportunistic infections (at any site), including febrile neutropenia	Bacterial, Fungal, Viral	Any HM +/- therapy	General (fever, malaise) or organ specific, sepsis, septic shock	Antimicrobial, source control, Immune restauration
Effect of therapy	Toxicity to chemo-, radio-, immuno-, or targeted therapy	Organ dysfunction; cytopenia; CRS/ICANS; Differentiation syndrome	Chemo/RDT; CAR T-cells or BsAs; APL on ATRA/ATO; any treated HM	Manifestations of organ dysfunction; fever, hypotension, capillary leak syndrome; neurological dysfunction	Corticosteroids; transfusion, G-CSF; Tocilizumab (CRS), Anakinra (ICANS)

B

Fig. 1 (continued)

time of HM diagnosis or during relapsed/refractory disease. Examples include ARF due to leukemic infiltration or leukostasis in AML, and airway obstruction or superior vena cava syndrome due to a mediastinal lymphoma, among others. In such cases, initiating emergent chemotherapy in the ICU may improve prognosis [13].

Other considerations

Multidisciplinary collaboration and expert advice are vital in managing critically ill HM patients with emergent complications. Involvement of hematologists, intensivists, pharmacists, and other specialists improves outcomes [14]. Given the variable prognosis of HM and challenges in identifying patients most likely to benefit from ICU care, new approaches such as time-limited trials have emerged. These strategies should be accompanied by discussion with patients and their representatives regarding goals of care [15]. Frailty and the potential impact of ICU admission on continuation of HM treatment post-discharge must be considered, as they are strongly linked to long-term outcomes in ICU survivors [16].

Future perspectives

Recognition and management of hematological emergencies require structured clinical reasoning and timely action. Multiple interventions may improve outcomes in this population. Further research and international multicenter trials are needed to refine best practices and strengthen the evidence base in these complex patients.

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Data availability statement

No new data were generated or analyzed in this study. Data sharing is not applicable to this article.

Declarations

Conflicts of interest

The authors declare that they have no conflicts of interest related to the content of this manuscript.

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