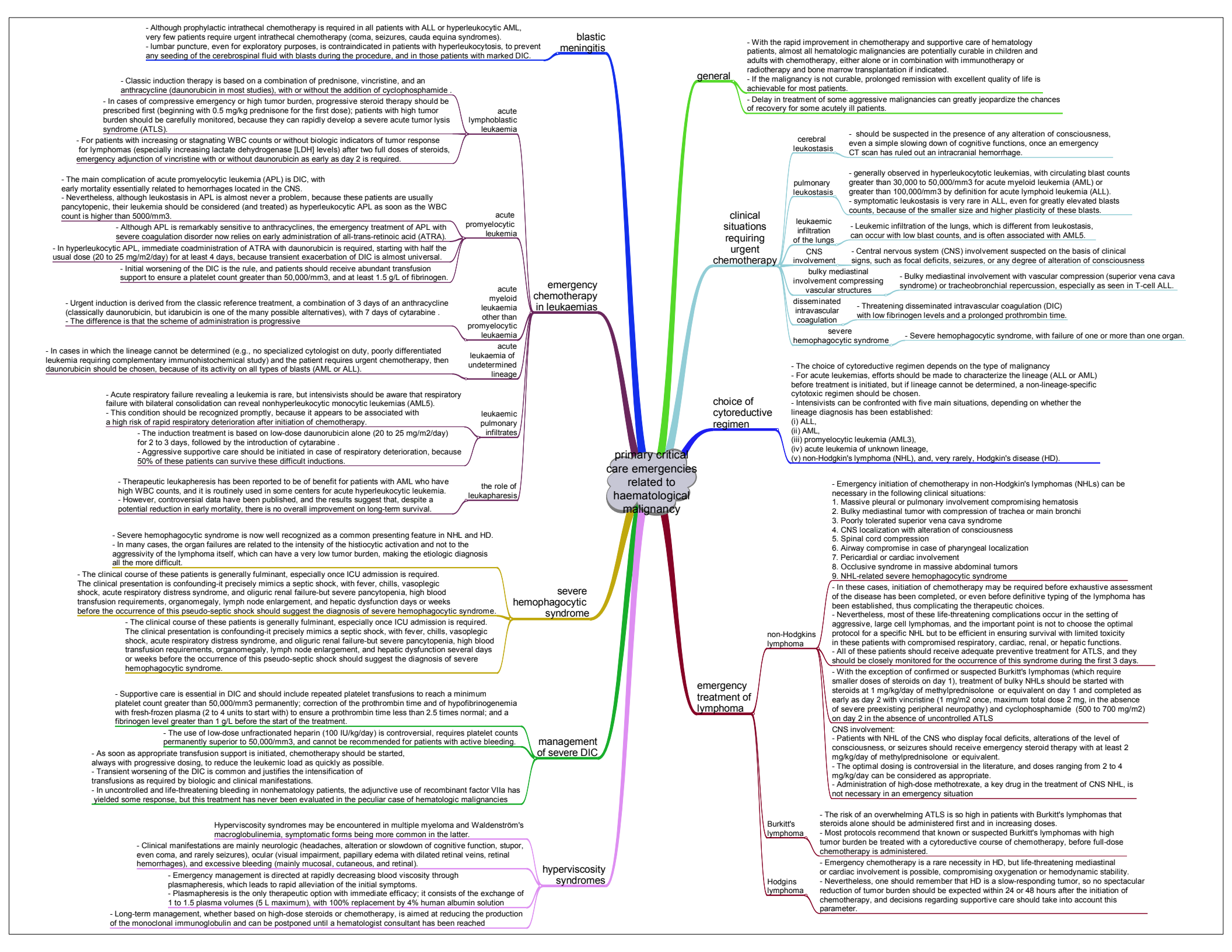
primary critical care emergencies related to haematological malignancy
blastic meningitis
- Although prophylactic intrathecal chemotherapy is required in all patients with ALL or hyperleukocytic AML, very few patients require urgent intrathecal chemotherapy (coma, seizures, cauda equina syndromes).
- lumbar puncture, even for exploratory purposes, is contraindicated in patients with hyperleukocytosis, to prevent any seeding of the cerebrospinal fluid with blasts during the procedure, and in those patients with marked DIC.
emergency chemotherapy in leukaemias
acute lymphoblastic leukaemia
- Classic induction therapy is based on a combination of prednisone, vincristine, and an anthracycline (daunorubicin in most studies), with or without the addition of cyclophosphamide .
- In cases of compressive emergency or high tumor burden, progressive steroid therapy should be prescribed first (beginning with 0.5 mg/kg prednisone for the first dose); patients with high tumor burden should be carefully monitored, because they can rapidly develop a severe acute tumor lysis syndrome (ATLS).
- For patients with increasing or stagnating WBC counts or without biologic indicators of tumor response for lymphomas (especially increasing lactate dehydrogenase [LDH] levels) after two full doses of steroids, emergency adjunction of vincristine with or without daunorubicin as early as day 2 is required.
acute promyelocytic leukemia
- The main complication of acute promyelocytic leukemia (APL) is DIC, with early mortality essentially related to hemorrhages located in the CNS.
- Nevertheless, although leukostasis in APL is almost never a problem, because these patients are usually pancytopenic, their leukemia should be considered (and treated) as hyperleukocytic APL as soon as the WBC count is higher than 5000/mm3.
- Although APL is remarkably sensitive to anthracyclines, the emergency treatment of APL with severe coagulation disorder now relies on early administration of all-trans-retinoic acid (ATRA).
- In hyperleukocytic APL, immediate coadministration of ATRA with daunorubicin is required, starting with half the usual dose (20 to 25 mg/m2/day) for at least 4 days, because transient exacerbation of DIC is almost universal.
- Initial worsening of the DIC is the rule, and patients should receive abundant transfusion support to ensure a platelet count greater than 50,000/mm3, and at least 1.5 g/L of fibrinogen.
acute myeloid leukaemia other than promyelocytic leukaemia
- Urgent induction is derived from the classic reference treatment, a combination of 3 days of an anthracycline (classically daunorubicin, but idarubicin is one of the many possible alternatives), with 7 days of cytarabine .
- The difference is that the scheme of administration is progressive
acute leukaemia of undetermined lineage
- In cases in which the lineage cannot be determined (e.g., no specialized cytologist on duty, poorly differentiated leukemia requiring complementary immunohistochemical study) and the patient requires urgent chemotherapy, then daunorubicin should be chosen, because of its activity on all types of blasts (AML or ALL).
leukaemic pulmonary infiltrates
- Acute respiratory failure revealing a leukemia is rare, but intensivists should be aware that respiratory failure with bilateral consolidation can reveal nonhyperleukocytic monocytic leukemias (AML5).
- This condition should be recognized promptly, because it appears to be associated with a high risk of rapid respiratory deterioration after initiation of chemotherapy.
- The induction treatment is based on low-dose daunorubicin alone (20 to 25 mg/m2/day) for 2 to 3 days, followed by the introduction of cytarabine .
- Aggressive supportive care should be initiated in case of respiratory deterioration, because 50% of these patients can survive these difficult inductions.
the role of leukapharesis
- Therapeutic leukapheresis has been reported to be of benefit for patients with AML who have high WBC counts, and it is routinely used in some centers for acute hyperleukocytic leukemia.
- However, controversial data have been published, and the results suggest that, despite a potential reduction in early mortality, there is no overall improvement on long-term survival.
severe hemophagocytic syndrome
- Severe hemophagocytic syndrome is now well recognized as a common presenting feature in NHL and HD.
- In many cases, the organ failures are related to the intensity of the histiocytic activation and not to the aggressivity of the lymphoma itself, which can have a very low tumor burden, making the etiologic diagnosis all the more difficult.
- The clinical course of these patients is generally fulminant, especially once ICU admission is required. The clinical presentation is confounding-it precisely mimics a septic shock, with fever, chills, vasoplegic shock, acute respiratory distress syndrome, and oliguric renal failure-but severe pancytopenia, high blood transfusion requirements, organomegaly, lymph node enlargement, and hepatic dysfunction days or weeks before the occurrence of this pseudo-septic shock should suggest the diagnosis of severe hemophagocytic syndrome.
- The clinical course of these patients is generally fulminant, especially once ICU admission is required. The clinical presentation is confounding-it precisely mimics a septic shock, with fever, chills, vasoplegic shock, acute respiratory distress syndrome, and oliguric renal failure-but severe pancytopenia, high blood transfusion requirements, organomegaly, lymph node enlargement, and hepatic dysfunction several days or weeks before the occurrence of this pseudo-septic shock should suggest the diagnosis of severe hemophagocytic syndrome.
management of severe DIC
- Supportive care is essential in DIC and should include repeated platelet transfusions to reach a minimum platelet count greater than 50,000/mm3 permanently; correction of the prothrombin time and of hypofibrinogenemia with fresh-frozen plasma (2 to 4 units to start with) to ensure a prothrombin time less than 2.5 times normal; and a fibrinogen level greater than 1 g/L before the start of the treatment.
- The use of low-dose unfractionated heparin (100 IU/kg/day) is controversial, requires platelet counts permanently superior to 50,000/mm3, and cannot be recommended for patients with active bleeding.
- As soon as appropriate transfusion support is initiated, chemotherapy should be started, always with progressive dosing, to reduce the leukemic load as quickly as possible.
- Transient worsening of the DIC is common and justifies the intensification of transfusions as required by biologic and clinical manifestations.
- In uncontrolled and life-threatening bleeding in nonhematology patients, the adjunctive use of recombinant factor VIIa has yielded some response, but this treatment has never been evaluated in the peculiar case of hematologic malignancies
hyperviscosity syndromes
Hyperviscosity syndromes may be encountered in multiple myeloma and Waldenström's macroglobulinemia, symptomatic forms being more common in the latter.
- Clinical manifestations are mainly neurologic (headaches, alteration or slowdown of cognitive function, stupor, even coma, and rarely seizures), ocular (visual impairment, papillary edema with dilated retinal veins, retinal hemorrhages), and excessive bleeding (mainly mucosal, cutaneous, and retinal).
- Emergency management is directed at rapidly decreasing blood viscosity through plasmapheresis, which leads to rapid alleviation of the initial symptoms.
- Plasmapheresis is the only therapeutic option with immediate efficacy; it consists of the exchange of 1 to 1.5 plasma volumes (5 L maximum), with 100% replacement by 4% human albumin solution
- Long-term management, whether based on high-dose steroids or chemotherapy, is aimed at reducing the production of the monoclonal immunoglobulin and can be postponed until a hematologist consultant has been reached
general
- With the rapid improvement in chemotherapy and supportive care of hematology patients, almost all hematologic malignancies are potentially curable in children and adults with chemotherapy, either alone or in combination with immunotherapy or radiotherapy and bone marrow transplantation if indicated.
- If the malignancy is not curable, prolonged remission with excellent quality of life is achievable for most patients.
- Delay in treatment of some aggressive malignancies can greatly jeopardize the chances of recovery for some acutely ill patients.
clinical situations requiring urgent chemotherapy
cerebral leukostasis
- should be suspected in the presence of any alteration of consciousness, even a simple slowing down of cognitive functions, once an emergency CT scan has ruled out an intracranial hemorrhage.
pulmonary leukostasis
- generally observed in hyperleukocytotic leukemias, with circulating blast counts greater than 30,000 to 50,000/mm3 for acute myeloid leukemia (AML) or greater than 100,000/mm3 by definition for acute lymphoid leukemia (ALL).
- symptomatic leukostasis is very rare in ALL, even for greatly elevated blasts counts, because of the smaller size and higher plasticity of these blasts.
leukaemic infiltration of the lungs
- Leukemic infiltration of the lungs, which is different from leukostasis, can occur with low blast counts, and is often associated with AML5.
CNS involvement
- Central nervous system (CNS) involvement suspected on the basis of clinical signs, such as focal deficits, seizures, or any degree of alteration of consciousness
bulky mediastinal involvement compressing vascular structures
- Bulky mediastinal involvement with vascular compression (superior vena cava syndrome) or tracheobronchial repercussion, especially as seen in T-cell ALL.
disseminated intravascular coagulation
- Threatening disseminated intravascular coagulation (DIC) with low fibrinogen levels and a prolonged prothrombin time.
severe hemophagocytic syndrome
- Severe hemophagocytic syndrome, with failure of one or more than one organ.
choice of cytoreductive regimen
- The choice of cytoreductive regimen depends on the type of malignancy
- For acute leukemias, efforts should be made to characterize the lineage (ALL or AML) before treatment is initiated, but if lineage cannot be determined, a non-lineage-specific cytotoxic regimen should be chosen.
- Intensivists can be confronted with five main situations, depending on whether the lineage diagnosis has been established:
(i) ALL,
(ii) AML,
(iii) promyelocytic leukemia (AML3),
(iv) acute leukemia of unknown lineage,
(v) non-Hodgkin's lymphoma (NHL), and, very rarely, Hodgkin's disease (HD).
emergency treatment of lymphoma
non-Hodgkins lymphoma
- Emergency initiation of chemotherapy in non-Hodgkin's lymphomas (NHLs) can be necessary in the following clinical situations:
1. Massive pleural or pulmonary involvement compromising hematosis
2. Bulky mediastinal tumor with compression of trachea or main bronchi
3. Poorly tolerated superior vena cava syndrome
4. CNS localization with alteration of consciousness
5. Spinal cord compression
6. Airway compromise in case of pharyngeal localization
7. Pericardial or cardiac involvement
8. Occlusive syndrome in massive abdominal tumors
9. NHL-related severe hemophagocytic syndrome
- In these cases, initiation of chemotherapy may be required before exhaustive assessment of the disease has been completed, or even before definitive typing of the lymphoma has been established, thus complicating the therapeutic choices.
- Nevertheless, most of these life-threatening complications occur in the setting of aggressive, large cell lymphomas, and the important point is not to choose the optimal protocol for a specific NHL but to be efficient in ensuring survival with limited toxicity in these patients with compromised respiratory, cardiac, renal, or hepatic functions.
- All of these patients should receive adequate preventive treatment for ATLS, and they should be closely monitored for the occurrence of this syndrome during the first 3 days.
- With the exception of confirmed or suspected Burkitt's lymphomas (which require smaller doses of steroids on day 1), treatment of bulky NHLs should be started with steroids at 1 mg/kg/day of methylprednisolone or equivalent on day 1 and completed as early as day 2 with vincristine (1 mg/m2 once, maximum total dose 2 mg, in the absence of severe preexisting peripheral neuropathy) and cyclophosphamide (500 to 700 mg/m2) on day 2 in the absence of uncontrolled ATLS
CNS involvement:
- Patients with NHL of the CNS who display focal deficits, alterations of the level of consciousness, or seizures should receive emergency steroid therapy with at least 2 mg/kg/day of methylprednisolone or equivalent.
- The optimal dosing is controversial in the literature, and doses ranging from 2 to 4 mg/kg/day can be considered as appropriate.
- Administration of high-dose methotrexate, a key drug in the treatment of CNS NHL, is not necessary in an emergency situation
Burkitt's lymphoma
- The risk of an overwhelming ATLS is so high in patients with Burkitt's lymphomas that steroids alone should be administered first and in increasing doses.
- Most protocols recommend that known or suspected Burkitt's lymphomas with high tumor burden be treated with a cytoreductive course of chemotherapy, before full-dose chemotherapy is administered.
Hodgins lymphoma
- Emergency chemotherapy is a rare necessity in HD, but life-threatening mediastinal or cardiac involvement is possible, compromising oxygenation or hemodynamic stability.
- Nevertheless, one should remember that HD is a slow-responding tumor, so no spectacular reduction of tumor burden should be expected within 24 or 48 hours after the initiation of chemotherapy, and decisions regarding supportive care should take into account this parameter.