TABLE 132-4 INITIAL DIAGNOSTIC EVALUATION AND MANAGEMENT OF ADULT PATIENTS WITH AML

History
Increasing fatigue or decreased exercise tolerance (anemia)
Excess bleeding or bleeding from unusual sites (DIC, thrombocytopenia)
Fevers or recurrent infections (neutropenia)
Headache, vision changes, nonfocal neurologic abnormalities (CNS leukemia or bleed)
Early satiety (splenomegaly)
Family history of AML (Fanconi, Bloom, or Kostmann syndromes or ataxia-telangiectasia)
History of cancer (exposure to alkylating agents, radiation, topoisomerase II inhibitors)
Occupational exposures (radiation, benzene, petroleum products, paint, smoking, pesticides)
Physical Examination
Performance status (prognostic factor)
Ecchymosis and oozing from IV sites (DIC, possible acute promyelocytic leukemia)
Fever and tachycardia (signs of infection)
Papilledema, retinal infiltrates, cranial nerve abnormalities (CNS leukemia)
Poor dentition, dental abscesses
Gum hypertrophy (leukemic infiltration, most common in monocytic leukemia)
Skin infiltration or nodules (leukemia infiltration, most common in monocytic leukemia)
Lymphadenopathy, splenomegaly, hepatomegaly
Back pain, lower extremity weakness [spinal granulocytic sarcoma, most likely in t(8;21) patients]
Laboratory and Radiologic Studies
CBC with manual differential cell count
Chemistry tests (electrolytes, creatinine, BUN, calcium, phosphorus, uric acid, hepatic enzymes, bilirubin, LDH, amylase, lipase)
Clotting studies (prothrombin time, partial thromboplastin time, fibrinogen, D-dimer)
Viral serologies (CMV, HSV-1, varicella-zoster)
RBC type and screen
HLA typing for potential allogeneic HSCT
Bone marrow aspirate and biopsy (morphology, cytogenetics, flow cytometry, molecular studies for *NPM1* and *CEBPA* mutations and *FLT3*-ITD)
Cryopreservation of viable leukemia cells
Myocardial function (echocardiogram or MUGA scan)
PA and lateral chest radiograph
Placement of central venous access device
Interventions for Specific Patients
Dental evaluation (for those with poor dentition)
Lumbar puncture (for those with symptoms of CNS involvement)
Screening spine MRI (for patients with back pain, lower extremity weakness, paresthesias)
Social work referral for patient and family psychosocial support
Counseling for All Patients
Provide patients with information regarding their disease, financial counseling, and support group contacts

Abbreviations: AML, acute myeloid leukemia; BUN, blood urea nitrogen; CBC, complete blood count; CMV, cytomegalovirus; CNS, central nervous system; DIC, disseminated intravascular coagulation; HLA, human leukocyte antigen; HSCT, hematopoietic stem cell transplantation; HSV, herpes simplex virus; IV, intravenous; LDH, lactate dehydrogenase; MRI, magnetic resonance imaging; MUGA, multigated acquisition; PA, posteroanterior; RBC, red blood (cell) count.

cerebellar toxicity. All patients treated with high-dose cytarabine must be closely monitored for cerebellar toxicity. Full cerebellar testing should be performed before each dose, and further high-dose cytarabine should be withheld if evidence of cerebellar toxicity develops. This toxicity occurs more commonly in patients with renal impairment and in those older than age 60 years. The increased toxicity observed with high-dose cytarabine has limited the use of this therapy in older AML patients.

Incorporation of novel and molecular targeting agents into these regimens is currently under investigation. For patients with *FLT3*-ITD AML, trials with tyrosine kinase inhibitors are ongoing. Patients with CBF AML may benefit from the combination of gemtuzumab ozogamicin, a monoclonal CD33 antibody linked to the cytotoxic agent calicheamicin, with induction and consolidation chemotherapies. This agent, initially approved for older patients with relapsed disease, has been withdrawn from the U.S. market at the request of the U.S. Food and Drug Administration due to concerns about the product's toxicity, including myelosuppression, infusion toxicity, and venoocclusive disease and the clinical benefit of the initially recommended higher doses. However, the aforementioned recent results are encouraging and support the reintroduction of this agent into the therapeutic armamentarium for AML.

In older patients (age ≥60 years), the outcome is generally poor likely due to a higher induction treatment–related mortality rate and frequency of resistant disease, especially in patients with prior hematologic disorders (MDS or myeloproliferative syndromes) or who have received chemotherapy treatment for another malignancy or harbor cytogenetic and genetic abnormalities that adversely impact on clinical outcome. These patients should be considered for clinical trials. Alternatively, older patients can be also treated with the 7 and 3 regimen with standard-dose cytarabine and idarubicin (12 mg/m^2), daunorubicin (45–90 mg/m^2), or mitoxantrone (12 mg/m^2). For patients older than 65 years, higher dose daunorubicin (90 mg/m^2) has not shown benefit due to the increased toxicity and is not recommended. The combination of gemtuzumab ozogamicin with chemotherapy reduces the risk of relapse for patients age 50–70 years with previously untreated AML. Finally, older patients may be considered for single-agent therapies with clofarabine or hypomethylating agents (i.e., 5-azacitidine or decitabine). The latter are often used for patients unfit for more intensive therapies.