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75-year-old Woman with Thoracic Spinal Cord Compression and Chloroma (granulocytic sarcoma)

Madhava Baikaidi, MD,

Northeastern Radiation Oncology Center, Scranton, PA

Stephen S. Chung, MD,

Memorial Sloan-Kettering Cancer Center, New York, New York

Martin S. Tallman, MD,

Memorial Sloan-Kettering Cancer Center, New York, New York

Lloyd Damon, MD,

UCSF Helen Diller Family Comprehensive Cancer Center, University of California at San Francisco

Alison Walker, MD [Assistant Professor],

Division of Hematology, The Ohio State University

Guido Marcucci, MD,

Division of Hematology, The Ohio State University

Abdalla Sholi, MD, and

Boca Raton Oncology Associates, Mount Sinai Hospital of Queens, Long Island City, NY

Gloria J Morris, MD, PhD

Mount Sinai Hospital of Queens, Long Island City, NY

CASE PRESENTATION

A 75-year-old-woman with a history of hypertension, coronary artery disease, dyslipidemia, osteoarthritis, and rheumatoid arthritis was admitted to the hospital after a 3 month history of worsening back pain during rehabilitation and physical therapy. She had been treated with chronic corticosteroids and most recently adalimumab (Humira) for her arthritides. She was ambulatory, but had developed gait dysfunction over a several-week period, describing symptoms consistent with a neuropathic process over the left anterior thigh and pain down the left leg. Computerized tomography (CT) of the spine showed an acute abnormality at T12. Confirmatory magnetic resonance imaging (MRI) of the thoracic spine demonstrated multiple infiltrative lesions involving almost all thoracic vertebrae, with high T2 signal suggestive of a marrow infiltrative processes, most marked at T10 and T12, as well as moderate to severe compression of the T12 vertebra with posterior bulging, causing spinal cord and thecal sac compression (Figure One). A paravertebral soft tissue density with mild enhancement was also seen bilaterally at the T12 level. A biopsy of the T12 vertebral lesion was attempted but was of insufficient quantity for a definitive diagnosis, recovering only atypical mononuclear cells. She was started on high dose dexamethasone and evaluated for urgent radiation therapy, as she was not felt to be a candidate for emergent neurosurgical stabilization due to her medical comorbidities.

To investigate the etiology of the cord compression a CT scan of the chest, abdomen, and pelvis was performed, which revealed no obvious lesions, masses, or lymphadenopathy. Complete blood count showed a normal hemoglobin and platelet count, while the white blood cell count was mildly elevated ($12.52 - 16.1 \times 10^3/\text{microliter}$ [normal $4.1 - 10.9 \times$

$10^3/\text{microliter}]$), with an elevated neutrophil count, but no abnormalities in the proportion of lymphocytes, eosinophils, basophils, or early myeloid precursors. Examination of the peripheral blood smear demonstrated normal appearing white and red cells without identification of blast-like cells, and immunophenotyping by flow cytometry of the peripheral blood did not detect any clonal proliferation. Liver and renal function tests were normal, as was the serum calcium level. Breast examination and CA 27-29 levels were normal. CA-125, CEA and CA 19-9 levels were normal. A serum protein electrophoresis was normal, as were quantitative immunoglobulin levels and serum free light chain levels (kappa and lambda), but there was a slight elevation of protein on a random urinalysis; this prompted a 24-hour urine collection for confirmation, which was negative for any detectable proteinuria or Bence-Jones proteins.

A bone marrow biopsy showed a hypercellular (80-90%) bone marrow, with a slightly increased myeloid:erythroid ratio of 5:1, and 60% involvement with atypical immature appearing hematopoietic cells in a background of trilineage hematopoiesis (Figure Two). Immunohistochemistry showed expression of CD43, CD117, weak positivity for CD30, and a subset of cells positive for P-selectin and CD33; the cells did not express CD34, PLAP, EBER, CD20, CD79a, PAX5, CAM5.2, TdT, CD3, CD15, CD5, CD2, CD4, CD8, CD7, CD56, TCL1, EMA, ALK1, CD138, and CD123. The diagnosis of acute myeloid leukemia with megakaryocytic lineage was established, but the leukemic cells did not express Factor VIII. Cytogenetics showed numerous hyperdiploid cells, 8 of which showed a translocation $t(9;22)(q34;q11.2)$ as the sole chromosomal abnormality, and FISH studies confirmed rearrangement of *Bcr-abl* in diploid and hyperdiploid cells.

She completed a course of radiation therapy to the spine and was evaluated for antileukemia therapy, which was initiated in the form of decitabine, followed by imatinib in order to target the cells harboring the $t(9;22)$ translocation.

INTRODUCTION

Acute Myeloid Leukemia (AML) in adults is an often heterogeneous disease entity in its etiology and presentation, but recent advances have certainly shown that effective treatments may result in complete remission at substantial rates (1). According to American Cancer Society statistics (2), 12,330 people were diagnosed with AML in 2010, with 8,950 deaths from the disease, and an estimated 12,950 new cases and 9,050 deaths in 2011 (3). As indicated by these approximations, the incidence of AML appears to be rising, likely due to the increasing age of the population, with etiologies in the elderly more likely to include AML arising in a background of myelodysplasia, related to chemical exposures, or related to treatment for other previous cancers (1).

A “typical” presentation of AML may present with sequelae of cytopenias, including bleeding and petechial rashes, infection, fatigue and weakness, weight loss and systemic symptoms. However, there are interesting unusual presentations of AML that may manifest with alarming clinical findings. These can include pericardial and pleural effusions (4a-Rege K et al), as well as rare cases of atrial involvement (5b- Tirado et al). CNS infiltration (6c-Schumann et al) has also been reported and is more likely in monocytic-lineage leukemias that may favor sanctuary sites (1), and these leukemias may also present with gum and soft tissue infiltration (7a). Neurologic complications have indeed been seen and reported in the literature as far back as the 1960’s and 1970’s with descriptions of meningitis, encephalitis, hemi- or paraplegias, involvement of cranial or peripheral nerves, and spinal cord compression (7d- Anjaria et al). Even more specifically, however, leukemias giving rise to spinal cord involvement due to vertebral destruction or epidural masses have been reported in the literature by Wildydes in 1963, and summarized by Anjaria. Myeloid sarcoma arises

as a subacute form of AML, with a male:female ratio of 2:1, increased incidence in children or young adults, and presentation as a single or multiple tumor masses made up of immature leukemic cells with or without green pigments, and located in the subperiosteum or bone marrow. It can appear in the orbit, anywhere in the skull, sinuses, spine, sacrum, or ribs, with radiologic features of local erosion, cortical thinning, compression at extradural or peripheral nerves sites, but not necessarily causing invasion of the dura (7d-Anjaria et al, referencing 8e-Aita 1964, 9f- Rao 1962).

We report here the presentation of AML as a “surprise” finding in an elderly female with virtually no obvious peripheral pancytopenias or abnormalities of her complete blood count, but who presented with an acute spinal cord compression and bony destruction in the spine.

In particular, this patient’s leukemia cells also exhibited a t(9;22) translocation in addition to an unusual FAB classification of AML with megakaryocytic differentiation as the phenotype.

We ask the following questions: **(a)** What treatment options would you offer this patient? Is she a candidate for aggressive induction chemotherapy? Biological therapy? **(b)** How would you monitor her for response to treatment? **(c)** How would you recommend and tailor maintenance therapy for this individual?

HEMATOLOGIC ONCOLOGISTS’ EXPERT OPINIONS

The differential diagnosis for the above constellation of diagnostic findings includes blast-phase chronic myeloid leukemia (CML), *de novo* acute myeloid leukemia (AML) harboring t(9;22), and Philadelphia (*Ph*)-positive acute lymphoblastic leukemia (ALL). The absence of any lymphoid antigens, particularly CD10, CD19, or TdT, exclude the possibility of *Ph*-positive B-lineage ALL (*Ph* positivity is quite rare in T-lineage ALL). Thus, by exclusion, this appears to represent blast phase CML or *de novo* AML.

Although *de novo* AML harboring t(9;22) is very rare (estimated 0.35% of all AML), several characteristics of this case are highly suggestive of this diagnosis. Based on a case series from the Massachusetts General Hospital, Brigham and Women’s Hospital, and the MD Anderson Cancer Center, patients with *de novo* AML with t(9;22) are much less likely than those with blastic-phase CML to exhibit basophilia and splenomegaly, neither of which was observed in our patient (11). Other notable findings in this case series were a lower BM cellularity in *de novo* AML (mean 80% compared with 98% in blastic-phase CML), as well as the absence of additional chromosomal abnormalities associated with blastic-phase CML (trisomy 8, trisomy 19, isochromosome 17q, and an additional *Ph* chromosome), and the presence of the p190 isoform of *Bcr-abl*. Our patient had a less elevated BM cellularity (80-90%), none of the chromosomal abnormalities typical of blastic phase CML, and the p190 isoform of *Bcr-abl*, further supporting the diagnosis of *de novo* AML. Finally, although chronic-phase CML can occasionally progress to blastic-phase CML without an intervening accelerated phase, it would be somewhat unusual to have no preceding detected chronic phase, particularly in a patient who was otherwise under constant medical attention for other medical issues.

One can still make an argument for the alternative diagnosis of blast-phase CML. Although CML typically harbors the p210 isoform of *Bcr-abl*, the p190 isoform has been described in approximately 1% of cases (notably more frequent than the 0.35% frequency of *Ph* positivity in *de novo* AML) and appears to predict for high rates of progression to blast phase, as well as tyrosine kinase inhibitor (TKI) resistance (12). The important clinical data in this case suggesting the possibility of blast-phase CML are the concurrent presence of a marked peripheral granulocytosis and peripheral blood cytogenetics revealing the presence

of t(9;22) in the absence of circulating blasts [77% by fluorescence *in situ* hybridization (FISH) and 100% by karyotype]. Quite peculiar in this case is the presence of an elevated circulating granulocyte count in the absence of circulating blasts, despite a bone marrow demonstrating 60% blasts. This might represent chronic-phase CML with evolution to blast crisis largely restricted to the BM. Alternative explanations for granulocytosis, such as corticosteroid use and an alternative myeloproliferative neoplasm, seem less likely given the presence of t(9;22) and the absence of JAK2 or MPL mutations.

In conclusion, the weight of evidence (absence of splenomegaly, absence of eosinophilia or basophilia, relatively low BM cellularity, absence of blast-phase CML associated cytogenetics, and presence of the p190 isoform of *Bcr-abl*) supports a diagnosis of *de novo* AML harboring t(9;22), but we admit that this does not explain her peripheral t(9;22) positive granulocytosis.

Presuming a diagnosis of *de novo* AML, she would be considered as having adverse-risk cytogenetics by virtue of a complex karyotype (13). Furthermore, the presence of megakaryocytic lineage markers such as P-selectin is associated with a worse prognosis (as well as MPO negativity, also seen in this case)(14). The overall poor prognosis of *de novo* AML associated with t(9;22) and blast-phase CML will be reviewed below.

In this older patient with *de novo* AML associated with adverse-risk cytogenetics and not fit for standard induction therapy, we would favor a low-intensity therapy, best supportive care, or enrollment on a clinical trial. When we first saw the patient in consultation, she had been started on decitabine at a dose of 20 mg/m², given for five consecutive days each month. We agreed that this represents a reasonable “low-intensity” option, with acceptable toxicity and a consistent response rate across all risk groups, including those with poor risk cytogenetics (15). However, it is important to note that the reported overall response rate to this agent is quite modest (25%), even lower (21%) in patients older than 70. Thus, strong consideration should be given to alternative and innovative therapies, particularly TKIs, as well be discussed in the following section.

When we saw this patient in clinic she had been started on imatinib at a dose of 400 mg, which she received for six days before discontinuation for neutropenia. In the above referenced case series of *Ph*-positive *de novo* AML by Soupir *et al.* (11), seven of the 16 patients received imatinib (five in combination with standard induction chemotherapy and two imatinib alone), with six having at least a partial hematologic response, and a median duration of response of only 2.5 months. The median survival was nine months, comparable to the seven month median survival reported for blast-crisis CML. These data are clearly limited, but suggest a very modest benefit from TKI therapy in this condition.

The data for TKI therapy in blastic-phase CML are more robust, with two multi-center phase II trials demonstrating limited efficacy. In a trial led by Sawyers *et al.*, 229 patients with blast-phase CML received imatinib alone at doses ranging from 400 to 800 mg daily, with 52% of patients sustaining hematologic responses (16). Thirty-one percent of patients had a sustained response and the median remission duration was ten months. Median overall survival remained poor at 7.9 months. In another trial led by Kantarjian *et al.*, a comparable response rate and overall survival of 54% and 6.5 months, respectively, was observed (17). An important observation in the trial by Sawyers *et al.*, particularly pertinent to our case, was that 64% of patients developed grade III or IV neutropenia, with 47% prompting dose reduction of imatinib. However, using a stopping criterion of an ANC of less than 0.5 for greater than 2 weeks, along with a marrow cellularity of less than 10%, only 5% of patients required discontinuation of imatinib. This strongly supports the notion that neutropenia in this context reflects disease response and is usually transient.

More recently, phase II trials have demonstrated efficacy for second-generation TKIs in patients with imatinib resistant, accelerated or blast-phase CML. In this context, hematologic and major cytogenetic responses of 47% and 29%, respectively, have been obtained with nilotinib (18), and 64% and 33%, respectively, for dasatinib (19). Most encouragingly, overall survival at 10-12 months was greater than 75% in both trials.

In summary, the above data suggest that if this patient were to have blast-phase CML, she would stand to benefit from imatinib, with potential additional benefit from a second-generation TKI at the time of progression. And although the data are extremely limited, there is some suggestion that we might be able to extend this treatment paradigm to *de novo* AML harboring t(9;22).

When we first saw this patient in consultation, she was neutropenic and had received one cycle of decitabine and a short course of imatinib. Although it was not possible to determine which agent was responsible for her neutropenia, we strongly suspected that it reflected treatment response to imatinib, as can occur as described in the above referenced trial by Sawyers *et al* (16). Thus, we recommended continuation of imatinib, preferring to treat her through a nadir in blood counts to maximize the chance of disease eradication, akin to the strategy used in standard induction chemotherapy for acute leukemia. A reasonable approach would be to use holding criteria for imatinib similar to that which were followed in the trial by Sawyers *et al.*, (holding for an ANC of less than 500/uL for greater than two weeks in the setting of a marrow cellularity of less than 10%).

The addition of decitabine to imatinib is of uncertain benefit in this situation. Although it has a non-trivial response rate (21%), the patient's preserved hemoglobin and platelet counts reduce the urgency of treating her leukemia with a more conventional agent such as this. We recommended assessing her response to TKI therapy alone (perhaps even with a trial of a second-generation TKI should she progress), reserving further decitabine for TKI-refractory disease.

In terms of the combination of decitabine with imatinib, the only available data come from a phase II study from the MD Anderson Cancer Center that demonstrated safety and efficacy of this regimen in accelerated or blast phase CML (32% complete hematologic response, 18% major cytogenetic response)(20). Taking into account these data, along with the above-discussed data for decitabine in *de novo* AML, one could argue to include decitabine in the initial therapy of either possible diagnosis. Clearly, prospective randomized trial data with which to base this decision are lacking.

To summarize, we strongly suspect that this patient has *de novo* AML associated with t(9;22), with an alternative diagnosis of blast-phase CML also possible. We believe that the ideal initial therapy for either diagnosis should include imatinib or a second-generation TKI. Acknowledging clinical equipoise in this situation, we recommend holding further decitabine, reserving its use for TKI refractoriness.

HEMATOLOGIST'S EXPERT OPINION

This case demonstrates the *de novo* presentation of AML as a granulocytic sarcoma (GS) arising in the thoracic spine with spinal cord compression. GS can occur as a single mass or as multifocal masses in virtually any organ, but predominantly lymph nodes, soft tissue, bone, and pleura (21-23). Although many GS occur as relapse after a bone marrow leukemia presentation and initial remission, nearly half of the cases occur before, or simultaneous with, a medullary myeloid leukemia (AML, MDS, or CML)(21). Histologically, these lesions are often first diagnosed as undifferentiated lymphoma, but histochemistries and immunophenotyping nearly invariably demonstrate the tumors express CD117, MPO, and

lysozyme, although only one-half express CD34 (21,23). GS represent 3-5% of all *de novo* AML cases and there is no clear FAB subtype predilection (21).

GS are enriched for certain non-random karyotypic abnormalities, especially those considered 'favorable'. GS will be present in 9-24% of patients with the t(8;21)(21, 24, 25). Patient with GS and the t(8;21) seem to have a high propensity for paraspinous disease and spinal cord compression (24). Numerous cases of the inv(16) and/or the CBFβ/MYH11 transcript have been reported (26). The prognosis of GS harboring core binding factor transcripts is uncertain, but is felt to be less favorable than their medullary leukemia counterparts (24,26). One case of t(9;22)(q34;q11) in a patient with a *de novo* GS and no evidence for CML has been reported (27). Our patient might represent the second reported case.

Whenever the Philadelphia chromosome or t(9;22)(q34;q11) and/or *Bcr-abl* transcript appears in a case of what otherwise appears to be *de novo* AML [*Ph*-positive AML], one must include in the differential diagnosis the possibility of myeloid blast crisis of an undiagnosed CML. *Ph*-positive AML is rare, representing 0.35-2% of all new cases of AML (11, 28). Three quarters of such patients express the p210 *bcr/abl* transcript length (11). Clinical and laboratory features that help distinguish *Ph*-positive AML from CML myeloid blast crisis include: lack of a prior hematologic abnormality, lack of basophilia, lack of splenomegaly, and fewer than 100% of metaphases showing the *Ph* chromosome or t(9;22)(q34;q11) and/or the *Bcr-abl* transcript. These findings would support, but not prove, that the malignancy represents *de novo Ph*-positive AML. After remission induction of *Ph*-positive AML, the marrow karyotype should revert to normal, whereas in CML myeloid blasts crisis, the *Ph* chromosome or equivalent would almost always remain evident (i.e. "second" chronic phase)(11). The prognosis of *Ph*-positive AML is poor, with a median overall survival of 9 months in one report (11). The *Ph* chromosome (or equivalent) has also been reported to be present in *de novo* acute biphenotypic leukemia (acute leukemia of ambiguous lineage) with one report describing this finding in 38% of such cases (28).

The treatment of GS, even if isolated without medullary leukemia, should involve systemic chemotherapy. As in low stage diffuse large B-cell lymphoma, GS is a systemic malignancy, and isolated GS is a harbinger of eventual bone marrow leukemia. The question is not whether to add chemotherapy to radiation therapy, but the opposite, whether to add radiation therapy to chemotherapy. In the CALGB experience, 4 of 8 patients with GS and the t(8;21) entered complete remission with induction chemotherapy and the overall survival was poor at a median of 5.4 months (24). The only long-term survivor received high-dose cytarabine consolidation therapy. The authors attributed part of the poor outcomes in this group to the avoidance or delay of local radiation therapy in the five patients with paraspinous disease. Three developed permanent paraplegia and their poor performance status obviated their ability to receive consolidation chemotherapy. This message favors the early use of local radiation therapy in patients with organ compromise from GS tumors, such as paraspinous disease, but in combination with systemic chemotherapy, regardless whether the bone marrow shows overt AML.

This case opens up the possibility of the adjunctive use of tyrosine kinase inhibitors (TKI), active in both CML and *Ph*-positive ALL. Although a TKI alone is often the initial treatment of choice for the myeloid blast crisis of CML (2), TKIs are best utilized in conjunction with chemotherapy in *Ph*-positive ALL (29, 30). There is one case report of a long-term complete cytogenetic remission of a patient with *Ph*-positive GS who received 7+3 induction chemotherapy followed by imatinib mesylate maintenance (27). In this current case, I recommend her radiation therapy be followed by standard induction chemotherapy (provided her performance status is robust) followed by a TKI, or a

hypomethylating agent (31) (if her performance status is moderate) in conjunction with a TKI, or followed by a TKI alone (if her performance status is poor).

HEMATOLOGISTS' EXPERT OPINIONS

A rare presentation of an uncommon hematologic malignancy, extramedullary manifestations (EM) of acute myeloid leukemia (AML) have been reported in 2 to 9% of patients at the time of diagnosis with marrow disease, however is more frequent in those with certain cytogenetic abnormalities such as t(8;21)(q22;q22), inv(16)(p13;q22) and t(9;11)(p21;q23)(25, 32-34). Most commonly arising within subcutaneous tissues, lymph nodes or bone, extramedullary leukemia (EL) has also been found within the visceral organs of the chest and abdomen (33). Isolated granulocytic sarcomas without marrow involvement are more rare, and therefore their incidence is less well defined (33, 35).

Therapeutic decision making for these patients presents many challenges, not only with regard to the modality utilized for induction (i.e., chemotherapy versus radiation therapy versus combined modality therapy), but also the appropriate consolidative therapy that will offer the best chance for long term disease free and overall survival (33). Although there is conflicting data on the prognostic significance of EL, it is considered to be an adverse risk factor associated with worse survival, even in those patients with favorable risk t(8;21)(q22;q22) AML (25, 33, 36, 37). As with all new diagnoses, a consideration of patient specific factors, as well as an understanding of achievable goals of care, is necessary prior to initiation of treatment, regardless of the type. If there had been an opportunity for this patient to have enrolled on a clinical trial, that would be our first recommendation as currently there is no standard approach to the management of patients 60 years of age with AML, regardless of the presence of extramedullary disease (38). The only way to systematically study and ultimately determine the best treatment for these patients is to analyze their outcome following uniform treatment, although the rarity of this disease makes accomplishing this challenging.

The acute issue of moderate to severe compression of the T12 vertebra causing spinal cord and thecal sac compression with neurologic symptoms warranted urgent intervention with corticosteroids and radiotherapy (39). Now that the diagnosis of AML is known, risk stratification based on cytogenetic and molecular analysis (*KIT*, *FLT3*, *NPM1* and *CEBPa* mutational status), as well as a consideration of her comorbid conditions and current performance status, will need to be taken into account prior to the initiation of therapy. Although older age alone or the presence of comorbidities is not a reason to withhold therapy, older patients are more likely to suffer treatment-related early death and to exhibit therapeutic resistance, both of which are concerns in this patient (40). Therapy-related AML (t-AML), which occurs following exposure to radiation or cytotoxic agents, is associated with a worse overall survival when compared to patients with *de novo* disease (41). This patient reported prior treatment with the tumor necrosis factor-alpha inhibitor adalimumab (Humira®) for her long standing history of rheumatoid arthritis. Interestingly, rare cases of AML arising during therapy with this class of agents have been reported in pediatric patients (42). Relevant to this case, AML following adalimumab exposure has been reported in an adult, although this patient had also received chemotherapeutic agents with known leukemogenic potential that may have contributed to the development of disease (43). Nonetheless this raises the possibility that this patient could have a t-AML, an important factor to consider when determining treatment. Patients with t-AML are more likely to have chromosomal abnormalities associated with unfavorable risk, and have a higher incidence of relapse and worse overall survival following conventional chemotherapy as compared to those with *de novo* AML (38, 41). Therefore, consideration of an alternative to an anthracycline and cytarabine based induction (ie. 7+3), for example treatment with the

hypomethylating agent decitabine which also has a favorable toxicity profile, should be considered for this patient. Blum *et al*, reported the experience of 53 patients with newly diagnosed AML who had received treatment with decitabine, where forty-eight of the patients had at least two of the following high risk characteristics: age ≥ 70 years, an antecedent hematologic disorder, unfavorable karyotype, or WHO performance status ≥ 2 (44). Despite these adverse features, a complete remission was achieved in 47% of patients and a response was seen in all cytogenetic subsets, including those with a complex karyotype or therapy related disease. While infection and febrile neutropenia were common in patients prior to neutrophil response, the regimen was relatively well tolerated with few non-hematologic toxicities that were grade 3 or higher. An effective low-intensity regimen such as this is ideal for patients who are not candidates for standard induction chemotherapy.

Another factor to consider in the development of a personalized therapeutic plan for this patient is the presence of the t(9;22)(q34;q11.2) found on cytogenetic analysis. More commonly associated with chronic myelogenous leukemia (CML) and precursor B acute lymphoblastic leukemia (ALL), t(9;22)(q34;q11.2) is an infrequent abnormality seen in fewer than 1% of newly diagnosed patients with AML (45, 46). Clinical criteria such as a lack of a preceding hematologic disorder, basophilia or splenomegaly at presentation, and a return to chronic or accelerated phase CML after induction chemotherapy, aid in differentiating CML in myeloid blast crisis (CML-MBC) from Philadelphia chromosome (*Ph*) positive AML (*Ph*+ AML)(47,48). Based on this patient's clinical information, it appears as though her diagnosis is most consistent with *Ph*+ AML rather than CML-MBC. Patients with *Ph*+ AML have an aggressive course characterized by resistance to conventional chemotherapy and frequent relapse in those with chemotherapy-responsive leukemia (11, 45, 46). Given the effectiveness of the tyrosine kinase inhibitor (TKI) imatinib mesylate in inducing hematologic, cytogenetic and molecular remissions in CML (49), this agent has been used alone and in combination with conventional chemotherapy in patients with *Ph*-positive AML, including those with an isolated granulocytic sarcoma (11, 27, 50, 51). These limited cases report hematologic, cytogenetic and molecular responses to TKI based therapy, although there have been few durable remissions. Those treated with intravenous (IV) chemotherapy received sequential therapy where imatinib mesylate began after completion of the IV treatment (27, 51, 52).

Given the above considerations and the patient's age and comorbid conditions, once stabilized we would initiate treatment with decitabine 20mg/m²/d for 10 days every 28 days as has been previously described (44). We would also consider initiation of imatinib mesylate 400mg daily. Unfortunately there is no data available to suggest whether imatinib mesylate should be administered with each cycle soon after completion of decitabine, or if it should be started only after achievement of disease remission. In the absence of data our preference would be the former rather than the later approach. Imatinib mesylate was chosen rather than the second generation TKIs nilotinib or dasatinib given the published reports of its use in similar patients with *Ph*-positive AML, and the lack of data with either of the other agents. However, should this patient respond to decitabine therapy and subsequently develop progressive disease on imatinib mesylate, it would be reasonable to consider a trial with either of these agents. With regard to additional local treatment of the CNS aside from the radiotherapy that she has received, intrathecal chemotherapy could be considered, although if the cerebrospinal fluid analysis was negative for myeloid blasts, this may not be necessary.

It is unlikely that this patient will be a candidate for potentially curative therapy with an allogeneic stem cell transplant, and therefore it is important to maintain her quality of life and minimize therapy related toxicity as much as possible. We believe that this regimen will accomplish this while also offering a chance for remission.

DISCUSSION AND CONCLUSIONS

We present here the complex case of a 75-year-old female with an unusual presentation of AML, in which workup for spinal cord compression led to the discovery of multiple osseous lytic lesions with abnormal radiographic enhancement suggestive of bone marrow involvement. This AML was classified as a megakaryocytic subtype, and it was also found to harbor the t(9;22) chromosomal translocation. Whether the megakaryocytic lineage of this patient's AML has an impact upon the biologic and metastatic behavior of this presentation remains in question (54). In addition to debate over the optimal induction therapy in an elderly individual, the presence of t(9;22) also raises questions regarding the role for tyrosine kinase inhibitor (TKI) therapy for this individual. We know historically that cytogenetic abnormalities which portend a better prognosis include t(8;21), t(16;16), t(15;17), and inversion of (16), (1), with normal cytogenetics portending an intermediate risk, and deletions of the long arms or monosomies of chromosomes 5 or 7, translocations or inversions of chromosome 3, t(6;9), or t(9;22) associated with poorer risk; these can further predict clinical outcome in older as well as younger individuals (53).

Discussion is relayed here as to specific tailoring of induction therapy, whether low- or high-intensity, for an elderly individual, with specific molecular targeting, after urgently intervening with radiation therapy to address the patient's spinal cord compression. A consensus in this situation is to offer both low-intensity therapy so as to reduce toxicity and morbidity associated with high intensity therapy in a poor-risk situation, as well as targeted therapy. There is no guidance in the literature, however, as to the use of supportive bisphosphonate therapy, in the situation of this hematologic malignancy, to stabilize and strengthen her spine despite lytic lesions and to further alleviate vertebral pain, as there is established with multiple myeloma, for example. We appreciate the expertise of the hematologists and oncologists who have assisted in formulating a treatment plan for this patient, whose further course was initiated with imatinib, and hematologic and radiologic surveillance planned (55). We welcome further comments and discussion toward the improvement of treatments and research for poor-risk leukemias in the elderly.

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TSE T1 Sag FS Image 6

T1 tse Axial Fat Sat image 42

FIGURE ONE LEGEND.

MRI of thoracic spine, showing spinal cord compression at T12 area, as **(a)** Turbo spin echo (TSE) T1 sagittal view; **(b)** TSE T2 sagittal residual view; **(c)** TSE T1 sagittal and fast spin view; **(d)** TSE T1 TEE Axial Fat Sat. Courtesy of Dr. Sunil Patel, and Elieen Davis, Administrator, Department of Radiology, Regional Hospital of Scranton, PA.

FIGURE TWO LEGEND.

(a) Fine needle aspiration smear from T12 area, Diff-Quik stain at 400× magnification, showing rare leukemia cell. (b) Bone marrow aspirate, Wright stain, at 400× magnification, showing leukemia cells. (c) Bone marrow core biopsy, Hematoxylin & Eosin stain, at 40× magnification, showing cellular marrow. (d) Bone marrow core biopsy, Giemsa stain, at 100× magnification, showing immature mononuclear cell infiltrate with blastic features, consistent with acute myeloid leukemia. (e) Bone marrow core biopsy, Hematoxylin & Eosin stain, at 400× magnification, showing leukemia cells. (f) Bone marrow core biopsy, Hematoxylin & Eosin stain, at 400× magnification, showing interface between leukemia cells (**lower**) and normal (**upper**). Courtesy of Dr. Abdalla Sholi, hematology and oncology associates of Boca Raton, FL, and Dr. Hamar Hamati, Department of Pathology, Regional Hospital of Scranton.