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Case Report

Myeloid Sarcoma of the Stomach Post-Bone Marrow Transplant for Myelodysplastic Syndrome

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Abstract

Myeloid Sarcoma (MS), an extra-medullary tumor of immature myeloid cells, is a rare finding in patients with other hematopoietic diseases such as AML, CML, and MDS. It can also be found in isolation, termed non-leukemic MS, but often portends the arrival of AML at a later date. MS tends to present in skin, bones, lymph nodes, and other locations associated with specific genetic abnormalities, such as ocular or testicular presentations. GI presentations are particularly rare, though they have been reported in the literature. Our patient is a 66-year-old male with a past medical history of AML, and MDS treated with Vidaza and eventually bone marrow transplant. Despite achieving complete remission, he presented on follow up with loose stools and abdominal pain, which on endoscopy and biopsy was revealed to be gastric MS. He was placed on Vidaza once again: He continues treatment at this time. Literature review reveals no ideal method for treatment of MS localized to the GI system. Hematopoietic stem cell transplant along with systemic chemotherapy remains the cornerstone of treatment, with the added benefit of excision surgery or radiotherapy being unclear at this time.

Keywords: Sarcoma; Myeloid; Gastric; Leukemia; Gastrointestinal

Introduction

Myeloid Sarcoma (MS), also known as granulocytic sarcoma, myeloblastoma or chloroma (owing to its greenish hue on pathological examination from the presence of myeloperoxidase), is a rare extra-medullary tumor of immature myeloid cells that disrupts the normal tissue architecture [1,2]. Extramedullary disease sites can be found anywhere in the body, including the skin, CNS, eyes, gastrointestinal tract, and testicles. Gastrointestinal manifestations, although not uncommonly reported in the literature, are more rare than skin or lymph node manifestations, with a reported occurrence of only 6.5% in a study of 92 patients done by Pileri, et al. [3,4]. MS has been associated with diseases involving myeloid cell line proliferation including Acute Myeloid Leukemia (AML), Chronic Myeloid Leukemia (CML), Myelodysplastic Syndrome (MDS), and Myeloproliferative Syndrome (MPS). Most often it presents concomitantly with known or previously known AML. It can also present as an isolated tumor, preceding bone marrow disease, or as a sign of relapse of disease [5,6]. Involvement of the GI tract clinically presents with nonspecific abdominal symptoms and anorexia; disease progression can result in possible obstruction or in bleeding due to perforation [7].

In this report, we present a particularly rare case of MS found in a patient with a history of treated Chronic Lymphocytic Leukemia (CLL) as well as intermediate-risk MDS treated with six cycles of chemotherapy and bone marrow transplant. The patient presented with loose stools and occasional stomach pains two years after the transplant, with subsequent endoscopy revealing the diagnosis.

Case Presentation

A 66-year-old man presented to clinic with an extensive past medical history including: B-cell CLL diagnosed in 2006, RAI Stage 0, with 13q deletion treated with multiple chemotherapy regimens; superficial transitional cell bladder carcinoma that was excised; and Intermediate II risk Myelodysplastic Syndrome (MDS) diagnosed in 2011 and believed to be related to the treatment of the patient's CLL. Cytogenetics of his MDS involved the translocation t (7:22) (q22; q14) and was classified as refractory anemia according to the French-British-American classification and Refractory Cytopenia with Multilineage Dysplasia (RCMD) according to the WHO classification. The patient was treated with six cycles of azactidine (Vidaza) for his MDS. He underwent chemotherapeutic conditioning with busulfan and fludarabine followed by a 10/10 HLA-matched unrelated donor hematopoietic stem cell transplant about 10 months after the initial diagnosis. Complications from the therapy included the development of veno-occlusive disease and Graft-Versus-Host Disease (GVHD) confirmed by liver biopsy despite GVHD prophylactic treatment with tacrolimus and sirolimus. Sirolimus was discontinued due to side effect of neutropenia, and budesonide and beclomethasone were added to the treatment regimen.

He presented to clinic for follow-up two years status post the allogenic stem cell transplant with complaints of loose stools occurring approximately four times daily despite use of loperamide once a day. The patient was without nausea or vomiting at the time but did note a "stomach ache". Review of systems was otherwise negative for signs of infection or other gastrointestinal symptoms. Vital signs were all within normal limits. Physical examination revealed a 66-year-old man appearing stated age, in no acute distress, without significant weight loss and with an abdomen that was non-tender, non-distended and having no palpable masses. Other than a port present on the right chest, there were no skin changes. Complete blood count at the time showed a normal white blood cell count of

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6.87 × 103 /uL, normal hemoglobin and hematocrit of 15.1 g/dL and 45.7% respectively, and slight thrombocytopenia of 121 × 103 /uL. Etiology of the diarrhea was thought to be either due to the GVHD or an infectious process. Infectious workup was negative, and the next step in management was to perform endoscopy.

Esophagogastrodudoenoscopy (EGD) showed patchy erythema in the gastric body and in the antrum with biopsies taken at these sites. Two biopsies were also taken from normal appearing distal duodenum for evaluation of GVHD. The pathology report described normal duodenal mucosa from the latter biopsies; however, the gastric biopsy showed a mononuclear infiltrate diffusely positive for CD43, CD34, and CD117 markers. The infiltrate appeared to expand the in to interstitial space with possible effacement of underlying architecture and was comprised of round, somewhat monotonous cells with fine chromatin and increased nuclear to cytoplasmic ratio. A prominent subset of the blasts expressed myeloperoxidase, confirming myeloid lineage. According to the pathology report, this was consistent with involvement of Acute Myeloid Leukemia (AML). Subsequent bone marrow biopsy was performed and was consistent with allogenic stem cell transplant with no evidence of residual or recurrent CLL. The patient was restarted on Vidaza and completed three cycles of treatment. EGD was repeated twice more, three and nine months after the original diagnosis, to assess for persistent disease of the stomach. Despite grossly improved appearance of the erythematous areas in gastric folds and in the antrum, pathology continued to show a CD34 and myeloperoxidase-positive mononuclear infiltrate consistent with granulocytic sarcoma.

On the most recent follow-up with the patient, repeat EGD confirmed granulocytic sarcoma in the gastric folds refractory to treatment with resolution of the gross appearance of the lesion. Repeat bone marrow biopsy was also negative for recurrent disease. The patient continues to have multiple symptoms likely due to underlying GVHD, including lack of appetite, fatigue, mild nausea, sclerosis of the skin, and dry eyes. The patient continues to take Vidaza for treatment.

Discussion

Myeloid Sarcoma (MS) is defined as a discrete mass of immature myeloid cells that presents at an extra-medullary site. The lineage of cells that makes up a particular phenotype of MS varies, but tends to be of myeloblastic or monocytic origin. Rarely are erythroblastic, megakaryocytic, or mature neutrophilic cells found in MS [4,8]. This disease can occur with AML, CML, MDS, or myeloproliferative disorders. The incidence of MS in patients with AML has been reported to be 2-8%, with the majority of cases presenting after the diagnosis of AML (50%), followed by appearance simultaneously with AML (15-35%), and appearance preceding AML (25%) [9]. Extramedullary disease in patients with CML blast disease has been reported to occur in 7-17% of cases [5]. One particular study that looked at the frequency of MS in non-leukemic *vs.* AML-associated vs. high-risk MDS over a 12 year span at MD Anderson Cancer Center found 5.2% of high-risk MDS patients to have MS [10]. In general, the appearance of MS portends a recurrence of bone marrow disease in AML or a blastic change in CML. Certain cytogenetics, such as the 8;21 translocation in AML-M2, have been associated with higher frequency of myeloid sarcoma [11].

The development of MS after allogeneic Hematopoietic Stem Cell Transplant (HSCT) is exceedingly rare and has been reported to be 0.2%-1.3% with poor overall survival [12-14]. Békássy, et al. describes a retrospective analysis of 5,824 patients from 1981 to 1992 who received bone marrow transplantation for AML, CML, or MDS. Of the CML/MDS subgroup, only six out of 2,753 grafted patients (0.22%) developed myeloid sarcoma [14]. Prognosis was poor for the total of 26 patients among all subgroups with MS post-bone marrow transplant in this study, with a 5-year survival of 33%. Szomor, et al. published an article one year after Békássy, et al. describing only three cases out of 229 that relapsed with myeloid sarcoma (1.3%). There was considerably long interval between bone marrow transplant and relapse with myeloid sarcoma in these three cases: 2, 6, and 13 years. Two of the cases involved tumors in the ovaries and one patient presented with disease in the CNS [13]. These sites are considered immunologic "sanctuaries" where malignancy can remain dormant and escape treatment, and thus appear as a relapse.

Yoshihara, et al. pooled data from nine studies that looked at extramedullary relapse after HSCT. They suggest that the incidence of relapse may be greater than that suggested by Békássy and Szomor. More recent studies have shown that extramedullary relapse of AML occurs in 5% to 12% of patients who receive allogenic stem cell transplant, accounting for 7% to 46% of total relapses. And review of the European Bone Marrow Transplant Registry database shows that incidence of relapse is higher in patients who underwent allogeneic versus autologous bone marrow transplant (11% *vs.* 6%; P=0.2) [15]. Others have noted that there exists a correlation found between chronic GVHD and extramedullary relapse, implicating that the expected graft-versus-leukemia effect in patients with chronic GVHD may maintain marrow remission without preventing extramedullary relapse [6,15].

The most common sites of involvement of MS include bone, periosteum, soft tissue, lymph node and skin, although the literature describes diverse locations of presentation from duodenal to vulvar presentations. In a study of 92 patients, Pileri, et al. found the most common site to be skin (28.2% of patients), followed by lymph nodes (16.3%), testes (6.5%), intestines (6.5%), bones (3.25%) and CNS (3.25%) [3]. Both Neiman, et al. and Antic, et al. who looked at 62 and 61 cases of myeloid sarcoma respectively, found similar rates of GI presentations of MS, about 7% [16,17]. Within the GI tract, the most common site of involvement is the small bowel, followed by colon, appendix, biliary tract, and stomach [18].

The presence of tumor cells outside the bone marrow suggests a change in the signaling pattern of the malignant cells that allows invasion of tissue and for extramedullary localization [9]. Immunohistochemical staining shows that the most commonly expressed markers are CD68/KP1 (100% of cases), followed by myeloperoxidase (83.6%) and CD117 (80.4%). Other common markers include CD99, CD68/PG-M1, CD34, terminal-deoxy-nucleotidyl-transferase, and CD56 [3]. The difficulty in the diagnosis of MS is in differentiating it from Hodgkin's lymphoma, large B cell lymphoma, and T cell lymphoma among others, due to the presence of B and T cell marker in certain cases. Establishing a myeloid lineage is then a critical step in diagnosing MS; myeloperoxidase and lysozyme are two critical markers for this purpose. In the rare cases where

these two markers fail, CD43 and CD68 can catch the remaining MS variants and usually place MS diagnosis on the differential [8].

In general there are three approaches to treatment of MS: systemic chemotherapy, bone marrow transplant, and radiotherapy. As with our patient, chemotherapy regimens tend to mirror those used to achieve complete remission in AML patients. However, previous studies have been performed which show that allogeneic HSCT, along with systemic chemotherapy, is superior to either one alone in the induction of complete remission of MS. Five year survival varies by study but has been reported from 21-25%, with mean survival ranging anywhere from 9-15 months [19]. Owing to the rarity of the disease, radiotherapy has not been effectively studied, nor has a standard chemotherapy regimen been devised [20]. It is generally agreed upon that systemic chemotherapy is needed to prevent progression to AML even in cases of isolated MS, although further systematic reviews are necessary to elucidate an algorithmic approach. Radiotherapy, a rarely studied modality, appears to be very effective locally. Per previous studies with GI involvement of MS, radiotherapy proved effective in local control of the tumor and inducing complete remission, while allogeneic HSCT provided long term "systemic" treatment to prevent future MS or progression to AML [21]. Further studies are also needed to assess the role of radiotherapy in the induction of remission or post-remission control of recurrence.

Myeloid sarcoma of the stomach is particularly rare given its location, and a relapse of hematologic disease with this tumor after chemotherapy and allogeneic HSCT for myelodysplasia is likely even more rare. Treatment protocols are not well established given the rarity of disease, and local therapy by surgical excision or radiotherapy has shown progression to systemic relapse [22]. Future therapies may include a combination of systemic and local treatments, but for now more studies need to be done. Prognosis remains poor in these patients, although it is slightly better than patients with bone marrow relapse [15]. Risk factors have yet to be fully elucidated, however our case suggests chronic GVHD may be a contributing factor.

References

1. Paydas S, Zorludemir S, Ergin M. Granulocytic sarcoma: 32 cases and review of the literature. Leukemia & lymphoma. 2006; 47: 2527-2541.
2. Campidelli C, Agostinelli C, Stitson R, Pileri SA. Myeloid sarcoma: extramedullary manifestation of myeloid disorders. American journal of clinical pathology. 2009; 132: 426-437.
3. Pileri SA, Ascani S, Cox MC, Campidelli C, Bacci F, Piccioli M, et al. Myeloid sarcoma: clinico-pathologic, phenotypic and cytogenetic analysis of 92 adult patients. Leukemia. 2007; 21: 340-350.
4. Huang XL, Tao J, Li JZ, Chen XL, Chen JN, Shao CK, et al. Gastric myeloid sarcoma without acute myeloblastic leukemia. World journal of gastroenterology. 2015; 21: 2242-2248.
5. Levy RA, Mardones MA, Burch MM, Krause JR. Myeloid sarcoma as the presenting symptom of chronic myelogenous leukemia blast crisis. Proceedings. 2014; 27: 246-249.
6. Nazer A, Al-Badawi I, Chebbo W, Chaudhri N, El-Gohary G. Myeloid sarcoma of the vulva post-bone marrow transplant presenting as isolated extramedullary relapse in a patient with acute myeloid leukemia. Hematology/oncology and stem cell therapy. 2012; 5: 118-121.
7. Narayan P, Murthy V, Su M, Woel R, Grossman IR, Chamberlain RS. Primary myeloid sarcoma masquerading as an obstructing duodenal carcinoma. Case reports in hematology. 2012; 2012: 490438.
8. Audouin J, Comperat E, Le Tourneau A, Camilleri-Broet S, Adida C, Molina T, et al. Myeloid sarcoma: clinical and morphologic criteria useful for diagnosis. International journal of surgical pathology. 2003; 11: 271-282.
9. Avni B, Koren-Michowitz M. Myeloid sarcoma: current approach and therapeutic options. Therapeutic advances in hematology. 2011; 2: 309-316.
10. Tsimberidou AM, Kantarjian HM, Estey E, Cortes JE, Verstovsek S, Faderl S, et al. Outcome in patients with nonleukemic granulocytic sarcoma treated with chemotherapy with or without radiotherapy. Leukemia. 2003; 17: 1100-1103.
11. Tallman MS, Hakimian D, Shaw JM, Lissner GS, Russell EJ, Variakojis D. Granulocytic sarcoma is associated with the 8;21 translocation in acute myeloid leukemia. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 1993; 11: 690-697.
12. Bakst RL, Tallman MS, Douer D, Yahalom J. How I treat extramedullary acute myeloid leukemia. Blood. 2011; 118: 3785-3793.
13. Szomor A, Passweg JR, Tichelli A, Hoffmann T, Speck B, Gratwohl A. Myeloid leukemia and myelodysplastic syndrome relapsing as granulocytic sarcoma (chloroma) after allogeneic bone marrow transplantation. Annals of hematology. 1997; 75: 239-241.
14. Bekassy AN, Hermans J, Gorin NC, Gratwohl A. Granulocytic sarcoma after allogeneic bone marrow transplantation: a retrospective European multicenter survey. Acute and Chronic Leukemia Working Parties of the European Group for Blood and Marrow Transplantation. Bone marrow transplantation. 1996; 17: 801-808.
15. Yoshihara S, Ando T, Ogawa H. Extramedullary relapse of acute myeloid leukemia after allogeneic hematopoietic stem cell transplantation: an easily overlooked but significant pattern of relapse. Biology of blood and marrow transplantation: journal of the American Society for Blood and Marrow Transplantation. 2012; 18: 1800-1807.
16. Neiman RS, Barcos M, Berard C, Bonner H, Mann R, Rydell RE, et al. Granulocytic sarcoma: a clinicopathologic study of 61 biopsied cases. Cancer. 1981; 48: 1426-1437.
17. Antic D, Elezovic I, Bogdanovic A, Vukovic NS, Pavlovic A, Jovanovic MP, et al. Isolated myeloid sarcoma of the gastrointestinal tract. Internal medicine (Tokyo, Japan). 2010; 49: 853-856.
18. Sekaran A, Darisetty S, Lakhtakia S, Ramchandani M, Reddy DN. Granulocytic Sarcoma of the Stomach Presenting as Dysphagia during Pregnancy. Case reports in gastrointestinal medicine. 2011; 2011: 627549.
19. Antic D, Elezovic I, Milic N, Suvajdzic N, Vidovic A, Perunicic M, et al. Is there a "gold" standard treatment for patients with isolated myeloid sarcoma? Biomedicine & Pharmacotherapy. 2013; 67: 72-77.
20. Yilmaz AF, Saydam G, Sahin F, Baran Y. Granulocytic sarcoma: a systematic review. American journal of blood research. 2013; 3: 265-270.
21. Yagi T, Ishikawa J, Takahashi M, Yamashita Y, Kusakabe S, Yoshinami T, et al. Successful treatment of duodenal myeloid sarcoma with allogeneic bone marrow transplantation and additional radiotherapy. Internal medicine (Tokyo, Japan). 2012; 51: 769-772.
22. Koc Y, Miller KB, Schenkein DP, Daoust P, Sprague K, Berkman E. Extramedullary tumors of myeloid blasts in adults as a pattern of relapse following allogeneic bone marrow transplantation. Cancer. 1999; 85: 608-615.

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