Relapse Acute Myeloid Leukemia after Allogeneic Stem Cell Transplantation with Rare Extramedullary Granulocytic Sarcomas

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22 years old lady

Admitted to the hospital with fatigue, whole body ache and pain.
- WBC: 51880/microlitre (51% lymphocytes, 44% LUC-large unstained cells)
- Hb: 9.9 g/dl
- Thrombocyte: 110000/microlitre
- LDH: 530 IU/L
- Sedimentation rate and CRP: Normal
- Other biochemical tests were within normal limits.
Flow cytometric analysis: 86 % blasts.
Diagnosed AML M0-M1 (24.11.2014)
Cytogenetic analysis: -7 chromosomal deletion
*High risk group
Peripheral blood smear: Dense atypical mononuclear cells.
26.11.2014 After 3+7 induction chemotherapy molecular analysis revealed refractory disease

26.12.2014-16.02.2015 After two FLAG-IDAs, morphologic analysis revealed complete remission-1 but MRD + (flow cytometric analysis: 3% blasts)
Because of the high risk disease (chromosome 7 deletion), previously diagnosed invasive fungal infection and severe mucositis and typhilitis, no more chemotherapy was given. Allogeneic transplantation, decreasing dosing of immunsuppressives at posttransplant third month and prophylactic DLI were planned.
27.02.2015 She had allogeneic stem cell transplantation from her full matched sibling (Bu12.8 Flu150 ATG30 TBI400/CsA-Mtx)

02.03.2015 Early complication: Mucositis

29.04.2015 At day 60, the patient was in complete remission 1 (CR1) and MRD negative.

12.05.2015 Acute Liver GVHD Gr2 (Bilirubine > 3mg/dl or enzyme 2-4xULN), Skin GVHD Gr1 (20% BSA with disease signs but no sclerotic features) had developed.

06.06.2015 At day 100 the patient was in CR1 and MRD negative.
27.08.2015 At day 180 the patient was MRD positive (2% blasts). By decreasing doses cyclosporin therapy was stopped.

18.09.2015 Azacytidin therapy was planned for six cycles. After the six cycle-therapy the patient was in complete remission and MRD was negative.
05.08.2016 Five months after the last azacytidin therapy (18 months posttransplantation), there were more than one masses in the right breast at physical examination.

There were lesions in right breast, gastric and pancreatic regions with increased FDG uptake at PET CT.
Interestingly, we did not see any symptoms of the involved organs in our patient.
Gastric endoscopic biopsy and right breast tru-cut biopsy resulted dense blastic cell infiltration, CD117 and CD34 positivity.

Bone marrow aspiration was normocellular.
20.08.2016 MEC chemotherapy was started.
20.09.2016 Bone marrow aspiration was evaluated as normal and MRD was negative. No granulocytic sarcomas were detected at PET CT, the patient was in complete remission.
27.09.2016 Donor lymphocyte infusion was applied.
• Complete blood count and blood biochemical tests were within normal limits
• PET-CT was reported as complete metabolic response.
• Bone marrow aspiration showed complete remission and MRD was negative.
Considering that the patient responded well and had a complete remission after the previous azacytidine therapy, azacytidine therapy (75 mg/m$^2$/day for 7 days, every month) was planned for six cycles. Our aim was to reduce the tumor burden and to induce the graft versus leukemia effect.
3.10.2016-27.03.2017 Azacytidin therapy was administered for six cycles. After the second cycle, second DLI was applied.

The patient is still in complete remission.
Granulocytic sarcoma, also called chloroma or extramedullary myeloblastoma, is a rare malignant hematologic tumor composed of immature myeloid cells at an extramedullary site.

It most often presents secondary to acute or chronic myeloid leukemia; however, it can also precede myeloid leukemia [1]

Granulocytic sarcomas are seen in regions where graft-versus-host effect is less visible after transplantation, this affects the multiplication of all the escaping tumor cells.
The most common sites of granulocytic sarcoma are the central nervous system, subcutaneous tissue and genitourinary system.

Less common sites include the bones, soft tissues of the head and neck, skin and breast.
The incidence of relapse of extramedullary AML following allogeneic stem cell transplantation varies from 0.8% to 10% [2-4].


Multiple factors that may contribute to extramedullary relapse after allogeneic stem cell transplantation have been suggested, including the disease status at the time of transplant, T-cell depletion of the cell graft, lack of GVHL and leukemia subtype.

However, to what extent each of these factors contribute is still in dispute, and further investigation is needed to determine the cause.
Pancreas involvement is rare. Simultaneous involvement of pancreas, stomach and breast has not been reported.

The first case report of the granulocytic sarcoma of the pancreas was submitted in December 2016.

Ishii, Akira MD; Kondo, Tadakazu MD, PhD; Oka, Tomomi MD; Nakamoto, Yuji MD, PhD; Takaori-Kondo, Akifumi MD, PhD (2016). Granulocytic sarcoma of the pancreas on 18F-FDG PET/CT: A case report. Medicine: - [Volume 95 - Issue 49 - p e5570](https://www.mdpi.com/2072-6694/95/49/e5570)
In patients with AML who develop granulocytic sarcoma, the prognosis is poor.

Symptoms associated with the involved organs can be seen.

Sometimes they can be isolated and they can be mixed with solid tumors. Granulocytic sarcomas must be kept in mind at the differential diagnosis.