LETTER TO THE EDITOR

Extramedullary relapse of acute myeloid leukemia in a surgical wound

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A 52-year-old woman diagnosed with Graves’ thyroiditis 2 years previously was evaluated for surgical management due to medical non-compliance and a reluctance to pursue radioiodine ablation. A routine complete blood count (CBC) was within normal limits. There was no history of head or neck irradiation, and her family history was unknown, as she was adopted. She denied any bleeding or bruising difficulties. Thyroid ultrasound revealed a slightly heterogeneous gland without discrete nodules. There was no abnormal cervical adenopathy. Total thyroidectomy was performed, with some difficulty achieving hemostasis after the specimen was removed from the field. She was discharged on the first postoperative day, but had to be seen in the office on postoperative day 2 because of a large ecchymotic area around the incision. The wound edges had also separated. Pathology findings were consistent with Graves’ disease without evidence of malignancy.

On postoperative day 4 she was readmitted to the hospital for ongoing bleeding and pain at her thyroid incision. On admission, her platelet count was 79 × 10^9/L and her white blood cell (WBC) count was 20.0 × 10^9/L. Her platelet count continued to decrease, and the Hematology and Oncology service was consulted. Peripheral smear showed 35% blasts. Based on this finding, an acute leukemia was suspected. A bone marrow biopsy performed on postoperative day 6 demonstrated 70% cellularity with 82% blasts.

Immunophenotyping by flow cytometry showed that blasts were positive for myeloperoxidase (MPO), CD33, CD15, CD36, CD64, and CD4 with minimal expression of CD14. Cytogenetic studies showed a karyotype 46,XX,i(8)(q10),der(22)t(8;22)(q13;q13) in 19 out of 20 metaphases. Based on the World Health Organization WHO classification of tumours of haematopoietic and lymphoid tissues, the patient was diagnosed with acute monoblastic leukemia. Induction chemotherapy was initiated with daunorubicin (60 mg/m^2/day, days 1–3) and cytarabine (100 mg/m^2/day, days 1–7). On day 14 after induction chemotherapy, her bone marrow biopsy showed a cellularity of 15% with 2% blasts. Two weeks later, the patient was discharged in a stable condition. However, 2 weeks after discharge, she presented with an enlarging neck mass. On physical examination, she had developed an infiltrating irregular mass in the subcutaneous tissue beneath the thyroidectomy incision, which was painful and tender to palpation (Figure 1, upper). Ultrasound examination showed it to be very heterogeneous and hypervascular.

A fine needle aspiration biopsy of the neck mass was performed. Morphologically, the cells resembled leukemic blasts. Immunohistochemistry showed positivity for CD45, CD15, CD4, and MPO. A computed tomography (CT) scan demonstrated a large anterior neck mass within the subcutaneous tissues, extending into the paratracheal space bilaterally without compression of the airways (Figure 1, lower). Prior to the procedure, her CBC was within normal limits, but in 48 h her white blood cell (WBC) count increased to 10.7 × 10^9/L with 18% blasts. A bone marrow biopsy showed 55% cellularity and 25% blasts. The immunophenotype of the leukemic cells was similar to the one previously described. She was admitted to the hospital and received reinduction chemotherapy consisting of...
mitoxantrone (6 mg/m²/day, days 1–6), etoposide (80 mg/m²/day, days 1–6), and cytarabine (1 g/m²/day, days 1–6). The leukemic infiltrate in her neck decreased in size, and a 14-day bone marrow biopsy showed a markedly decreased hematopoiesis with 5% cellularity. Due to her aggressive clinical course, she was referred for hematopoietic stem cell transplant (HSCT). Unfortunately, while undergoing the work-up for her HSCT, she developed seizures secondary to an intracranial hemorrhage and was found unresponsive at her home. Her CBC at the time of admission to the ICU was within normal limits. Due to her severe anoxic brain injury, her family decided to withdraw medical care and she was then transferred to an inpatient hospice facility, where she expired a few days later.

Acute myeloid leukemia (AML) is a clonal proliferation of malignant myeloid precursors in which the normal bone marrow maturation process is interrupted, leading to an accumulation of immature blast forms. Based on the French–American–British (FAB) classification system, this patient would have presented with the FAB M5 subtype of AML, which has been associated with a poor prognosis. However, in accordance with the WHO classification, this case was diagnosed with AML, not otherwise specified, acute monoblastic leukemia subtype [1]. Acute monoblastic leukemia accounts for less than 5% of all cases of AML, and is considered a rare disease by the Office of Rare Diseases of the National Institutes of Health since it affects fewer than 200,000 people in the United States. The prognosis of patients with this specific variant of AML is currently unknown [1]. The specific cytogenetic finding of complete or partial tetrasomy 8 (four or more copies), however, portends a worse outcome, with a survival reported between 6 and 8 months despite the use of anthracycline-based chemotherapy [2,3]. Tetrasomy 8 has rarely been reported in AML, but, when present, is usually the sole cytogenetic abnormality seen associated with monocytic variants [2–5]. Interestingly, leukemic cells carrying tetrasomy 8 have also shown a background of trisomy 8, suggesting a biological relationship (i.e., clonal evolution) [6]. Our patient had a partial tetrasomy 8, a much less common, but recurrent, finding than trisomy 8 in AML.

When leukemic cells develop as a solid tumor at extramedullary sites, they are called ‘granulocytic sarcoma.’ In 1853, these tumors were given the name...
of ‘chloroma,’ because of the greenish color imparted by the presence of MPO. Large retrospective studies note the incidence of granulocytic sarcoma in patients with AML to be approximately 3% [7], and occasionally these tumors may be the initial presentation of AML [8,9]. Monocytic variants of AML often develop extramedullary disease involving skin, gingiva, and central nervous system. Several factors play a role in the increased rate of extramedullary involvement seen in acute monoblastic leukemia. In an early study, Lichtmann and Weed showed that malignant monocytic cells had an increased adhesiveness, deformability, and motility, features that facilitate their exit from the circulation [10]. Additionally, leukemic blasts are usually in G0 phase, but they retain the ability of reentering the cell cycle in a favoring environment and probably survive for extended periods of time, independent from their ability to divide [11]. The mechanisms behind the monoblastic survival/divisional advantage are not fully elucidated, but likely rely on cytokine release as well as cell-to-cell interactions within the chloroma microenvironment. Furthermore, since there is evidence that although a bone marrow remission is achieved and skin or gum infiltrations do not completely disappear [12], one could theorize that therapeutic levels of chemotherapy are not achieved in these blast sanctuaries, facilitating extramedullary relapses.

Although there have been a few reports of granulocytic sarcomas arising at the exit sites of Hickman catheters in patients with myeloproliferative disorders [13] and irradiated skin in a patient with breast cancer [14], the development of a leukemic infiltrate within a surgical wound has not been previously described. Theoretically, areas with acute inflammation would allow an increased extravasation followed by interstitial trapping of leukemic monoblasts. Furthermore, the healing tissue may have provided a pertinent microenvironment in which endothelial dysfunction, tissue permeability, and angiogenic growth factors, among others, facilitate the survival and multiplication of leukemic blasts, allowing the formation of extramedullary leukemic infiltrates.

References