and CD25 [5].

Being an extremely sensitive method, FCM is useful in detecting neoplastic mast cells even with a low burden of the disease and expected to identify even those cases which do not fulfill the diagnostic criteria for SM [4]. It proved to be an important diagnostic tool in the present case as mast cells may be increased in many reactive conditions as well.

Conclusion

The diagnosis of SM requires a cognisance of this rare entity along with a high index of suspicion. It should be considered as one of the differential diagnoses in cases with massive splenomegaly especially when the usual causes have been excluded. The assessment of the immunophenotype of mast cells is helpful in establishing the diagnosis of SM. This case also highlights the role of FCM in identifying abnormal mast cells based on routinely available markers in laboratories performing leukemia FCM.

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Emergence of chronic myeloid leukemia following autologous stem cell transplantation in a young woman with multiple myeloma

TO THE EDITOR: We read with great interest the recent paper "A case of synchronous multiple myeloma and chronic myeloid leukemia" published by Lee *et al.* [1] and report here a similar case that further highlights the management challenges in such complex cases. A 39-year-old female presented with left hip pain 5 years ago and a plain film showed a large lytic lesion in the neck of the femur. Her complete blood count revealed a hemoglobin level of 12 g/dL, platelet count of 233×10^9/L and total white blood cell (WBC) count of 10.8×10^9/L with normal serum calcium and creatinine levels. A bone marrow biopsy showed 40% bone marrow plasma cells (Fig. 1), lambda chain levels were elevated at 2,760 mg/L with a free light chain ratio of 0.0004, resulting in a diagnosis of multiple myeloma (MM). She completed 6 cycles of cyclophosphamide, bortezomib and dexamethasone chemotherapy in conjunction with radiation therapy to the fracture site and received monthly bisphosphonate infusions. This was consolidated with a melphalan-conditioned autologous stem cell transplant. She did not receive maintenance lenalidomide therapy given a previous history of pulmonary embolism. Two and a half years following her initial diagnosis, despite a normal serum free light chain ratio, it was noted that she had a rising WBC count with a peak level of 40.2×10^9/L, and a platelet count of 204×10^9/L, neutrophil count of 32.2×10^9/L, monocyte count of 2.7×10^9/L and basophil count of 0.59×10^9/L. Molecular analysis of the peripheral blood did not identify a *JAK-2* mutation, however the *BCR-ABL* ratio, measured by real-time quantitative polymerase chain reaction, was elevated at 140.6%. Bone marrow (BM) sampling showed marked granulocytic hyperplasia without excess blasts consistent with chronic-phase chronic myeloid leukemia (CML) (Fig. 2). There was no increase in plasma cells and BM karyotype confirmed the presence of an abnormal clone that contained a translocation between the long arms of chromosomes 9 and 22 with breakpoints at 9q34 and 22q11.2. This *BCR-ABL* rearrangement was analyzed in 192 out of 200 cells and the results were consistent with CML. The patient initially commenced imatinib therapy at 400 mg daily, but at 6 months, her disease control was suboptimal with a *BCR-ABL* ratio of 23%. She subsequently started nilotinib 400 mg twice daily resulting in an improved molecular response with a most recent transcript ratio of 1.4%. Her most recent BM aspirate showed CML in morphological remission and her free light chain ratio remained normal in line with ongoing MM remission.

The co-diagnosis of MM and CML is a vanishing rare

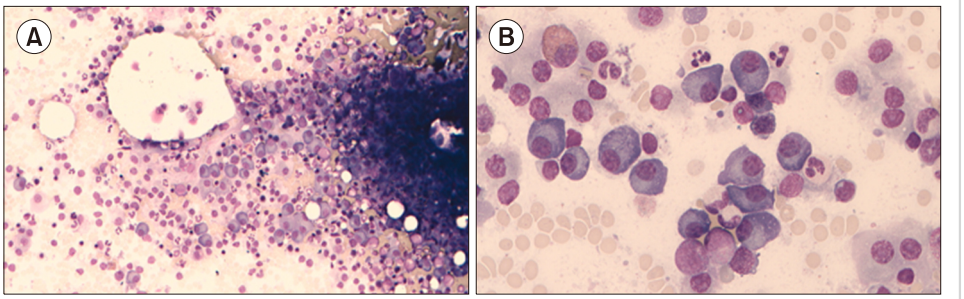

Fig. 1. Bone marrow at the time of multiple myeloma (MM) diagnosis. A hypercellular particle with atypical plasma cells under low power **(A)**. Numerous atypical plasma cells under high power **(B)**.

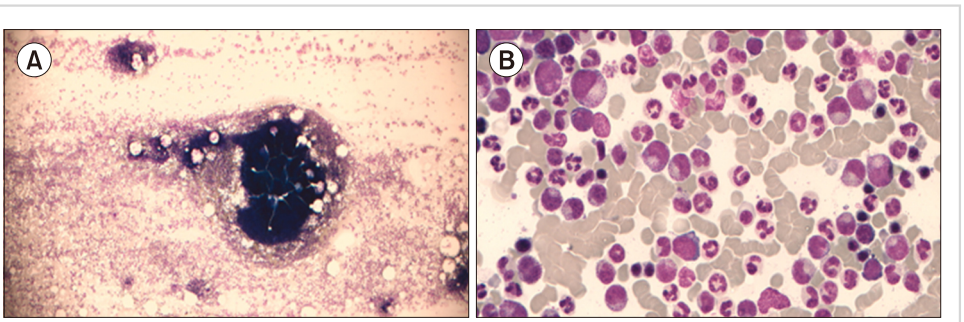

Fig. 2. Bone marrow at the time of chronic myeloid leukemia (CML) diagnosis. A hypercellular particle under low power **(A)**. A high-power view of granulocytic hyperplasia **(B)**.

phenomenon, with literature on this topic confined to case reports and small series. Clonal expansion in both the lymphoid and the myeloid cell lineages is implied as pathology of the disease. Possible hypotheses for this include the development of a common malignant pluripotent hematopoietic stem cell, treatment-related toxicity of myeloid cells and environmental factors [2]. To date, there have been 27 published reports of cases of co-diagnosis of MM and CML. Eight of these included patients who initially presented with MM and were subsequently diagnosed with CML, as in our case (Table 1) [3-10]. The mean time to CML diagnosis in this cohort was 30.6 months (4–53 mo), comparable to the 30 months till onset of CML in our case. Six of 8 patients were male, and the mean age of the cohort at first diagnosis was 63.3 years (47–77 yr). Therefore, our patient is the youngest recorded patient to have developed this disease. Additionally, of note, and to the best of our knowledge, there has been no other case described to date that developed CML following autologous stem cell transplant.

There are no evidence based-guidelines for the management of these patients. In 2 similar cases compared to our case, the use of imatinib led to stable remission of CML [3, 5], and in 1 other case treatment with the more recent tyrosine kinase inhibitor (TKI) dasatinib also led to remission [10]. Another report described an elderly male patient with relapsed MM who was diagnosed with CML at the time of relapse. His disease was controlled after 11 months of treatment with bortezomib, dexamethasone, and dasatinib before he died of pulmonary hypertension [4]. There are no reports thus far of a similar patient who underwent allogeneic stem cell transplantation.

Table 1. Reported cases of CML following MM diagnosis.

Reference	Gender	Age at first diagnosis (yr)	Time to onset of CML (mo)
1. MacSween *et al*. 1972	Male	77	33
2. Klenn *et al*. 1993	Male	71	24
3. Nitta *et al*. 1999	Male	70	33
4. Nakagawa *et al*. 2003	Male	47	33
5. Ragupathi *et al*. 2013	Female	62	17
6. Alsidawi *et al*. 2014	Male	60	48
7. Pessach *et al*. 2015	Male	68	53
8. Wolleschak *et al*. 2016	Female	51	4
9. Barrett *et al*. 2018	Female	39	30

Abbreviations: CML, chronic myeloid leukemia; MM, multiple myeloma.

In conclusion, we here reported the youngest patient diagnosed with CML following successful treatment of MM and the first patient who has developed CML following autologous stem cell transplantation. We also described the initial poor response to first-line TKI therapy with subsequent improved disease control after use of second-line therapy.

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Philadelphia-positive mixed phenotype acute leukemia presenting with *PML-RARα* fusion transcript without t(15;17) on cytogenetic studies

TO THE EDITOR: About 1–5% of the acute leukemias are not possible to assign a single lineage, which is designated as mixed phenotype acute leukemia (MPAL) [1, 2]. Promyelocytic leukemia (*PML*) and retinoid acid receptor α (*RARα*) fusion transcript is a product of translocation of chromosome 15 and 17, which is a hallmark of acute promyelocytic leukemia (APL). Cryptic or masked t(15;17) (q24;q21) in APL, which has morphological APL and *PML-RARα* fusion transcript but no t(15;17)(q24;q21) on routine cytogenetic analysis, has been noted [3]. The detection of t(15;17) in biphenotypic acute leukemia (BAL) with French-American-British (FAB) L2 morphology has been rarely reported, including one with *PML-RARα* fusion transcript [4] and the other without *PML-RARα* fusion transcript. However, by far, there is no report about the expression of *PML-RARα* fusion transcript in Philadelphia chromosome-positive (Ph+) MPAL patients.

A 37-year old female presented with a two-week history of neck and pelvic area pain, fever, and chills. On physical examination, the spleen was palpable 10 cm below the lower costal margin on the left mid-clavicular line. The liver and lymph nodes were not palpable.

Initial blood test revealed elevated white blood cell (WBC) count with blasts (WBC 287.520×10^9/L; segmented neutrophil 32%; metamyelocyte 2%; myelocyte 13%; eosinophil 2%; basophil 1%; blast 13%; Hb 9.6 g/dL; platelets 187×10^9/L). Prothrombin time (PT) and activated partial prothrombin time (aPTT) were in the normal range (PT 13.5 sec; aPTT 25.5 sec), and fibrinogen was slightly increased (467.5 mg/dL).

A bone marrow (BM) aspiration and biopsy showed markedly hypercellular marrow and increased blasts (about 23.8% of all nucleated cells) with predominantly lymphoblast morphology with scant cytoplasm without Auer rods (Fig. 1A). Special staining showed negativity to all of MPO, Sudan black B, and specific and nonspecific esterases and periodic acid-Schiff staining. On immunophenotyping, blast cells expressed myeloid (cytoplasmic MPO 54.58%, CD13 77.94%, CD33 75.4%), B-lymphoid (CD10 26.87%, CD19 83.94%), and stem cell markers (CD34 3.11%, CD71 53.7%). Chromosomal analysis by G-banding showed 46,XX,t(9;22)(q34;q11) in 23 cells among the 25 metaphase cells analyzed (Fig. 1B). The FISH signals from Vysis indicated abnormal *BCR/ABL1* fusions in 304 of 312 (97.4%) interphase nuclei examined (Fig. 1C), and the *PML-RARα* probe reported no fusion in 325 interphase nuclei examined (Fig. 1D). RT-PCR with a Hemavision kit showed a single *PML-RARα*