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The Cytologic Features of Chronic Myelogenous Leukemia and Its Lymphoid Blast Phase in Body Fluid
– A Case Report –

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Although chronic myelogenous leukemia (CML) may be involved in any part of the body, infiltration of the body fluid has rarely reported in the literature. Here we report on a 35 year-old male patient who was diagnosed chronic myelogenous leukemia ten years previously and he received allogenic hematopoietic stem cell transplantation. He then presented with left knee pain eight years after the initial diagnosis. MRI revealed a soft tissue mass at the distal femur. Cytology of the joint fluid revealed myeloblasts, promyelocytes, eosinophilic myelocytes, band neutrophils, megakaryocytes and orthochromatic erythroblasts, which was all consistent with leukemic infiltration of the knee joint fluid. The immunohistochemistry was positive for CD34, CD117 and myeloperoxidase (MPO). Despite that the patient underwent radiation therapy, MRI revealed growth of the mass, and ten months later, the lymphoid blast phase of CML was confirmed after biopsy. The patient received an above knee amputation. Five months later, multiple masses were revealed on PET-CT at the left iliopsoas muscle, abdominal wall and bones. Bilateral pleural effusion occurred shortly after this. Cytologic evaluation of the pleural fluid also revealed blast-like cells, and histologic evaluation of the abdominal mass confirmed the lymphoid blast phase of CML with positivity for CD3, UCHL-1, CD34 and CD117, but negativity for MPO.

Key Words : Chronic myelogenous leukemia; Lymphoid blast phase; Body fluid; Cytology

Chronic myelogenous leukemia (CML) is a myeloproliferative disease that originates from an abnormal pluripotent hematopoietic stem cell, and so this malady may be involved in any part of the body. However, its involvement in body fluids has rarely been reported.[1] We report here on a case of CML that involved the joint fluid with the associated histologic findings of the lymphoid blast phase of CML forming a knee joint mass, and the cytology showed the lymphoid blast phase of CML involving the pleural fluid.

CASE REPORT

A 35 year-old male patient was diagnosed with CML 10 years ago, and he then received allogenic hematopoietic stem cell transplantation. Eight years after the initial diagnosis, he presented with left knee pain. MRI revealed a 7.6×5.9 cm sized cauliflower-shaped signal intensity change of the bone marrow at the left distal femur. An anterolateral cortical break was noted and the mass lesion had extended to the prefemoral space. This lesion showed heterogenous signal intensity on both the T1 and T2 images, and it showed heterogeneous peripheral enhancement with gadolinium (Fig. 1).

Cytologic examination was performed on the joint fluid. The smears of the knee joint fluid were moderately cellular and they contained various types of small clustered or isolated cells. The backgrounds were clear without necrotic materials or blood. Some cells had a large round nucleus located at the center with a scant amount of cytoplasm without any granules. These cells were thought to be myeloblasts. A few cells were larger than the myeloblasts, and they had a slightly eccentric nucleus; their cytoplasm was more abundant compared to the myeloblasts and the cytoplasm contained granules. These cells were thought to be promyelocytes. Some cells were smaller than the promyelocytes, but they also showed slightly eccentric nucleus and a significant amount of cytoplasm. Some of these cells had eosinophilc gran-

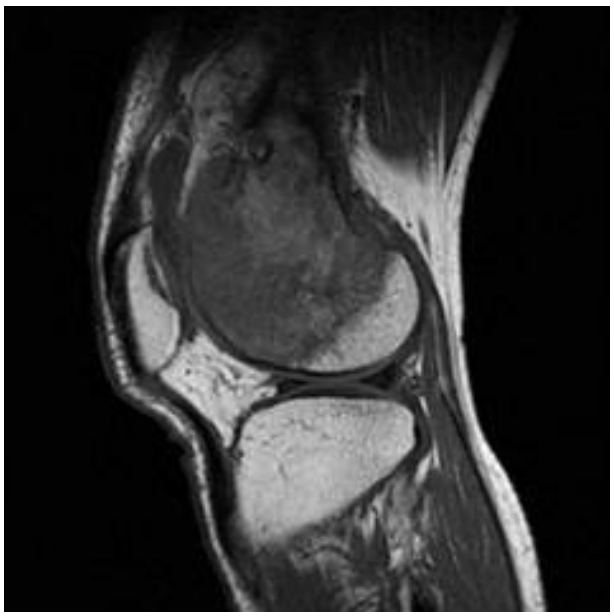

Fig. 1. Knee magnetic resonance image (MRI) revealed a 7.6×5.9 cm sized cauliflower shaped signal intensity change of the bone marrow at the left distal femur. An anterolateral cortical break is noted and the mass was extended to the prefemoral space.

ules in the cytoplasm, indicating these were eosinophilc myelocytes. Band neutrophils with a horseshoe shaped nucleus were also noted. Orthochromatic erythroblasts with an eccentric round condensed nucleus were also seen. There were a few multinucleated giant cells that could have been either megakaryocytes or osteoclasts when considering that the specimen had been obtained from the knee joint. Mature neutrophils and eosinophils were also seen (Fig. 2).

Immunohistochemical stains were performed on the cell block specimen of the joint fluid, and the suspicious hematopoietic precursor cells showed positivity for myeloperoxidase (MPO) and CD34. The multinucleated giant cells were positive for CD61 and they were also positive in periodic-acid-schiff (PAS) stain, which confirmed that the giant cells were megakaryocytes and not osteoclasts (Fig. 3) This confirmed the diagnosis of extramedullary relapse of CML. The bone marrow aspirate was unremarkable at this time period.

The patient received radiation therapy up to a total of 2000 cGy, but the mass did not respond, and the follow up MRI showed that the mass had grown from 7.6×5.9 cm to 17.0×8.6 cm.

Ten months later, biopsy was performed from the mass lesion of the left knee. On microscopic examination, the tumor cells were dyshesive and arranged in a sheet like pattern. The tumor cells had a round to oval nucleus located at the center of the cell with a modest to scanty amount of cytoplasm. The nucleoli were indistinct. These cells were thought to be myeloblasts. Mature lymphocytes were scattered within the mass (Fig. 4).

Immunohistochemical studies revealed that the tumor cells were positive for leukocyte common antigen (LCA), CD34, CD117 and UCHL-1, but they were negative for CD3, CD79a and myeloperoxidase (Fig. 4).

The peripheral blood smear, the bone marrow aspiration smear and the bone marrow biopsy specimens were all unremarkable. The extramedullary proliferation of blasts confirmed the blast phase of CML.

The patient underwent above the knee amputation surgery, and then the patient was stable for about five months. The follow up PET-CT revealed FDG uptakes at the left iliopsoas muscle, left femoral head, left proximal humerus, left anterior abdominal wall mass, scalp, C4 vertebra and the lymph nodes of the left external iliac chain, the paraaortic area and the abdominal wall. Bilateral pleural effusion was revealed on chest X-rays. Cytologic evaluation was performed of the pleural fluid with using the liquid-base cytology method.

The backgrounds were clear without necrotic materials or blood, and the specimen revealed clusters of cells with a large round nucleus located at the center and a modest amount of cytoplasm without any granules. These cells were thought to be blast cells. Some reactive lymphocytes and neutrophils were also scattered. Positive staining for CD34 confirmed the hematopoietic origin of these cells (Fig. 5).

Biopsy of the soft tissue nodule at the abdominal wall was also performed. The tumor cells were dyshesive and arranged in a sheet-like pattern in the dermis and subcutis. The tumor cells had a round to oval nucleus with moderate pleomorphism. The mitotic index was 12/10 HPF, and atypical mitoses were also observed. The cells had a coarse chromatin pattern, and some of the cells had a single nucleolus. These cells stained positive for LCA, CD34, CD117, CD3, and UCHL-1, and they were negative for MPO. The immunohistochemical results were suggestive of an extramedullary proliferation of the lymphoid blast phase. The peripheral blood smear, the bone marrow aspiration smear and the bone marrow biopsy specimens were all unremarkable.

The patient refused further evaluation or treatment and he was discharged.

DISCUSSION

In the CML-chronic phase, the leukemic cells are minimally invasive and their proliferation is largely confined to the hema-

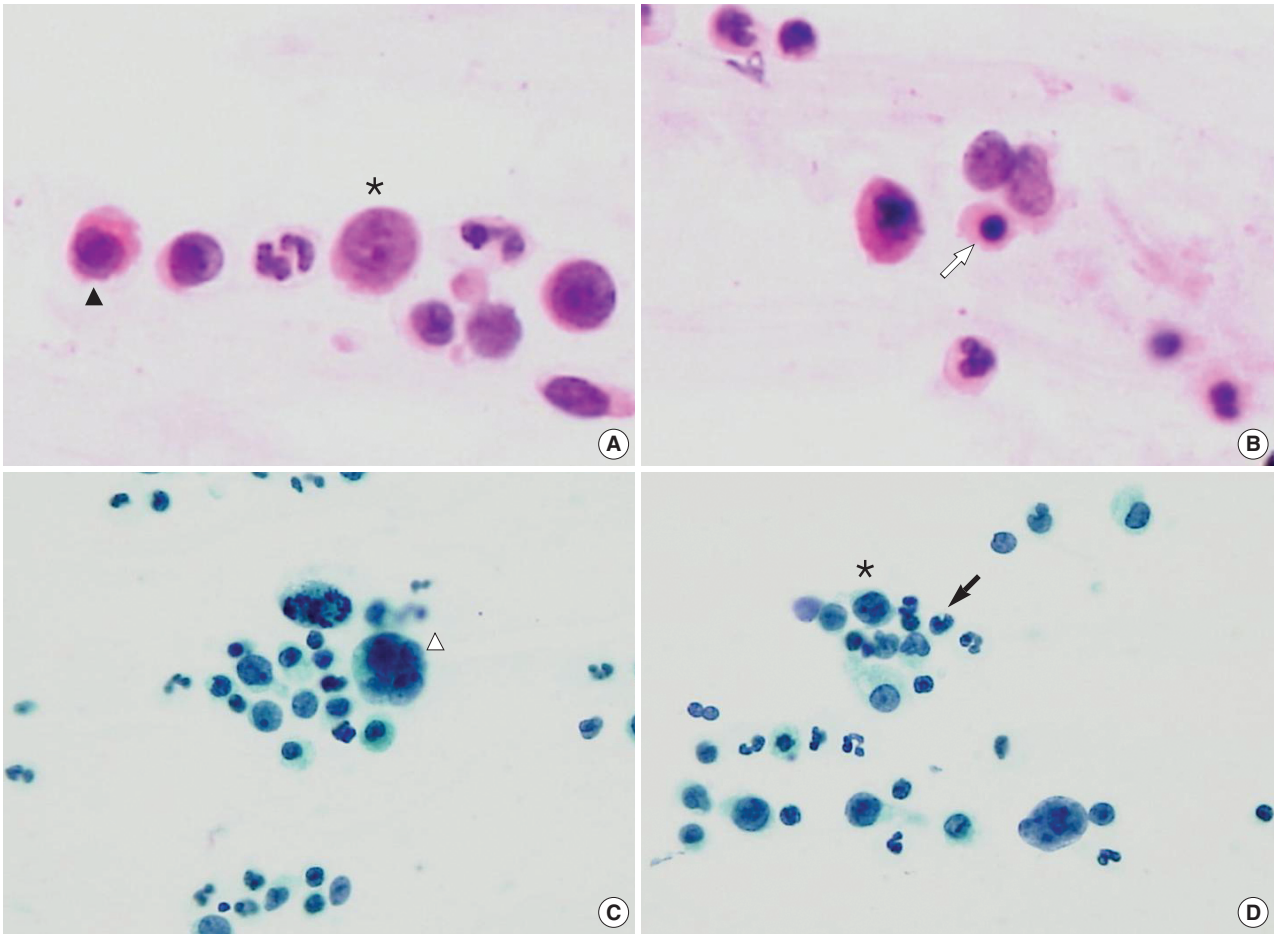

Fig. 2. Cytologic findings of the knee joint fluid. (A) Myeloblast with a large round nucleus located at the center without any granule and scant cytoplasm (*), and eosinophilic myelocytes with slightly eccentric nucleus and significant amount of cytoplasm containing eosinophilic granules (black arrowhead) is shown (H&E). (B) Orthochromatic erythroblast (white arrow) with an eccentric round condensed nucleus is noted (H&E). (C) Multinucleated giant cells (white arrowhead) which could be either megakaryocytes or osteoclasts. These cells were proven to be megakaryocytes later by positive staining for CD61 immunohistochemical stain (Papanicolaou). (D) Band neutrophil (black arrow) and myeloblast (*) were admixed with mature neutrophils (Papanicolaou).

topoietic tissues, and primarily the blood, bone marrow, spleen and liver.[1]

Serous effusions are a common complication of leukemias, but not all the effusions caused by leukemia contain neoplastic cells; such effusions may be a result of inflammation secondary to the neoplasm or to the neoplastic occlusion of vascular channels. All types of leukemia cells may be found in serous fluids, and the cells can be recognized according to the usual morphologic criteria featured in the atlases of hematology.[2] The cells may form loose aggregates. They have a variable appearance depending on the type of leukemia, but most of the cells have a primitive hematologic blast-like morphology, often with some degree of maturation along either the granulocytic or monocytic lines.[3]

The joint fluid cytology of this case revealed myelobasts, eosinophilic myelocytes, band neutrophils, orthochromatic erythroblasts and megakaryocytes that displayed various stages of multi-lineage differentiation and so this confirmed the diagnosis of extramedullary relapse of CML.

The most common site of extramedullary relapse are bones, followed by the head and neck area, the CNS and the skin/subcutaneous.[4] In this case, the primary site of extramedullary relapse was also thought to be the bone. The cortical break involving the anterior side of the distal femur must have enabled the leukemic infiltration of the joint fluid.

During the blast phase, not only the hematopoietic tissues, but also a number of extramedullary tissues that include the lymph nodes, skin, soft tissue and central nervous system may show infiltration of blasts. The diagnosis of the blast phase can be made if one or more of the following is present: 1) when the blasts make up more than 20% of the peripheral blood white cells or

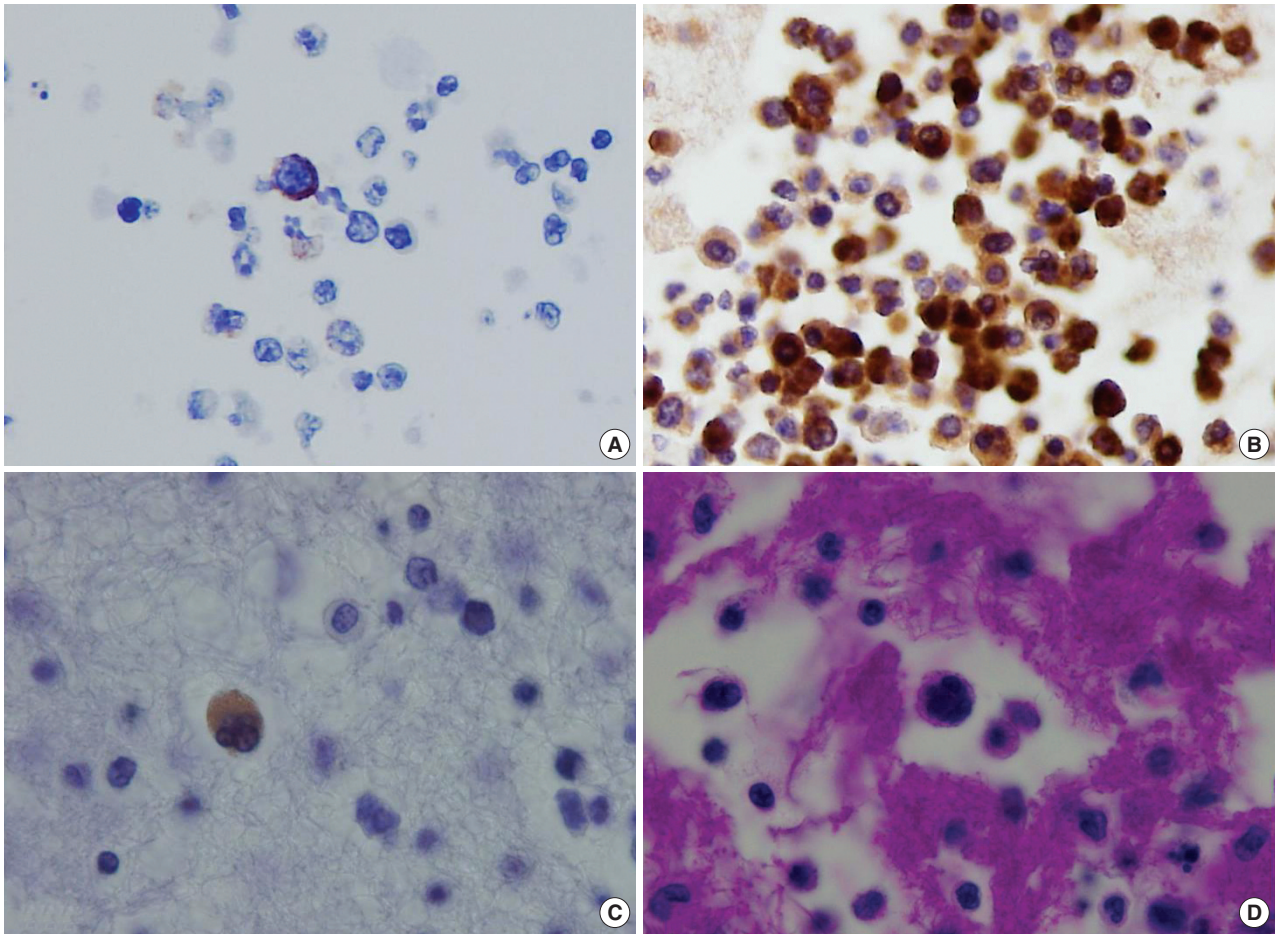

Fig. 3. Immunohistochemical stains and special stain with the cell block of the joint fluid. (A) The suspicious hematopoietic precursor cells showed positivity for CD34. (B) These cells showed strong positivity for myeloperoxidase. (C) The multinucleated giant cells were positive for CD61, which confirmed that the giant cells were megakaryocytes and not osteoclasts, and thus supports the diagnosis of leukemic infiltration of CML. (D) These cells were also positive in periodic-acid-schiff (PAS) stain, which also confirmed that the giant cells were megakaryocytes and not osteoclasts (PAS).

the nucleated cells in the bone marrow, 2) when there is an extramedullary proliferation of blasts and 3) when there are large aggregates and clusters of blasts in the bone marrow biopsy specimen.[1]

The present case had an extramedullary proliferation of blasts, and the blast cells displayed an interesting change of their immunohistochemical staining pattern during their transformation to the blast phase.

The joint fluid cytology revealed multi-lineage cells that were positive for CD34 and CD117, confirming that the cells originated from hematopoietic cells. Positivity for MPO was an indicator that these cells displayed a myeloid differentiation.

However, the biopsy obtained from the distal femur revealed that the mass was mainly composed of blasts and it had lost its various cellular components of different cell lineages and differentiations. The mass also displayed a change of immunohistochemical pattern. It had lost its positivity for MPO and it developed a new positivity for UCHL-1. This finding was suggestive of the blast phase of CML in the distal femur.

Five months later, another biopsy was performed on the abdominal soft tissue mass. This biopsy also shared characteristics of the previous biopsy, and the staining was negative for MPO and positive for UCHL-1. Interestingly, it had developed a new positivity for CD3.

It is widely accepted that the expression of MPO, which is a microbiocidal protein, is a golden marker to determine the myeloid hematopoietic lineage of immature blasts.[5] The blasts in this case had lost their positivity for MPO. The newly developed positivity for UCHL-1 and CD3 suggested that the blast phase in this case was a lymphoid blast phase.

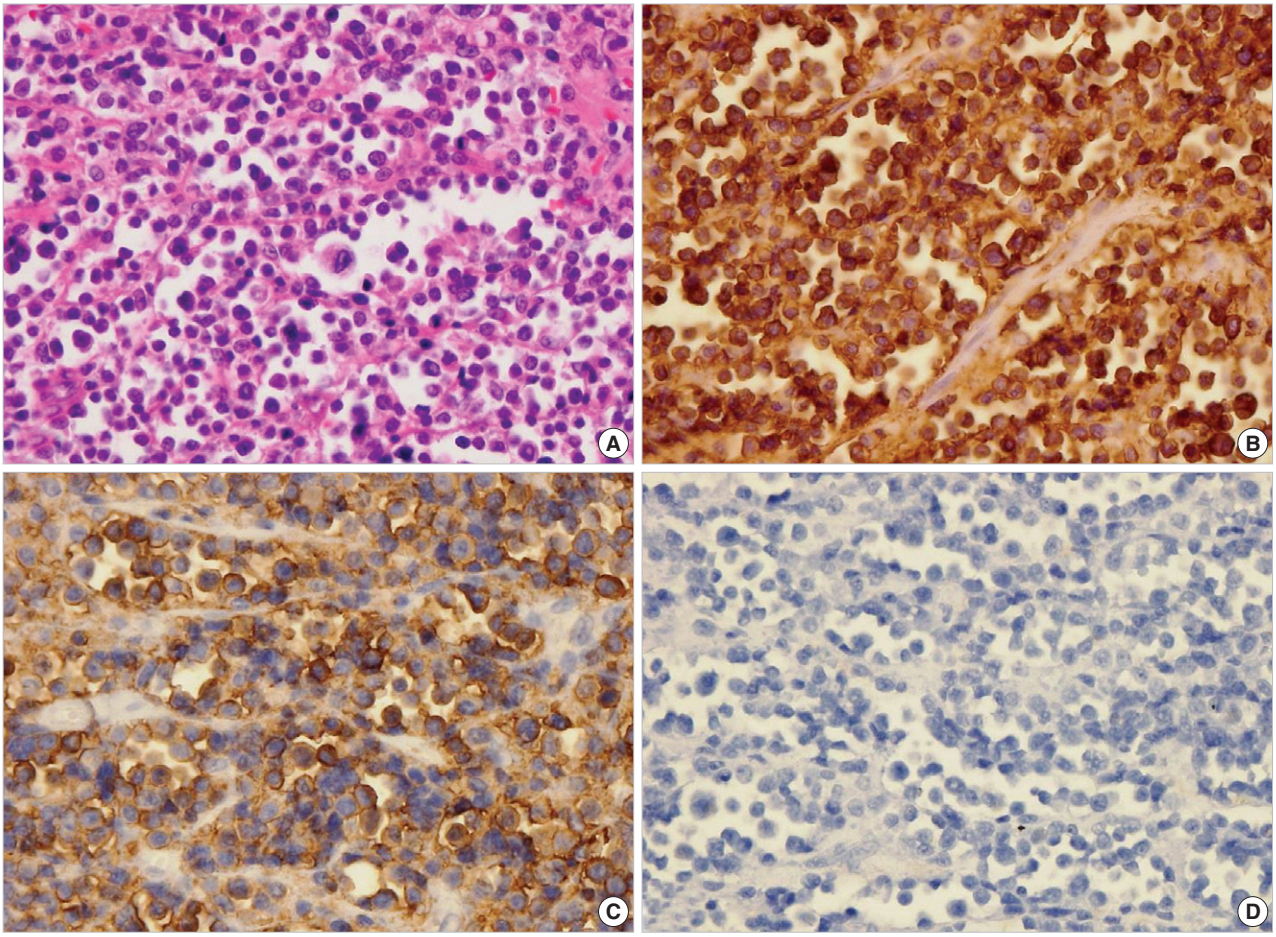

Fig. 4. Histologic findings of the distal femur mass. (A) The tumor cells were dyshesive and arranged in a sheet like pattern. It is mostly composed of myeloblasts with a round to oval nucleus located at the center of the cell with a modest to scant amount of cytoplasm (H&E). Immunohistochemical studies show the tumor cells were positive for CD34 (B) and UCHL-1 (C) but were negative for myeloperoxidase (D).

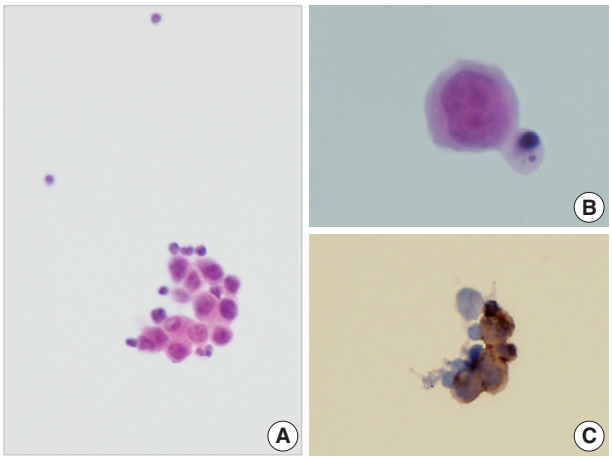

Fig. 5. Cytologic findings of the pleural fluid. (A) A Cluster of blasts admixed with a few scattered reactive lymphocytes (Papanicolaou). (B) A blast cell has a centrally located large round nucleus moderate amount of cytoplasm. It has two nucleoli (Papanicolaou). (C) Positive staining for CD34 confirmed the hematopoietic origin of these cells.

The pleural fluid cytology displayed mostly blasts and some scattered lymphocytes, and this was suggestive of the blast phase involvement of CML.

Leukemic infiltration that is seen on the body fluid cytology has been rarely described in literature, and this is easy to be neglected when analyzing a body fluid cytology specimen. This case revealed two types of CML involvement in the body fluid. The first type displayed the characteristic multi-lineage differentiation of the hematopoietic stem cells, and the immuhohistochemistry findings obtained from the cell block supported the diagnosis of chronic phase CML. The second type displayed mostly cells having a slightly enlarged round nucleus with a modest amount of cytoplasm with some scattered lymphocytes, and this indicated the blast phase of CML. The abrupt change of immunohistochemical staining indicating a lymphoid blast phase, and this was confirmed on the histologic evaluation.

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