INTRODUCTION

The incidence of second primary cancer following the first cancer increases progressively. Meta-analyses of several studies claim an incidence of 3-5% in second primary cancer, 0.5% in tertiary cancer and 0.3% in quaternary cancer. Probable underlying factors are persistence of environmental carcinogenic effect, genetic instability, use of systemic chemotherapy and radiotherapy, hormonal drugs, diagnostic radiological examinations, immune suppression, organ transplantation, and increased overall survival after the first tumour.

Here, we present a very rare case with variant hairy cell leukemia (HCL) occurring 2 years after papillary urothelial neoplasm of bladder. According to the search on PubMed database, association of bladder cancer with variant hairy cell leukemia was reported only once.

CASE REPORT

A 65 years old man was admitted with multiple lymphadenopathy, weight loss, night sweats and fatigue for 2 months. He had been treated for bladder cancer 2 years ago. Leukocyte count was 37.9 x 10\(^9\)/l. Peripheral blood smear had 91% lymphocytes. Lymphocytes had large nuclei with prominent nucleoli, heterogeneous appearance, and large cytoplasm with hairy projections. Flow cytometric immunophenotyping revealed CD20, CD22, CD24, CD45 and HLA-DR positivity. Atypical lymphocytes were stained with tartrate resistant acid phosphatase. Increased metabolic activity was detected in multiple lymph nodes, bone marrow and extremely enlarged spleen with positron emission tomography-computed tomography. Excisional biopsy of the left axillary lymph node revealed infiltration with diffuse B-cell leukemia/lymphoma. Immunohistochemistry showed CD20 positive atypical cells with weak expression of CD11c. The patient was diagnosed as a case of variant hairy cell leukemia and cladribine was administered. A probable second primary malignancy should be kept in mind in cases with a defined malignancy in the presence of unusual symptoms.

Key Words: Carcinoma, transitional cell. Leukemia, hairy cell. Neoplasms, second primary. Urinary bladder neoplasms.

ABSTRACT

A 65 years old man was admitted with multiple lymphadenopathy, weight loss, night sweats and fatigue for 2 months. He had been treated for bladder cancer 2 years ago. Leukocyte count was 37.9 x 10\(^9\)/l. Peripheral blood smear had 91% lymphocytes. Lymphocytes had large nuclei with prominent nucleoli, heterogeneous appearance, and large cytoplasm with hairy projections. Flow cytometric immunophenotyping revealed CD20, CD22, CD24, CD45 and HLA-DR positivity. Atypical lymphocytes were stained with tartrate resistant acid phosphatase. Increased metabolic activity was detected in multiple lymph nodes, bone marrow and extremely enlarged spleen with positron emission tomography-computed tomography. Excisional biopsy of the left axillary lymph node revealed infiltration with diffuse B-cell leukemia/lymphoma. Immunohistochemistry showed CD20 positive atypical cells with weak expression of CD11c. The patient was diagnosed as a case of variant hairy cell leukemia and cladribine was administered. A probable second primary malignancy should be kept in mind in cases with a defined malignancy in the presence of unusual symptoms.

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CASE REPORT

A 65 years old man was admitted with complaints of cervical, axillary and inguinal lymphadenopathy, weight loss, night sweats and fatigue for 2 months. He had bladder cancer (high grade papillary urothelial carcinoma) 2 years ago. Tumour had infiltrated the muscular tissue and partially had high-grade invasive non-papillary carcinoma nature. He had transurethral resection combined with four cycles of cisplatin and gemcitabine chemotherapy. Bilateral cervical, axillary and inguinal lymph nodes and moderate splenomegaly were detected on physical examination. Complete blood count revealed leukocyte count 37.9 x 10\(^9\)/l, red blood cell count 4.26 x 10\(^12\)/l, haemoglobin 13.1 g/dl, hematocrit 39.6%, mean corpuscular volume 93.0 fl, mean corpuscular haemoglobin 30.7 pg and platelet count 108 x 10\(^9\)/l. Peripheral blood smear had 91% lymphocytes, 8% neutrophils, and 1% monocytes. Lymphocytes had large nuclei with prominent nucleoli, heterogeneous appearance, and large cytoplasm with hairy projections. No basket cells were detected and platelets were normal with enough clumps. Morphology of the lymphocytes on peripheral blood smear resembled HCL or prolymphocytic leukemia; therefore, flow cytometric immunophenotyping was planned. Flow cytometric immunophenotyping revealed CD3 11.0%, CD4 6.3%, CD5 11.3%, CD7 9.2%, CD8 3.4%, CD10 0.5%, CD11c 0.3%, CD13 0.7%, CD19 0.8%, CD20 85.2%, CD22 82.7%, CD23 0.6%, CD24 84.3%, CD25 0.9%, CD33 3.8%, CD38 3.0%, CD34 0.9%, CD45 99.1%, CD103 0.3%, CD5 + CD19 + 0.1%, CD5+CD20 + 0.1%, CD13+HLA-DR + 1.0%, CD34 + HLA-DR + 0.6%, HLA-DR 86.1%, CD23 + HLA-DR + 1.0%, CD45 + CD38 + 3.0% and ZAP-70 7.4%. Atypical lymphocytes were stained with tartrate resistant acid phosphatase. Increased metabolic activity was detected in bilateral cervical, supraclavicular, axillary, inguinal and femoral, paratracheal, bilateral hilar, partially conglomerated lymph nodes, bone marrow and extremely large spleen with positron emission tomography-computed tomography scanning. Excisional biopsy of left axillary lymph node revealed "infiltration of
diffuse B-cell leukemia/lymphoma*. Immunohistochemistry showed CD20 positive atypical cells with weak expression of CD11c. Reactive cells were positive for CD5 and CD3. CD23, CD10 and cyclin-D1 were negative and Ki-67 proliferation index was 30%.

Based on clinical and laboratory findings, the patient was diagnosed as a case of variant HCL. The diagnosis was predicted the variant form HCL different from classical type because extreme leukocytosis, morphology of the lymphocytes had large nuclei with prominent nucleoli, positively staining with tartrate resistant acid phosphatase, and negativity of CD25 and CD103 antigens by flow cytometric immunophenotyping. Cladribine 0.1 mg/kg daily continuous intravenous infusion for 7 days was administered. The patient's signs and symptoms with laboratory values totally regressed 2 - 3 weeks after the completion of chemotherapy.

**DISCUSSION**

Urothelial carcinoma of the bladder (transitional cell carcinoma) is the most commonly seen cancer in the urinary tract. Cisplatin-based chemotherapy regimens increase the life expectancy in cases with advanced urothelial carcinoma. Recently, in patients with locally advanced or metastatic urothelial carcinoma, treating with gemcitabine/cisplatin combination is the common approach.3 This case that had locally advanced papillary urothelial carcinoma was also treated with the gemcitabine/cisplatin combination chemotherapy. Two years after completion of chemotherapy regimen, the primary tumour was still in remission.

HCL is an uncommon but distinct form of chronic B-cell lymphoproliferative disorder, comprising about 2% of lymphoid leukemias. The diagnosis of HCL usually is made by examining the morphologic features of the peripheral blood which shows irregular cytoplasmic extensions of leukemic cells. It is more common in elderly men. Pathogenesis of HCL is unknown but exposure to ionizing radiations, Epstein-Barr virus, organic chemicals, and employment in woodworking or farming are possible risk factors.4

Splenectomy, interferon, cytotoxic chemotherapy and purine analogs are the treatment options for symptomatic HCL patients.5 Purine analogs, cladribine and pentostatin are first line treatment options instead of splenectomy and interferon. Cladribine is the most commonly used one because of easy administration. Cladribine chemotherapy was preferred for this case.

The unique association of bladder cancer and HCL was reported by Paydas.6 Paydas implied the importance of exposure to chemicals (dye) for both HCL and urothelial cancers. This case was a farmer working in cheese production. There was no exposure to chemicals and ionizing radiation.

In conclusion, variant hairy cell leukemia following papillary urothelial neoplasm of bladder was diagnosed by careful evaluation of new symptoms. A probable second primary malignancy should be kept in mind in cases with a defined malignancy in the presence of unusual symptoms.

**REFERENCES**


