

Quiz

CORRECT ANSWER TO THE QUIZ. CHECK YOUR DIAGNOSIS

“DOUBLE TROUBLE” – SYNCHRONOUS MANTLE CELL LYMPHOMA AND METASTATIC SQUAMOUS CELL CARCINOMA IN AN INGUINAL LYMPH NODE

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Multiple primary neoplasms may also occur synchronously. Lymphoma may coexist with second malignant tumor in its primary location or malignant tumor may metastases to lymphomatous lymph nodes. Most often lymphoid component is a low grade lymphoma and coexistence of mantle cell lymphoma (MCL) and second malignant tumor is much rarer.

In this report, we describe a case of synchronous squamous cell carcinoma and mantle cell lymphoma coexisting in an enlarged inguinal lymph node. To the best of our knowledge, this is the second report of synchronous metastatic squamous cell carcinoma and MCL in a lymph node.

Key words: synchronous primary neoplasm, mantle cell lymphoma, metastatic squamous cell carcinoma.

Introduction

Infrequently, a patient may develop more than one neoplasm. It is well described for a variety of cancer predisposition syndromes including neurofibromatosis, Lynch syndrome, multiple endocrine neoplasia syndromes, and much more. However, several malignancy may occur in a person without precise genetic predisposition. In those cases environmental factors (e.g. ultraviolet light) or immunosuppression may trigger carcinogenesis [1]. The risk for developing a cancer is significantly increased by prior chemotherapy and radiation therapy, which may explain development of metachronous (diagnosed at greater than 6-month intervals) primary malignant tumors [2]. Multiple primary neoplasm may also occur synchronously, within a 6-month period and for some of them common possible causative agent may be sus-

pected e.g. *Helicobacter pylori* infection, which may lead to the development of primary lymphoma and adenocarcinoma of the stomach [3].

Among synchronous and metachronous multiple primary malignant tumours, melanomas and lymphomas are the most frequently encountered components. Lymphoma may coexist with second malignant tumor in its primary location (most commonly in the digestive tract, lung or skin) or malignant tumor may metastases to lymphomatous lymph nodes. Commonly, lymphoid component is a low grade lymphoma, primarily chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) [2]. Long lasting, indolent behavior of CLL/SLL accompanied by immunosuppression may predispose to the development of second malignant tumor [4]. Indeed, it was proven that presence of CLL/SLL constitutes a risk factor for developing another neoplasm in gen-

eral (risk increased three times), most significantly for skin cancers (risk increased eight times) [5]. Coexistence of mantle cell lymphoma and second malignant tumor is much rarer. Described in the literature cases include synchronous as well as metachronous MCL and primary cancers involving lung, breast and gastrointestinal tract [3, 6, 7, 8, 9, 10], chronic myeloid leukemia [11] and melanoma [12, 13].

In this report, we describe a case of synchronous squamous cell carcinoma and mantle cell lymphoma, which coexists in an enlarged inguinal lymph node. To the best of our knowledge, this is the second report of synchronous metastatic squamous cell carcinoma and MCL in a lymph node. In the first published report MCL involving cervical and mediastinal lymph nodes, which occurred synchronously with pulmonary squamous cell carcinoma with mediastinal lymph node metastases was described [14].

Case presentation

An 85-year-old male with anemia presented enlarged inguinal lymph node and was admitted to Institute of Hematology and Transfusion Medicine according to “fast tract” oncological diagnostics national program. In the excised lymph node an extensive metastasis of partially keratinising squamous cell carcinoma was detected (Fig. 1A). The periphery of the lymph node was occupied by diffuse infiltration from monotonous, small to medium-sized lymphoid cells characterized by scant cytoplasm, irregular nuclei and inconspicuous nucleoli (Fig. 1B). These cells presented B-cell markers i.a. CD20 and CD19 and co-expressed T-cell-associated antigen CD5 (weaker membrane reaction) (Fig. 2). Negative stains included CD23, CD43, CD10, BCL6, CD3. Positive cyclin D1 nuclear reaction (with variable intensity) confirmed the diagnosis of the classical mantle cell lymphoma (Fig. 2). In the trephine bone marrow biopsy

only isolated clusters of cells exhibited typical immunohistochemical reactions for MCL and allowed the minimal bone marrow involvement confirmation.

After time and thanks to the information obtained from the family we got a clue that patient has remained under urological control in Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology (MSCM CCIO). The medical history analysis revealed that 3 years ago the patient had distal penis resection with 5cm diameter tumor resection. The partially keratinising, invasive squamous cell carcinoma of penis, G3, pT2 was described (Fig. 3A). Before the inguinal lymph node investigation the patient was admitted to MSCM CCIO with sudden urinary retention with prostate cancer suspicion. The incidence repeated once again just after MCL detection and the transurethral resection of the prostate gland (TURP) was performed. The microscopic examination and immunohistochemical evaluation confirmed the mantle cell lymphoma infiltration of prostate gland (Fig. 3B-F).

Discussion

Majority of synchronous malignancies concern squamous cell carcinoma coexisting with low grade lymphoma, mainly CLL/SLL [1, 2]. Therefore, present case of squamous cell carcinoma and MCL in inguinal lymph node is unique. MCL component was classified as classic type with minimal bone marrow involvement. Our patient matches epidemiological and both morphological and immunohistochemical profile described below.

Generally, MCL is rare malignancy and considered as an aggressive disease with median overall survival of 4-5 years. It comprises about 3-6% of all non-Hodgkin lymphomas, with annual incidence of 0,5 per 100,000 population in Western countries. The disease affects mainly men, with male to female ratio

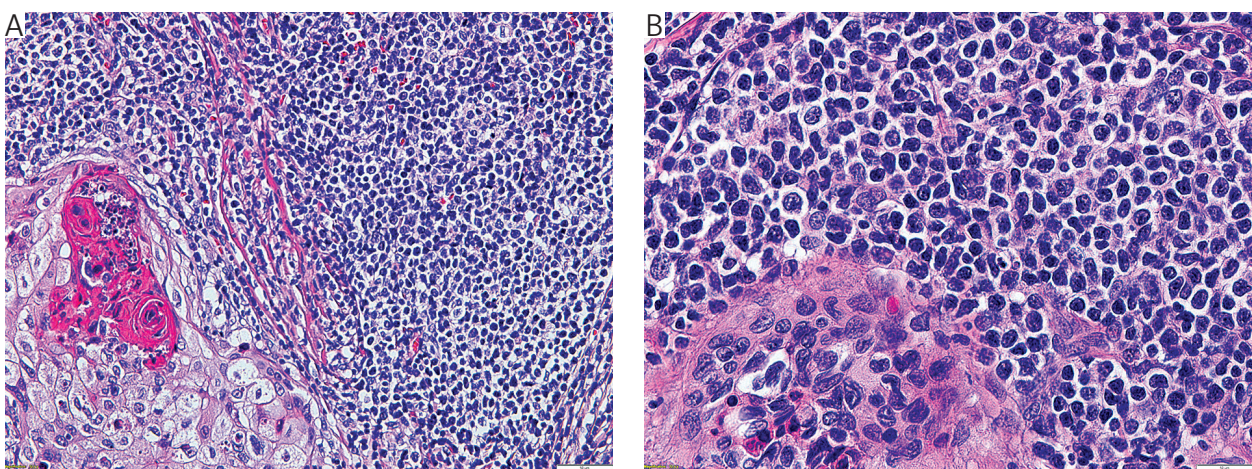


Fig. 1. Metastasis of partially keratinising squamous cell carcinoma coexisting with diffuse infiltration from mantle cell lymphoma, classical variant: A) HE, 20× magnification, B) HE, 40× magnification

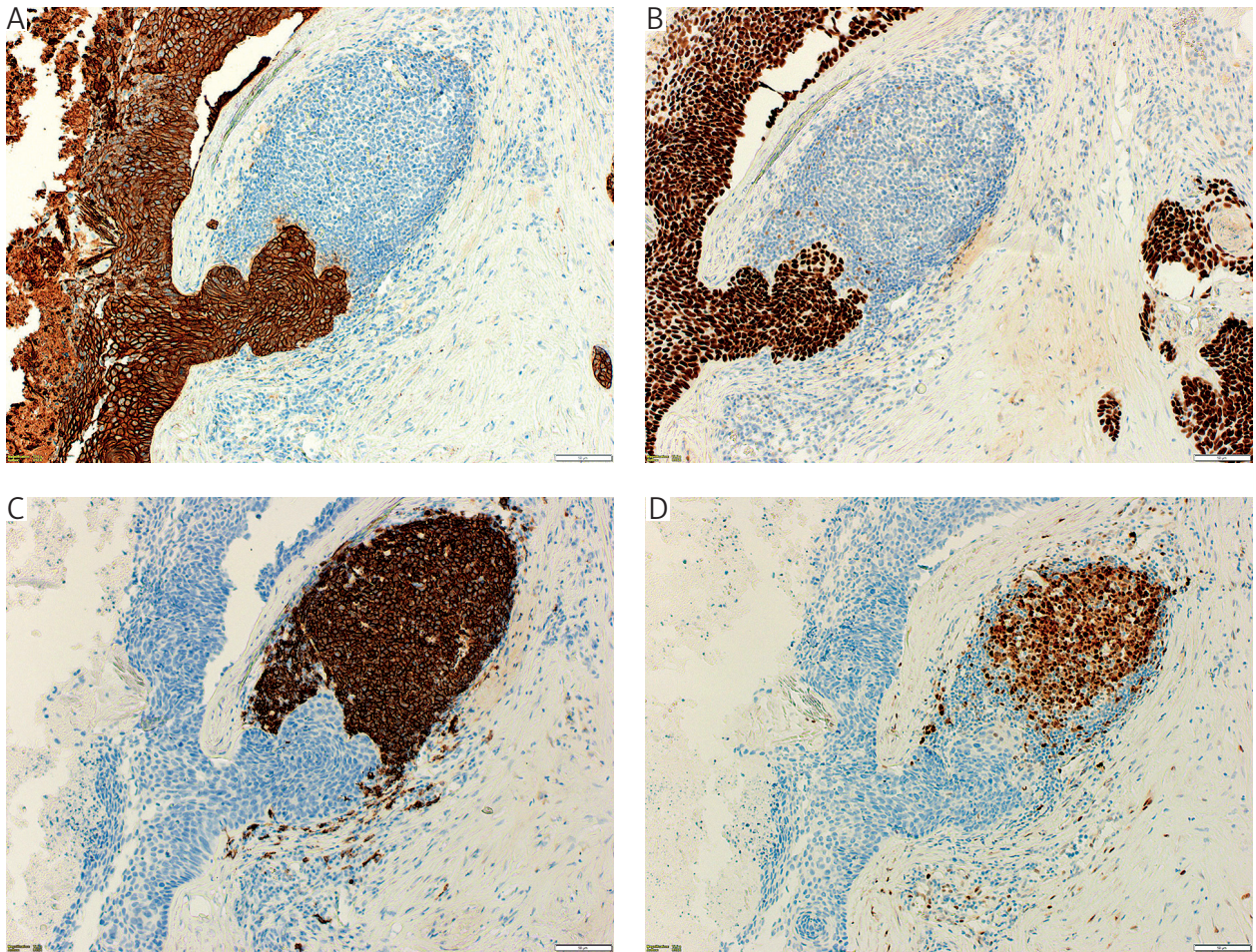


Fig. 2. Immunohistochemical evaluation of synchronous squamous cell carcinoma and mantle cell lymphoma, classical variant: A) CKAE1/AE3, 10× magnification, positive squamous cell carcinoma component, strong membrane reaction; B) p63, 10× magnification, positive squamous cell carcinoma component, strong nuclear reaction; C) CD20, 10× magnification, positive MCL component, strong membrane reaction; D) cyclin D1, 10× magnification, positive MCL component, strong nuclear reaction

being 2-3 : 1, and the median age at diagnosis equal 68 years. Typical presentation of MCL is generalized lymphadenopathy accompanied by splenomegaly as well as blood and bone marrow involvement. MCL may also occur extranodal including gastrointestinal tract, liver and Waldeyer's ring [15, 16]. The 2016 revision of the World Health Organization distinguish two types of MCL, which develop through distinct molecular pathways, both indolent but with potential for additional genetic changes and aggressive behavior. First (classic) type generally encompass lymph nodes and other extranodal sites and second is a leukemic non-nodal type with bone marrow, spleen and peripheral blood involvement [17]. Microscopically MCL infiltration consist of monotonous small to medium-sized cells characterized by irregular nuclei with condensed chromatin and inconspicuous nucleoli surrounded by scant, pale cytoplasm [18]. The molecular hallmark of MCL is t(11;14)(q13;q32) translocation, which results in relocation of *CCND1* gene close to the immunoglobulin heavy chain (*IGH*)

gene. The translocation leads to constant expression of *CCND1* protein which is one of the cell cycle regulators and its overexpression causes uncontrolled G1/S transition and cell cycle propagation [15]. Immunohistochemical detection of cyclin D1 (an intensive nuclear reaction) in lymphoma cells strongly favors diagnosis of MCL. Besides cyclin D1, MCL cells are positive for B cell markers including CD19, CD20, CD22, CD79a, as well as CD5 [18]. Classical MCL is SOX11 positive, whereas leukemic non-nodal type is usually SOX11 negative. Moreover, MCL cells do not express CD23, CD10 and BCL6 antigens.

In our case metastasis to lymph node was the first manifestation of the cancer of unknown primary site (CUP). It is estimated that 3-5% of all human cancers have a metastatic presentation without known primary site. The definition of CUPs include cases, where primary origin of tumour could not be detected by clinicians after standard diagnostic approach. In the USA statistics 7-12 cases of CUPs per 100 000 people are diagnosed each year and the age range at

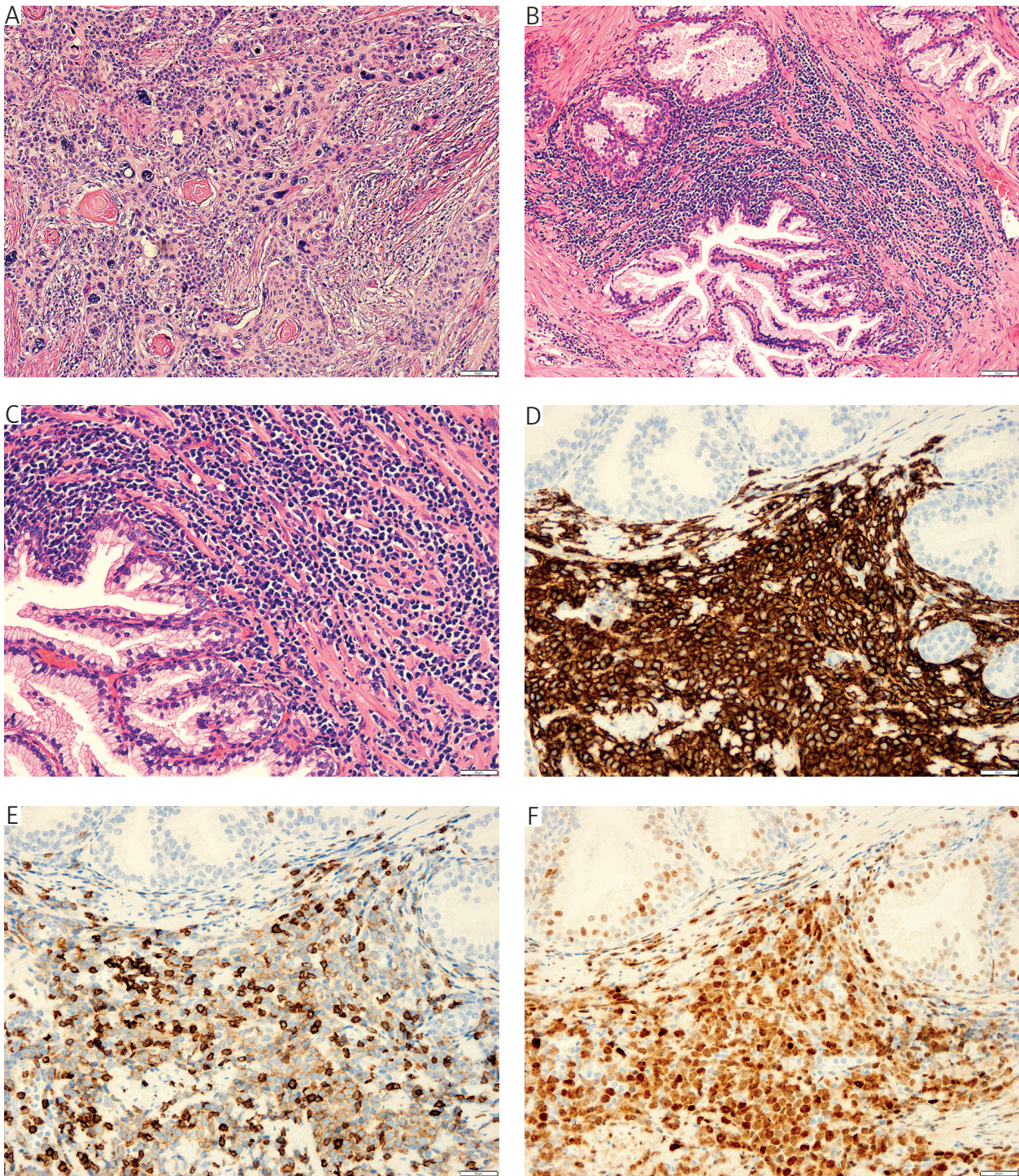


Fig. 3. Squamous cell carcinoma of penis and mantle cell lymphoma infiltration of prostate gland: A) HE, 20× magnification, squamous cell carcinoma of penis; B) HE, 10× magnification, MCL in prostate gland; C) HE, 20× magnification, MCL in prostate gland; D) CD20, 20× magnification, MCL in prostate gland; E) CD5, 20× magnification, MCL in prostate gland; F) cyclin D1, 20× magnification, MCL in prostate gland

the time of the diagnosis is 65-90 years. Most of the CUPs are carcinomas, predominantly adenocarcinoma (90%); squamous cell carcinoma and undifferentiated neoplasm are much rarer and their percentage does not exceed 5% [19]. Metastases of CUPs can be found in a variety of organs, mainly liver, lymph

nodes, peritoneal cavity, lungs or bones. Inguinal lymph nodes are relatively rare location of CUPs and are assessed to constitute 1-3.5% of all CUPs; among them, 10-15% of cases are diagnosed as squamous cell carcinoma [20]. Determination of the primary location of the squamous cell carcinoma with ingui-

nal lymph node metastases requires detailed clinical and endoscopic examination of anal, vulva, vagina, uterine cervix, penis and scrotum regions [19]. In our case squamous cell cancer of penis was previously identified nevertheless we did not obtain any information about prior medical history of this patient during diagnostic process. It is worth noting that having full access to clinical data greatly simplifies histopathological evaluation and is still one of the most important conditions determining the efficient and correct microscopic assessment.

In a lymph node with cancer metastasis diagnosis of lymphoma is especially difficult. Presence of metastasis may result in deterioration of normal lymph node architecture as well as cause significant reactive changes. What is more, in case of lymphadenopathy without prior history of lymphoid malignancy finding of metastatic cancer may lead to omission of discrete lymphoma infiltration. The additional immunohistochemical stains are obligatory to appropriate differential diagnosis. Therefore careful examination of architecture is still essential tool in every lymph node specimen.

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