Coincidence of chronic lymphocytic leukaemia with Merkel cell carcinoma: deletion of the RB1 gene in both tumors

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SUMMARY
The authors report a case of a 64-year-old man with chronic lymphocytic leukaemia (CLL) diagnosed 5 years ago. Recently, the patient was admitted with a tumour of the skin in the left lumbar region. Histological and immunohistochemical examinations established the diagnosis of Merkel cell carcinoma (MCC). Electron-microscopic examination revealed the formation of spherical aggregates of intermediate-sized filaments in the perinuclear region. The coincidence of MCC and CLL is rather rare and in published cases, no cytogenetic examinations were performed. We examined the RB1 gene using the interphase FISH method. A biallelic deletion in CLL tumour cells was detected; in MCC tumour cells, biallelic deletion was found in 33 % of the cells and monoallelic deletion in 57 % of the cells. In addition, chromosome 6 trisomy and 1p36 deletion were detected. Examination of non-neoplastic cells of the patient's skin showed a biallelic presence of the RB1 gene. According to the relevant literature, examination of the RB1 gene in CLL has informational value as a prognostic factor. The relationship between deletion of the RB1 gene and prognosis in MCC has not yet been determined and needs more research.

Keywords: Merkel cell carcinoma – chronic lymphocytic leukaemia – immunohistochemistry – RB1 gene

Koincidence chronické lymfatické leukémie a karcinomu z Merkelových buněk: delece RB1 genu v obou nádorech

SOUHRN
Autoři popsali případ 64-letého muže, u kterého byla zjištěna chronická lymfatické leukémie (CLL) před pěti lety. V současné době byl pacient přijat pro nádor kůže v lumbální oblasti vlevo. Histologické a imunohistologické vyšetření ukázalo, že jde o karcinom z Merkelových buněk (MCC). Elektronově mikroskopické vyšetření ukázalo charakteristické paranukleární globule tvořené intermediálními filamenty. Koincidence MCC a CLL je poměrně vzácná a cytogenetická vyšetření zde nebyla publikována. Vyšetřovali jsme RB1 gen pomocí interfázové FISH metody. Cytogenetické vyšetření RB1 genu ukázalo bialelickou deleci u nádorových buněk CLL; u MCC byla bialelická delece u 33 % a monoalelická delece u 57 % buněk. Současně byla prokázána trizomie 6 a delece 1p36. Vyšetření nenádorové kůže ukázalo přítomnost RB1 genu v obou alelách. Podle literárních údajů má vyšetření RB1 genu u CLL význam při stanovení prognózy onemocnění. Vztah mezi delecí RB1 genu a prognózou onemocnění nebyl dosud u MCC stanoven a vyžaduje vyšetření dalších případů.

Klíčová slova: karcinom z Merkelových buněk – chronická lymfatická leukémie – imunohistochemie – RB1 gen

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The coincidence of Merkel cell carcinoma (MCC) and chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL) was described in isolated cases (1–3). To distinguish the tumours, immunohistochemical or electron-microscopic examination is required in most cases. In cases where MCC occurs subsequently after the formation of CLL, it is necessary to eliminate the possibility of a transformation to lymphoma of a high grade of malignancy.

Cytogenetic examination of MCC reveals a deletion of the RB1 gene (location 13q14), trisomy 6 occurs in about 50 % of cases and distal deletion involving chromosome 1p35-36 is common; in CLL, 13q14 deletion is rather frequent as well (4,5). The goal of this study was to examine both tumours in histological, immunohistochemical and cytogenetic terms. The interphase FISH method was used to prove the presence of the tumour suppressor gene RB1.

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MATERIALS AND METHODS

In a 64-year-old patient, CLL was diagnosed 5 years ago by flow cytometry of peripheral blood – the lymphocytes were CD5 and CD19 positive. The disease did not progress, and the patient was followed in clinical conditions, but he was not treated (watch and wait management). Neither the lymph nodes, spleen nor liver were enlarged. During the examination, the number of lymphocytes in the peripheral blood was 47.2 x 10^9/L, erythrocytes 2.52 x 10^{12}/L,