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Case report/Kazuistyka

Extraneural relapse of medulloblastoma mimicking acute leukemia: A diagnostic challenge in adult patient

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ABSTRACT

Medulloblastoma is the most frequent malignant tumor of the central nervous system (CNS) in children, but it can rarely occur in adults. Extraneural relapse of medulloblastoma occurs very rarely and it is usually associated with dismal prognosis. We present a case of young adult with relapsed medulloblastoma with extraneural metastases in the bone marrow and expression of terminal deoxynucleotidyl transferase (TdT) on the malignant cells mimicking acute leukemia. To the best of our knowledge, this is the first report of medulloblastoma exhibiting expression of the TdT in adult. We would like to emphasize that in cases like this, differential diagnosis of anemia and thrombocytopenia in adults should include a consideration of primary or secondary bone marrow involvement by medulloblastoma or other rare malignancy.

Introduction

Medulloblastoma, an invasive embryonic tumor of cerebellum, is an infrequent primary malignancy of the central nervous system (CNS) in adults [1, 2]. While no clear etiology has been identified, a link may exist with maternal diet and blood or immune disorders during pregnancy, early John Cunningham polyomavirus infections in childhood, or human cytomegalovirus. The most common cytogenetic

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abnormality in medulloblastoma is i17q (isochromosome 17q), wherein the short arm (p) is absent, and there is a gain of genetic material from the long arm (q). The search for putative tumor suppressor genes on chromosome 17p in the context of medulloblastoma is ongoing [2].

Medulloblastoma presents with high invasive growth with spread of tumor cells into the leptomeningeal space along the neuroaxis early in the course of the disease [1]. It constitutes approximately 3% of primary CNS tumors [2]. Extraneural relapse of medulloblastoma occurs in 3–5% of patients and it is usually associated with dismal prognosis.

Here, we describe a case of young adult with relapsed medulloblastoma with extraneural metastases and expression of the terminal deoxynucleotidyl transferase (TdT) on the malignant cells mimicking acute leukemia.

Case presentation

A 19-year-old man was presented with headache and dizziness for one month. Magnetic resonance imaging (MRI) of the brain displayed a tumor in the right hemisphere of the cerebellum. The patient underwent surgical resection and histopathological diagnosis of medulloblastoma (WHO grade IV) was established. He then received adjuvant craniospinal radiation therapy with a boost to the posterior fossa.

One year later the patient complained of intense generalized bone pain. A positron emission tomography scanning showed a disseminated bone marrow and bone 18F-FDG uptake with SUVmax ranging from 3 to 8. Brain MRI revealed no signs of cancer relapse. The patient underwent preventive chemotherapy including carboplatin and etoposide.

Afterwards he developed prolonged anemia and thrombocytopenia. Bone marrow examination was performed and bone marrow cytology showed infiltrates with blast-resembling cells, mimicking morphologically low-differentiated acute leukemia and accounting for 92% of nucleated bone marrow cells (Fig. 1A).

However, flow cytometry of bone marrow showed that immunophenotype of the pathological cells was CD45(–), CD56(+), CD33(–), CD13(–), CD117(–), CD14(–), MPO(–), CD10(–), CD7(–), cytCD79α(–), and TdT(+) (Fig. 1B). Trephine biopsy revealed an extensive mass of cells positive for the

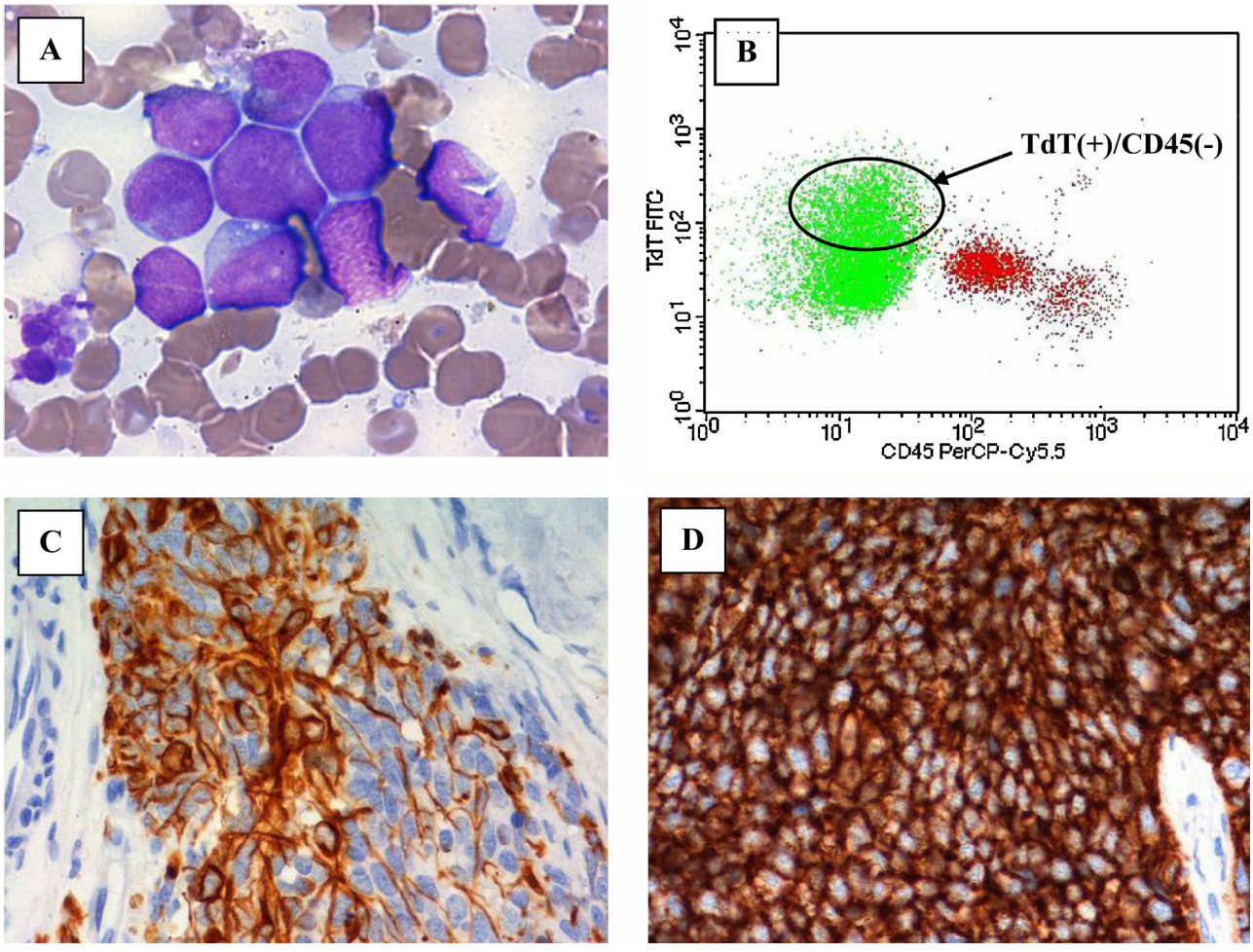

Fig. 1 – Medulloblastoma in the bone marrow: (A) bone marrow cytology. Large cells mimicking blasts with a high nuclear/cytoplasmic ratio, nucleus with a dispersed chromatin structure and prominent nucleoli (MGG stain, magnification 2000×); (B) flow cytometry result showing TdT(+)/CD45(−) cells (marked area); (C) trephine biopsy disclosing cells focally positive for GFAP stain (magnification 400×); (D) trephine biopsy showing cells strongly positive for CD56 stain (magnification 400×)

expression of vimentin, glial fibrillary acidic protein (GFAP) (Fig. 1C), neural cell adhesion molecule (CD56) (Fig. 1D), and neurone-specific enolase. These cells were negative with regard to myeloid and lymphoid antigens, cytokeratin, synaptophysin and chromogranin.

Metastases of medulloblastoma to the bone marrow were confirmed and the patient received a palliative chemotherapy with 3 courses of ICE (ifosfamide, carboplatin, etoposide). Unfortunately, he developed further metastases to lymph nodes, spleen and liver. The patient died 3 years after initial diagnosis of medulloblastoma.

Discussion

Medulloblastoma is the most common CNS tumor in children (15–30% of all primary CNS tumors in childhood), while it is extremely rare in adults [3]. The cerebellum and brain are common sites of metastases. The main sites of extraneural relapse are bones, bone marrow, lymph nodes, lungs, and liver (84%, 27%, 15%, 6%, 6% of cases, respectively). In adults, atypical metastatic sites are bones (80%) and lungs [2, 3].

Primitive neuroectodermal tumor can morphologically mimic acute leukemia [4]. In our patient, bone marrow cytology and histology revealed morphologically atypical cells resembling leukemic blasts. However, both immunophenotype and immunohistochemical examination were consistent with bone marrow involvement of relapsed medulloblastoma.

In the present report, the medulloblastoma cells showed expression of the precursor lymphoid antigen TdT in flow cytometry in the absence of other lymphoid and myeloid antigens. In the literature cases of medulloblastoma have been described that mimic acute leukemia and show the expression of myeloid antigens [4]. The expression of TdT has been described in non-hematopoietic malignancies such as Merkel carcinoma or pulmonary small cell carcinoma [5] and medulloblastoma in children [6]. To the best of our knowledge, this is the first report of medulloblastoma expressing the TdT in adult.

In cases like this, differential diagnosis of anemia and thrombocytopenia in adults should include a consideration of primary or secondary bone marrow involvement by medulloblastoma or other rare malignancy [4, 7]. Nevertheless, secondary acute leukemia or parallel occurrence of acute leukemia and medulloblastoma has also been reported [8–10]. In such cases, the results of flow cytometry, immunohistochemical staining, and sometimes genetic analyses are crucial in the process of establishing adequate diagnosis and treatment.

Authors' contributions/Wkład autorów

According to order.

Conflict of interest/Konflikt interesu

None declared.

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None declared.

Ethics/Etyka

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform Requirements for manuscripts submitted to Biomedical journals.

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