UNUSUAL MANIFESTATION OF MULTIPLE MYELOMA: FOCAL AFFECTION OF CENTRAL NERVOUS SYSTEM IN A PATIENT WITH CHRONIC LYMPHOCYTIC LEUKAEMIA

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Introduction: Involvement of the central nervous system as the first manifestation of multiple myeloma is very rare.

Aim: To present an unusual case of the primomanifestation of a multiple myeloma in the form of a focal affection of the central nervous system in a patient with chronic lymphocytic leukaemia.

Methods and results: A female patient diagnosed with chronic B-lymphocytic leukaemia with gradually increasing right-sided cerebellar symptomatology. The CT examination revealed expansion of the cranial vault with significant compression of brain structures. The tumour was extirpated and the histological examination led to a diagnosis of a plasmocytic myeloma. A thorough examination confirmed the diagnosis of multiple myeloma with significant osteolytic involvement of the skeleton. A combined chemo- and radiotherapy resulted in adjustment in the focal neurological finding, and a partial remission of the multiple myeloma was achieved.

Conclusion: The above presented case describes two very unusual states: the primomanifestation of a multiple myeloma in form of a focal affection of the central nervous system, and the coincidence of a multiple myeloma as the second haematological malignancy in a patient with chronic B-lymphocytic leukaemia.

INTRODUCTION

Multiple myeloma is a malignant hematologic disease belonging to the group of monoclonal gammopathies. Its incidence ranges from around 4–6 cases per 100,000 citizens/year with the predominant occurrence at a higher age. Multiple myeloma is characterised by proliferation and accumulation of clones of neoplastically transformed plasmocytes which produce molecules of monoclonal immunoglobulin detectable in serum and/or urine.

In addition to anaemia, hypercalcaemia, involvement of kidneys, and immunodeficiency, typical signs of the disease include various symptoms of the skeleton, while a first symptom of the central nervous system is extremely rare^{1,2}.

CASE DESCRIPTION

A 78-year-old female patient, observed for 5 years with chronic B-lymphocytic leukaemia (Immunophenotype CD 19+, CD20+, CD23+, CD5+) but without high-risk genetic modifications (with no deletion of ATM gene, p53, RB1, with no chromosome 12 trisomy) in the initial stage

(Binet A) with a therapeutic strategy of 'watch and wait', was examined over 3-months for gradually progressive vertigo with nausea, walking instability, and cephalgia. The objective neurological finding was dominated by a central right-sided reflexological accentuation, pallescerebellar and mild right-sided neocerebellar syndrome. Imaging methods (Computed tomography, Magnetic resonance imaging) revealed an expansion of the cranial vault 85 x 33 x 75 mm, showing characteristic signs – affinity of the tumour for the scleromeninx with intra- as well as extradural portion, and with extensive bone destruction (Fig. 1). Regarding the stealthy course of the disease, the patient was indicated for radical intervention under the diagnosis of meningeoma. The execution of the operation was difficult due to great blood loss, and penetration into the sinus transversus as well as sinus sagitalis did not allow for as radical an intervention as planned. The peri-operational and subsequent histological examination of the extirpated tissue revealed an infiltrate of mixtures of polymorphic plasmocytes with numerous precursor forms of plasmablast-appearance with expression of CD 138, CD79a, and light chains of the κ -type, while CD 20 and CD 56 markers were negative. The conclusion of the finding was thus a plasmocytic myeloma.

Fig. 1. Magnetic resonance image of the cranial vault, FLAIR sequence – temporooccipital expansion on the right with extra- as well as intra-cranial propagation, skeleton destruction, compression of the occipital and temporal lobes.

Fig. 2. An X-ray image of the skull after tumour extirpation, multiple osteolytic lesion of the cranial vault.

Fig. 3. Magnetic resonance image of the cranial vault, FLAIR sequence. Tumour residua after extirpation in the area of the right cerebellar hemisphere and the base of the right pyramid.

A detailed examination revealed an extensive lymphocytosis $38 \times 10^9/l$ in the peripheral blood image, without anaemia or thrombocytopenia. The immunophenotypisation of B-lymphocytes was positive for CD 19+, CD20+, CD23+ and CD5+ which belongs to the image of a chronic lymphocytic leukaemia. A bone marrow examination confirmed the image of the chronic lymphocytic leukaemia with a massive infiltration of the bone marrow by lymphocytes (44%), however, with a focal nest-like infiltration of atypical monoclonal plasmocytes with the expression of CD 138, and positive light chains of the kappa type, present in an amount exceeding 10%. Cytogenetic examination proved deletions in the area of 13q14. The serum revealed a small gradient of a monoclonal IgA kappa immunoglobulin (3.95 g/l), the examination of free light chains in the serum (Freelite™, The Binding Site) determined normal levels, including the index of κ/λ clonality. Also a higher level of β_2 microglobuline was indicated – 4.36 mg/l. Radiographic examination of the axial skeleton and the whole-body magnetic resonance imaging (WB-MRI) revealed a multiple osteolytic lesion in the area of the skull (Fig. 2), the skeleton of both glenohumeral joints, both femurs and in the area of both ischia of the pelvis. An asymptomatic compression fracture of the second lumbar vertebral body was also diagnosed. Densitometric examination of the skeleton (DEXA) confirmed a decline in bone matter in the zone of osteoporosis in the lumbar spine area (T-score -2.6); the findings of the whole-body examination corresponded to osteopenia. ^{99m}Tc -MIBI (methoxy-isobutyl-isonitrile) scintigraphic examination detected a mixed focal and diffuse activity, including 2 foci in the area of the cranial vault – viable re-

sidua in the area of the original extramedullar propagation of the tumour. The funding thus complied with the SWOG as well as IMWG criteria of a symptomatic IgA kappa multiple myeloma, IIA stage according to Durie-Salmon, II stage according to ISS (International Staging System). Therefore, chemotherapy was commenced in the CTD 'senior' regime (Cyclophosphamide 50 mg daily p.o., Thalidomide 100 mg daily p.o., Dexamethazone 20 mg p.o. always on the 1st, 8th, 15th and 22nd day of a 28-day cycle), due to a number of comorbidities (diabetes mellitus, ischemic heart disease) in the 'low-dose' dexamethazone modification, with the aim of therapeutically influencing the simultaneous chronic lymphocytic leukaemia, as well. The patient has received 5 cycles of chemotherapy which have resulted in partial remission of the myeloma shown by the disappearance of paraprotein by electrophoretic examination of serum (but with positive values by immunofixation electrophoresis), and with a significant decline in lymphocytes in the peripheral blood from the original $38 \times 10^9/l$ to $3.5 \times 10^9/l$. On the basis of the residual findings by the follow-up magnetic resonance of the cranial vault (Fig. 3), the treatment was complemented by focal radiotherapy of the cranial vault (30 Gy) with the aim of suppressing the residual extramedullar masses. The follow-up neurologic examination revealed complete resolution to the clinic findings, and the patient was referred to the outpatient care in a very good clinical state.

DISCUSSION

The presented observation describes a rare coincidence of two chronic B-lymphocytic neoplastic states – the chronic B-lymphocytic leukaemia, and the multiple myeloma diagnosed 5 years later and which manifested in the form of a focus in the central nervous system and which complied with the IMWG criteria for multiple myeloma. The simultaneous occurrence of a multiple myeloma and another myeloid or lymphoid malignancy is rather rare, and it is mostly discovered only several years after intensive chemotherapy or radiotherapy treatment of the primary neoplasia³⁻⁶.

In our observation, the present multiple myeloma and the chronic B-lymphocytic leukaemia represent neoplasias arising at different maturity stages of the B-lymphocytic elements within the natural occurrence, without previous therapy, suggesting the possibility of a natural maturity and transformation of part of the tumorous clone right into the plasma cell line. This has been referred by other studies based on cytogenetic and molecular analysis, as well⁷⁻⁸.

The invasion of the central system by the multiple myeloma in the form of a leptomeningeal myelomatosis, an extramedullar propagation, or more rarely an intracerebral expansion, are frequently related to a less differentiated cellular morphology, frequently of the plasmablastic type, with a high-risk genetic profile, and also intensive previous therapy; the further course of the disease in these patients is usually very complicated and difficult

to improve therapeutically⁹⁻¹¹. In our observation, the primomanifestation of multiple myeloma in form of a focal neurologic symptoms allowed effective treatment of the disease, i.e. it combined surgical intervention, focal actinotherapy and systemic chemotherapy with thalidomide. This resulted in adjustment of the clinical condition, and improvement of all key characteristics of both B-lymphoproliferative states. It is worth mentioning that not only the myeloma reacted favourably to the comprehensive chemo-radiotherapy following the operative intervention, but also the hematologic indicators of chronic lymphocytic leukaemia significantly improved, as shown by the considerable decline in the number of lymphocytes in the bone marrow as well as by the normalisation of the number of lymphocytes in the peripheral blood.

As this case reveals, the long term treatment of patients with chronic lymphocytic leukaemia may involve not only the natural progression of the primary disease but also the relatively frequent occurrence of duplicate neoplastic states including multiple myeloma.

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