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Case Report

IgD-λ multiple myeloma accompanying with elevated AFP level: a case report and literature review

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Abstract: Elevated blood Alpha-fetoprotein (AFP) level is of great significance to the diagnose of hepatocellular carcinoma (HCC) or embryonic tumor of the genital gland. However, no multiple myeloma (MM) case accompanying with elevated AFP Level has so far been reported. In this study, we reported a 66-year-old male patient who consulted in the Hematology Department due to repeated back pain for six months. The patient was diagnosed with IgD-λ light chain MM (Stage III B). The patient was then administered PD (bortezomib + dexamethasone), TCD (thalidomide + cyclophosphamide + dexamethasone), TAD (thalidomide + epirubicin + dexamethasone) and BDT (bendamustine + dexamethasone + thalidomide) regimens. His AFP level was progressively elevated, with the highest value of 578.80 μg/L. Meanwhile, space-occupying lesion was found in his liver, which was confirmed as plasmablastic neoplasm of the liver through liver biopsy. Moreover, a large amount of pleural effusion was found in his left chest after receiving BDT regimen again, which showed monoclonal plasma proliferation. Finally, the patient died of disease progression.

Keywords: IgD-λ, multiple myeloma, alpha-fetoprotein

Introduction

Alpha-fetoprotein (AFP) is an embryo protein mainly produced by human liver and yolk sac, which will be produced and circulate in human blood in the case of hepatocellular carcinoma (HCC) or embryonic tumor of the genital gland [1, 2]. Therefore, it is of great significance to check the AFP level in peripheral blood to diagnose these diseases. According to clinical reports, solid tumors also cause elevated AFP level [3-5]. However, no case has so far been reported in multiple myeloma (MM), which can result in markedly increased AFP level. In the current study, a 66-year-old male patient with IgD-λ light chain MM (Stage III B) was reported. Specifically, his AFP level had apparently increased during chemotherapy, meanwhile, occupying lesion had also been discovered in his liver, which was diagnosed with plasmablastic neoplasm of the liver rather than HCC through liver biopsy.

Case description

A 66-year-old man visited the Hematology Department of our hospital on July 21st, 2012 due to repeated back pain for six months. Six months ago, the patient visited the local hospital and biochemical routine examination showed globulin (GLB) of 36.5 g/L, creatinine (Cr) of 960 μmol/L, λ light chain in urine of 745 mg/dL. In addition, frontal cephalometric radiography revealed multiple bone destruction of skull. Emission computed tomography (ECT) suggested extremely active bone metabolism in multiple bilateral ribs, sternum, multiple thoracic vertebra, the first lumbar vertebral body, and right sacroiliac joint. Moreover, bone marrow examination demonstrated obviously active plasma cell proliferation; in the meanwhile, palsmablast + proplasmacyte accounted for 25.5% and plasmacyte occupied 32%. Bone marrow immunophenotyping indicated about 47.43% abnormal plasma cell populations of the non-erythroid cells, lambda (+), CD38 (+++), CD138 (+++) and CD20 (+) (bimodal expression). As a result, the patient was diagnosed with λ light chain MM (Stage III B) based on these examination results. The patient was administered the VAD regimen (vindesine 1mg d1-4+ epirubicin 15 mg d1-4+ dexamethasone 40 mg d1-4, 9-12, 17-20) on January 6th, 2012. In addition, the patient received hemodialysis treatment twice a week in outpatient clinic.

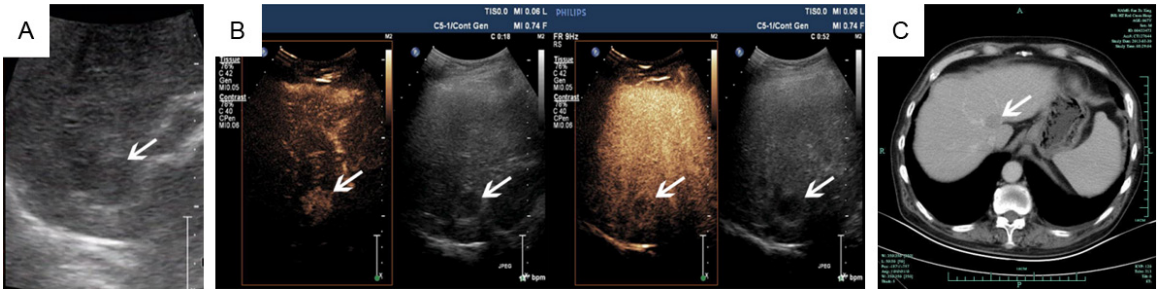

Figure 1. A: Abdominal ultrasound: a new space-occupying lesion was discovered in the second hepatic portal (arrow). B: Liver enhanced-contrast ultrasound: the hypoechoic nodules showed high perfusion, which was characterized by rapid increase and then decrease (arrow). C: Upper abdominal enhanced-contrast spiral CT: a low density shadow about 2.2 cm in diameter was found in the second hepatic portal, where contrast media could rapidly go in and out (arrow).

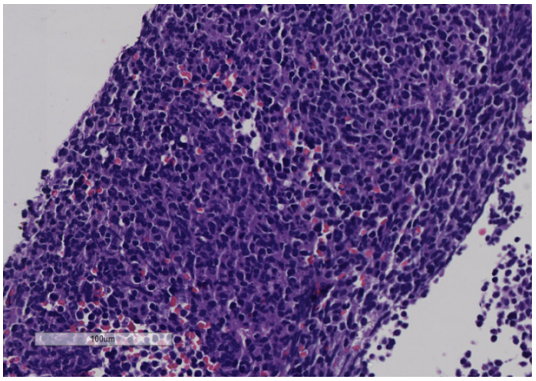

Figure 2. Tumor cells showed diffuse distribution, large nucleus, anachromasis, acidophilic cytoplasm and plasma cell differentiation (HE staining: 400×). Bar = 100 μm.

The severity of MM in the patient was evaluated using peripheral blood and bone marrow after admission into our hospital. Specifically, the biochemical routine examination suggested Cr of 679.9 μmol/L, albumin (ALB) of 44.4 g/L, GLB of 30.2 g/L, and calcium (Ca) of 3.08 mmol/L. Additionally, blood routine examination revealed white blood cell (WBC) of 4.3×10^9/L, hemoglobin (Hb) of 119 g/L, platelet (PLT) of 145×10^9/L, serum λ light chain of 1730 mg/dL, serum β2-microglobulin of 38.88 mg/L, urine β2-microglobulin of 12.2 mg/L, erythrocyte sedimentation rate (ESR) of 42 mm/h. Furthermore, serum and urine immunofixation electrophoresis (IFE) revealed IgD-λ monoclonal protein. Bone marrow routine examination suggested proplasmacyte of 8.0% and plasmacyte of 20.0%. The patient was thereby confirmed as IgD-λ light chain MM (Stage III B) in our hospital according to the above-mentioned findings. The patient had received chemotherapy regimens consisting of one PD (bortezomib 1.75 mg d1, 4, 8, 11+ dexamethasone 20 mg d1-2, 4-5, 8-9, 11-12) and three TCD (thalidomide 50 mg/d+ cyclophosphamide 0.2 d1-4+ dexamethasone 20 mg d1-4, 9-12) since July 27th, 2012. His bone marrow routine examination showed proplasmacyte of 2% and plasmacyte of 6.5% after chemotherapy.

Additionally, the patient had also received the TAD regimen (thalidomide 100 mg/d+ epirubicin 15 mg d1-4+ dexamethasone 20 mg d1-4, 8-11) since January 8th, 2013. His bone marrow routine examination revealed plasmablast of 40%, proplasmacyte of 18% and plasmacyte of 3.5% after chemotherapy. Furthermore, no mutations of genes *RB1, D13S319, p53, IgH* and *1q21* were found by fluorescence in situ hybridization (FISH) detection on the myeloma cells derived from the patient. However, his AFP level was up to 145.50 μg/L, while the alanine transaminase (ALT) fell within the normal range. Afterwards, diseases such as viral hepatitis, liver cirrhosis, focal hepatic lesions and germ cell tumors were excluded based on several examinations. Therefore, the BDT regimen (bendamustine 150 mg d1-2+ dexamethasone 15 mg d1-4+ thalidomide 100 mg/d) was employed on March 4th, 2013, in view of the elevated AFP level in the patient.

Nonetheless, reexamination showed that the AFP level had further increased after chemotherapy, which approached the peak at 578.80 μg/L. At the same time, a new space-occupying lesion about 2 cm in diameter was discovered in the second hepatic portal in abdominal ultrasound examination (**Figure 1A**). In addition, hepatic contrast-enhanced ultrasonography was

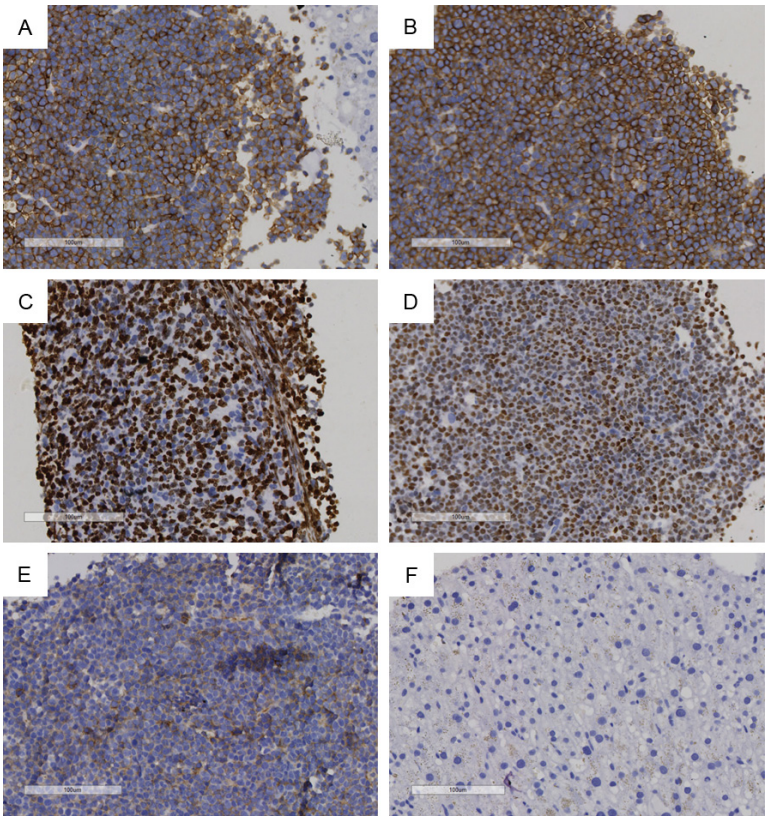

Figure 3. Immunohistochemical examination showed tumor cells positive for CD38 (A), CD138 (B), Ki67 (C), MUM1 (D), AFP in liver lesion (E) and negative for AFP in normal liver cells (F) (400×). Bar = 100 μm.

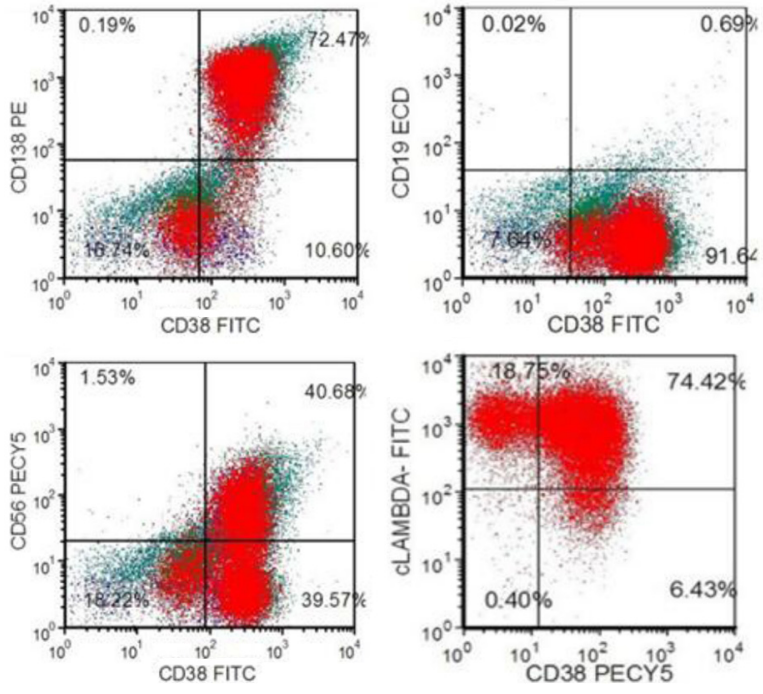

Figure 4. Immunophenotyping of pleural effusion showed CD38 (++), CD138 (+), CD19 (-), CD56 (partly+) and immunoglobulin λ light chain restriction.

also conducted, in which 2.4 ml contrast agent (SonoVue) was injected intravenously. The arterial phase at 19 seconds revealed rapider filling of contrast agent in hypoechoic nodules than in surrounding normal liver tissues. The portal venous phase at 35 seconds suggested less contrast agent in hypoechoic area than in surrounding normal liver tissues. The delayed phase displayed consistently lower contrast agent level in hypoechoic area than in surrounding normal liver tissues, which had quickly faded. On the whole, the hypoechoic nodules showed high perfusion, which was characterized by rapid increase and then decrease (**Figure 1B**). Moreover, upper abdominal enhanced-contrast spiral computed tomography (CT) was also performed, which indicated a small and round hypodense shadow about 2.2 cm diameter in the second hepatic portal. Besides, the lesion was well-defined, and the contrast media could rapidly go in and out of the margin after enhancement (**Figure 1C**). Liver biopsy pathology suggested that the tumor cells derived from the highly aggressive tumor of lymphoid hematopoietic system, which presented diffuse distribution, large nucleus, anachromasis, acidophilic cytoplasm and plasma cell differentiation (**Figure 2**); and immunohistochemistry revealed CD38 (+), CD138 (+), Ki67 (90%), MUM1 (+), CD45RO (+), CD43 (+), CD56 (partial+), AFP (+), CD3 (-), CD20 (-), Pax5 (-), EMA (-), HepPar (-), but AFP (-) in normal liver cells (**Figure 3**). Therefore, the patient was diagnosed with plasmablastic neoplasm of the liver. Serum and urine IFE indicated that the

IgD level had decreased by 30% compared with the last result. Biochemical routine examination suggested Cr of 401.4 μmol/L, ALB of 35.9 g/L, GLB of 23.2 g/L, and Ca of 3.18 mmol/L. Blood routine examination indicated WBC of 3.3×10^9/L, Hb of 67 g/L and PLT of 95×10^9/L; serum λ light chain of 427 mg/dL; and serum β2-microglobulin of 36.05 mg/L. Additionally, bone marrow routine examination suggested proplasmacyte of 6.0%, and plasmacyte of 27.0%. The patient returned to his local hospital after he received the BDT regimen (bendamustine 150 mg d1-2+ dexamethasone 15 mg d1-4+thalidomide 100 mg/d) on April 17th, 2013.

Unfortunately, the patient had massive pleural effusion in his left chest during his stay in the local hospital, which was drawn and appeared bloody. Meanwhile, the AFP level in pleural effusion was 214.25 μg/L. Immunophenotyping of pleural effusion showed monoclonal plasma proliferation of 72.5%, CD38 (++), CD138 (+), CD19 (-), CD56 (partly+), and immunoglobulin λ light chain restriction (**Figure 4**). The patient finally died of disease progression.

Discussion

IgD MM is a rare subtype of myeloma, which affects less than 2% of MM patients [6]. To be specific, IgD MM can be generally divided into κ and λ subtypes according to serum free light chain analysis, among which, the λ subtype is more common, accounting for about 70%-90% [7]. IgD content in patient is extremely low, which can maintain within the normal range. Monoclonal bands can hardly be found in common protein electrophoresis [7]. Nevertheless, the detection rate of IgD MM can be greatly improved using IFE [8]. If there is only monoclonal light chain detected without any heavy chain, IFE should also be performed to rule out the possibility of IgD MM before light chain MM is diagnosed. Only IFE of IgG, IgA and IgM was performed in the local hospital, the patient was initially diagnosed with λ light chain MM. However, the patient was finally diagnosed with IgD-λ MM in our hospital according to the results of all examinations performed, including IgD IFE.

AFP level is well recognized to elevate in patients with hepatocellular carcinoma (HCC), germ cell tumor and other gastrointestinal tumors. The AFP level is not recommended by the American Association for the Study of Liver Diseases (AASLD) as one of the diagnostic criteria of HCC. Nonetheless, it still emphasizes the important role of AFP elevation in the monitoring of HCC [9]. Meanwhile, it also points out that imaging evidence is one of the important diagnostic criteria of HCC. Some reports have shown that enhanced CT scan combined with contrast-enhanced ultrasound contributes to improving the imaging-diagnostic accuracy of HCC by up to 82% [10]. However, the serum AFP level still increased rapidly after the patient received the combined chemotherapy regimen, but AFP expression in normal hepatic cells adjacent to the tumor was negative. Meanwhile, new nodules could also be discovered in his liver. However, MM with extramedullary nodular infiltration in liver is rare [11]. Consequently, the patient was suspected of multiple primary cancers based on the above reasons. However, the diagnosis of multiple primary cancers should be confirmed based on definite pathology [12]. Therefore, liver pathological biopsy was performed on the patient.Unexpectedly, the pathological examination showed that the lesion was plasmablastic neoplasm of the liver. We suggest that a secondary puncture biopsy should be performed for a MM patient with new lesions in other parts of the body, so as to avoid misdiagnosis.

IgD MM is associated with poor response to general chemotherapy as well as dismal prognosis. Studies show that IgD MM is more sensitive to the initial treatment of VAD (vincristine, adriamycin and dexamethasone) and M2 (carmustine, cyclophosphamide, vincristine, melphalan and prednisone) regimens. However, patients have a shorter remission stage, a higher recurrence rate and a higher possibility of developing multidrug resistance [13]. Compared with other subtypes of MM, IgD MM has a similar response to autologous stem cell transplantation, but the survival rate after transplantation is lower [14]. Besides, IgD MM is usually complicated by various degrees of renal dysfunction, which appears to add to the difficulty in make treatment. Ramasamy *et al.* [15] suggested that bendamustine combined with thalidomide and dexamethasone was an effective therapy for myeloma patients with end stage renal disease. Moreover, Grey-Davies E *et al.* [16] also affirmed the importance of

BDT regimen and considered that it was an effective salvage treatment for advanced MM. In this case, the patient mainly received general chemotherapy at the early stage with a short remission. Afterwards, he received the BDT regimen, which had short curative effect. The patient subsequently suffered from plasmablastic neoplasm of the liver, abnormal AFP level and massive pleural effusion containing plasma cells, indicating that IgD MM was a highly invasive tumor.

IgD-λ MM with plasmablastic neoplasm of the liver accompanying with a high AFP level is a rare disease in clinic, which has not been reported so far. IgD-λ MM not only has high invasiveness, but also lacks effective approaches for treatment. Moreover, clinicians should pay more attention to puncture biopsy to avoid misdiagnosis.

Disclosure of conflict of interest

None.

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