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Case Report

Traumatic or pathological fracture?–A case report related to HOOK effect and brief literature review

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Abstract: The diagnosis of fracture is mainly based on patient's symptoms, physical examination and imaging examination. The possibility of a pathological fracture should be highly suspected if the fracture is caused by a minor external trauma or the patient has a history of malignancy, especially in the elderly. Here in, we report a 66-year-old female patient who was referred to our hospital suffering lumbar pain for 1 month with limited mobility due to minor trauma when doing housework. When the laboratory technologists reviewed the immuno-related test reports, they found that the result of serum IgA was suspect, and the response curve suggested the presence of Hook Effect. After reexamination, the patient's serum IgA level was found to be abnormally high, accompanied by the increment of lambda light chain abnormality. Combined with clinical symptoms and other related examinations, the diagnosis was finally confirmed as IgA-lambda multiple myeloma, which is the exact cause of the pathological fracture.

Keywords: Hook Effect, pathological fracture, multiple myeloma, case report

Introduction

HOOK Effect, also known as Prozone effect, refers to the phenomenon of an inappropriate concentration ratio of antigen and antibody in the immune response; and this leads to the occurrence of wrong or missed detection of qualitative and quantitative results. Fractures can result from trauma, which is a traumatic fracture and bone disease, such as osteomyelitis, bone tumors leading to bone destruction, where the fracture occurs when a minor force is applied: this is called pathologic fracture, pathologic fracture is mainly caused by primary or metastatic bone tumors.

Case presentation

A 66-year-old female patient suffered minor external trauma while doing housework one month prior to examination. Her lower back pain, accompanied by limited movement was not improved after conservative treatment in the local hospital. Her lower back pain gradually worsened and she was unable to sit or stand. Therefore, she came to our hospital for further treatment. The MRI showed "L2 vertebral compression changes with bone marrow edema", and the patient was admitted to hospital with a "lumbar compression fracture". In order to distinguish pathological fractures from traumatic fracture and determine whether there are surgical contraindications, the surgeon who was in charge of the operation issued the relevant testing items. Partial examination results of the patient are shown in **Table 1**.

When the laboratory technologist reviewed the results, it was found that the result of serum IgA test was 6.04 g/L, with the "X" symbol on the right side, indicating the result was unusual. After checking HIS (Hospital Information System) and the concentration response curve (see **Figure 1**), the "HOOK Effect" was highly suspected. After further centrifugation, the serum was placed in a clean drying tube (to exclude the matrix effect of the tube separating gel in the original container). The serum was re-determined after a dilution ratio of normal saline, the result of serum IgA level was 22.94 g/L, and the concentration response curve was normal (see **Figure 2**). To further clarify the increase of

Table 1. Partial examination results of the patient

Abbreviation	Project name	Result	Unit	Reference range
IgG	Immunoglobulin G	3.55	g/L	7.00-16.00
IgA	Immunoglobulin A	22.94	g/L	0.70-4.00
IgM	Immunoglobulin M	<0.175	g/L	0.40-2.30
KAP	KAP light chain	0.78	g/L	1.70-3.70
LAM	LAM light chain	6.79	g/L	0.90-2.10
K/L	KAP/LAM	0.11		1.35-2.65
RBC	Red blood cell	3.32	10^{12}/L	3.80-5.10
HGB	Hemoglobin	93	g/L	115-150
HCT	Hematocrit	28.7	%	35-45
Ca	Serum Calcium	3.14	mmol/L	2.20-2.65

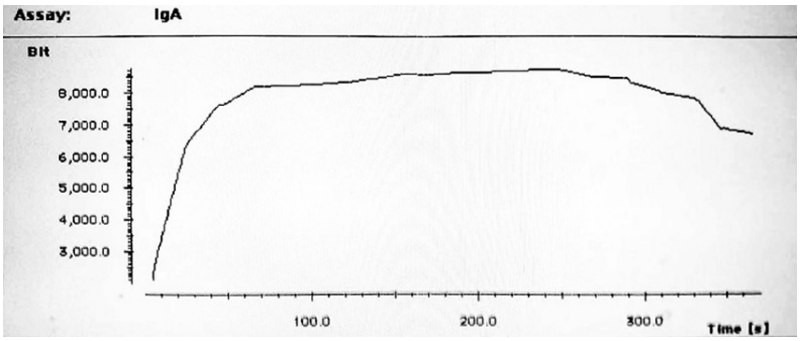

Figure 1. Concentration response curve.

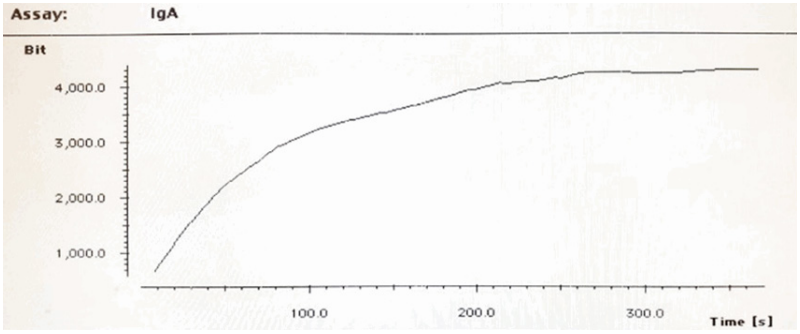

Figure 2. Concentration response curve (The serum was re-determined after dilution of the ratio of normal saline).

lambda light chain abnormality, the laboratory technologist suggested the surgeon should request a urinary kappa and lambda light chain examination (see **Table 1**), a serum immunofixation electrophoresis (see **Figure 3**) and a bone marrow cytology examination (see **Figure 4**). Eventually the patient was diagnosed with IgA-lambda multiple myeloma and immediately transferred to the hematological department with symptomatic treatments and chemotherapy of PAD (bortezomib + doxorubicin + dexamethasone).

Discussion

Multiple myeloma (MM) is a malignant tumor with abnormal proliferation of clonal plasma cells, where myeloma cells proliferate in the bone marrow, causing osteolytic bone destruction. MM is the second most common malignancy in the blood system. MM mainly occurs in middle-aged and elderly people. The ratio of males to females was 1.54 to 1 [1]. According to epidemiological statistics, there are about 86,000 new cases worldwide each year [2]. MM can be classified into IgG type, IgA type, IgD type, IgM type, and IgE type according to the type of immunoglobulin which has abnormal proliferation. In addition, there is the light chain type, the double clone type and the non-secretory type, according to the type of light chain, and it can be further divided into kappa type and lambda type. Clinically, MM of IgA type is prone to hyperviscosity syndrome (HVS); IgA easily forms polymers, and is high hydrophilic, which are the reasons for the high incidence of HVS. In this case, the inaccurate results of the patient's first serum IgA test suggested that the abnormal turbidity was probably caused by the increased plasma viscosity of MM.

Abnormal plasma cells and their products in MM result in a range of target organ dysfunctions and clinical manifestations, including bone pain and fracture, renal impairment, anemia, hypercalcemia, and repeated severe infections. Multiple myeloma bone disease (MMBD)

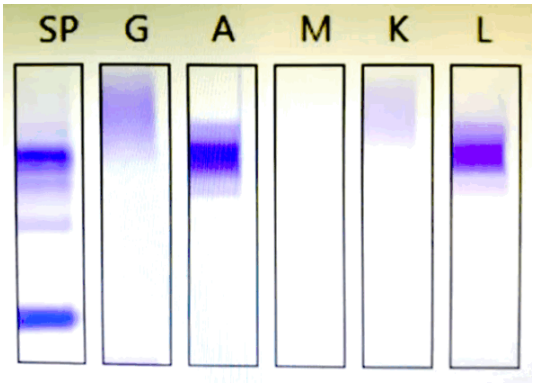

Figure 3. Serum immunofixation electrophoresis.

is the general name of a series of clinical complications including pathological fractures, spinal cord and nerve root compression, osteoporosis, hypercalcemia and bone pain caused by osteolytic destruction of myeloma: the incidence of MMBD in patients with myeloma is over 80% [3]. The pathogenesis of MMBD is mainly due to the fact that myeloma cells activate osteoclasts while inhibiting osteoblastic activity, resulting in the eventual imbalance of bone metabolism [4-6].

In this case, the discovery of Hook Effect was crucial to avoid misdiagnosis. Heidelberger first discovered the antigen-antibody reaction with band phenomenon in 1929. In 1977, Green called it the Hook Effect, which includes the front and back bands. The Hook Effect is most often found in ELISA, nephelometry, chemiluminescence and other immunological techniques. In this case IgA in serum was determined by nephelometry in our laboratory.

According to the patient's medical history, physical examination and auxiliary examination, including bone marrow puncture and biopsy, bone marrow cytology examination and bone marrow pathology; the patient was diagnosed with MM, and the patient's pathological fracture was also considered. The original operation plan was suspended, the related symptomatic treatments and chemotherapy of PAD were carried out clinically. In addition to patients with pathologic fractures of the long bone and acute paraplegia, other MM patients are recommended to receive more than one course of systemic chemotherapy in a hematological department before surgical treatment, and then the need for surgery is reassessed [7].

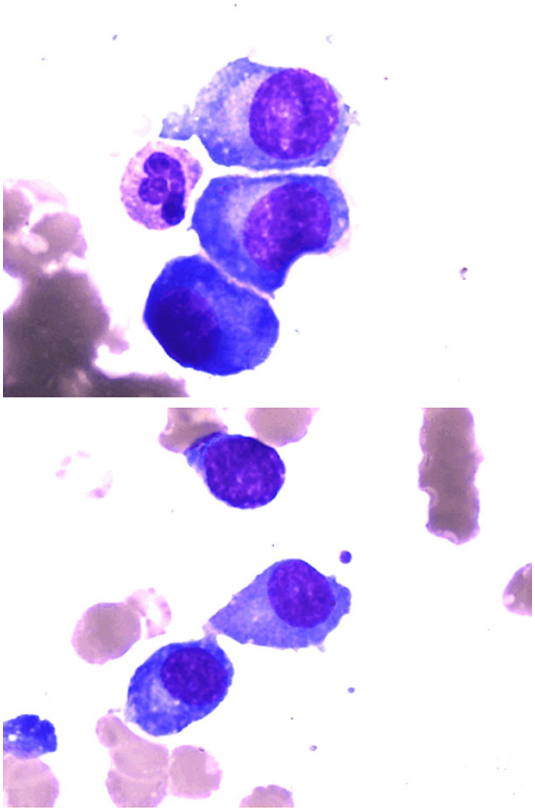

Figure 4. Bone marrow cytology examination.

Conclusions

Fracture was the first symptom in this case, therefore, for elderly patients with suspected pathological fracture, it is necessary to exclude potential neoplastic diseases, especially multiple myeloma (MM). In this situation, we suggest that: First, the detection of serum and urine immunological items should be required, and then perform serum immunofixation electrophoresis in patients with unusual outcomes, and finally, bone marrow cytology examination should be performed to confirm the diagnosis. Many primary and metastatic bone tumors are sometimes found after pathologic fracture. In MM, the clinical symptoms, especially the first symptom, is diversified and can occur in various systems of the body [8]. Therefore, in clinical work, we should actively carry out multidisciplinary treatment (MDT), the laboratory technologists and the clinicians can try to communicate in a more effective manner, so that patients can benefit more from inter-disciplinary cooperation.

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Disclosure of conflict of interest

None.

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