Journal of Zhejiang University SCIENCE B
ISSN 1673-1581 (Print); ISSN 1862-1783 (Online)
www.zju.edu.cn/jzus; www.springerlink.com
E-mail: jzus@zju.edu.cn

***Case Report:***

# IgE myeloma with elevated level of serum CA125

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Received Dec. 20, 2008; Revision accepted May 23, 2009; Crosschecked June 12, 2009

**Abstract:** Objective: To explore clinical and laboratory features and significance of detecting serum carbohydrate antigen 125 (CA125) in immunoglobulin E (IgE) multiple myeloma. Methods: We reported the clinical findings of a male patient with IgE myeloma and elevated level of serum CA125 and reviewed the literature. Results: Laboratory tests of this patient on admission showed extremely high serum IgE and CA125, a bone marrow aspirate revealed abnormal plasma cells (38.4% of nucleated cells: 16.4% mature and 22% atypical), and in bone marrow biopsy, immunoperoxidase staining showed positive cytoplasmic staining for IgE and κ light chain within the vast majority of plasma cells. Computed tomography (CT) bone scans indicated wedge shape change and compressive fracture of thoracic vertebrae, and emission computed tomography (ECT) discovered multiple punctiform aggregation of radiation in both cervical ribs and spine. The serum IgE and CA125 gradually decreased to normal limits after eight cycles of chemotherapy. This patient is alive well with an 18-month complete remission. Conclusion: We reported the first case of IgE myeloma with elevated level of serum CA125. To further evaluate clinical characteristics and significance of CA125 in IgE myeloma, more cases are needed.

**Key words:** Immunoglobulin E (IgE), Multiple myeloma, Carbohydrate antigen 125 (CA125)
**doi:**10.1631/jzus.B0820399 **Document code:** A **CLC number:** R55

## INTRODUCTION

Multiple myeloma (MM) is a plasma cell neoplasm, characterized by proliferation of a single line of plasma cells producing a specific monoclonal immunoglobulin, generally osteolytic lesion or osteoporosis, anemia, infection, and renal failure. IgG and IgA myelomas are the common forms, but IgE myeloma is rare. Since the first case of IgE myeloma was reported in 1967 (Johansson and Bennich, 1967), only about 40 cases have been described in the literature (Jako *et al*., 1997; Kairemo *et al*., 1999; Lloyd *et al*., 2003). The prevalence of IgE myeloma is about 0.01% in all plasmocytomas (Jako *et al*., 1997). Although signs and symptoms are similar, it is generally accepted that IgE myeloma has a more malignant clinical course than other forms of MM (Jako *et al*., 1997; Alexander *et al*., 1992). Carbohydrate antigen 125 (CA125) originates from epithelial tissue of fetus and is widely used as a kind of tumor markers especially in human ovarian carcinoma (Eagle and Ledemann, 1997). Although increased CA125 can also be detected in many benign or malignant conditions including several hematological diseases (Russo *et al*., 2007), so far the significance of serum CA125 level in patients with IgE myeloma has not been found. To our knowledge, the case we report is the first IgE myeloma with elevated level of serum CA125 in the literature.

## CASE REPORT

A 53-year-old man presented in May 2007 with a history of nonspecific back pain for at least half a year. The pain became so sharp during the month prior to admission that the patient had to lie in bed and could not turn over. There was no evidence of allergic diseases or solid tumors such as lung and gastrointestinal cancers. Results of pertinent laboratory tests on admission were: hemoglobin 117 g/L, total proteins 54.8 g/L, albumin 37.45 g/L, and $\beta_2$-microglobulin

3.17 mg/L. No circulating plasma cells were seen on the blood film. Routine chemistry values were within reference limits. Serum tumor markers were normal except that CA125 was as high as 1292.3 U/ml. Quantification of serum and urine proteins gave serum IgG 4.94 g/L, IgA <0.0667 g/L, IgM 0.20 g/L, IgE 534 U/ml (reference limits: 0~87 U/ml), κ light chain 3.92 g/L, λ light chain 1.87 g/L, and urine κ light chain 3670 mg/L and λ light chain <50 mg/L. Although his IgE value was high, the IgE monoclonal band was too small to be seen by serum protein electrophoresis. Immunofixation did not observe the presence of IgG, IgA, IgM, IgD, κ, or λ monoclonal protein. On Wright's stained smears of bone marrow aspirate, plasma cells made up 38.4% (16.4% mature and 22% atypical) of nucleated cells (Fig.1). Percentages of other bone marrow cells were decreased. Chromosomal analysis of the bone marrow cells was normal. A bone marrow biopsy revealed that the hematopoietic cells comprised 50% of nucleated cells, the three lineages were all observed, and lots of plasmoid cells were seen. The immunohistochemistry revealed plasma cell (+), CD138 (+), IgE (+) (Fig.2), IgG (+), IgA (–), IgM (–), κ (+) (Fig.3), λ (–), and CD20 (–). Skeletal roentgenograms found multiple osteolytic lesions in the skull. Bone scans by computed tomography (CT) of this patient showed wedge shape change and compressive fracture of T5, T6, T8, T9, and T12, and emission computed tomography (ECT) discovered multiple punctiform aggregation of radiation in both cervical ribs and spine. The patient was treated with bisphosphonates+vincristine-adriamycin-dexamethasone (VAD) for one cycle in late May 2007, and then bisphosphonates+liposomal doxorubicin-vincristine-dexamethasone (DVD) for seven cycles every four weeks. At the same time he took thalidomide orally 200 mg once daily. This regimen resulted in a considerable reduction in the skeletal pain and a gradual decline in serum IgE to 44.1 U/ml and CA125 to 28.33 U/ml after the total 8 cycles of chemotherapy.

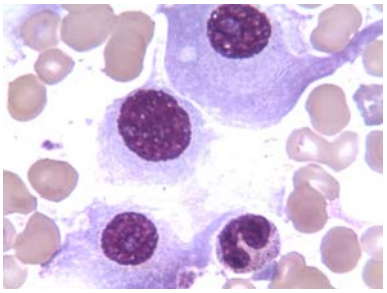

**Fig.1 Bone marrow aspirate showing atypical plasma cells with prominent nucleoli and open-weaved nuclear chromatin. Wright's stain (1000×)**

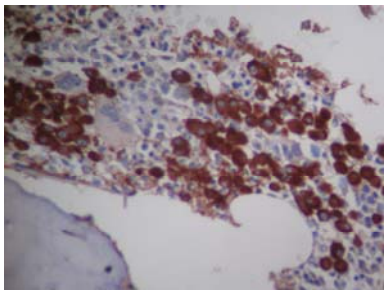

**Fig.2 Bone marrow biopsy, immunoperoxidase staining with antibody against IgE showing positive cytoplasmic staining for IgE within the vast majority of plasma cells (200×)**

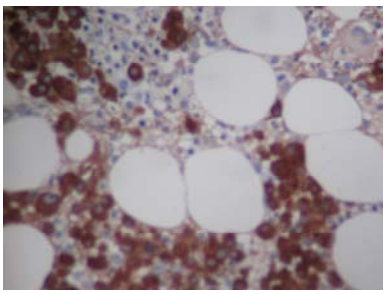

**Fig.3 Bone marrow biopsy, immunoperoxidase staining with antibody against κ light chain showing positive cytoplasmic staining for κ light chain within the vast majority of plasma cells (200×)**

## DISCUSSION

Since the first description of IgE myeloma by Johansson and Bennich (1967), about 40 cases have been reported. One case of IgE monoclonal gammopathy of undetermined significance was also described (Ludwig and Vormittag, 1980). IgE myeloma is in fact similar to classical myeloma in sex distribution and age of onset. Of the known cases of IgE myeloma including the one in the current report, the male-to-female ratio was 20:18, and ages of these patients ranged from 38 to 80 years (Jako *et al*., 1997; Kairemo *et al*., 1999; Lloyd *et al*., 2003). IgE myeloma has no specific or typical symptoms and findings when compared with the other forms of MM.

However, among those most often reported are bone pain, weight loss, fatigue, dyspnea, and anemia. Bone pain is usually present in patients with compressive fracture of the vertebrae and osteolytic lesions of the spine, chest, pelvis, and extremities. Our patient also complained of bone pain, because of multiple compressive fractures of vertebral bodies. Hepatosplenomegaly seemed to be more common in IgE myeloma as compared with other types, for of the 40 cases 11 patients presented with hepatomegaly and/or, splenomegaly, but none with lymphadenopathy (Alexander *et al*., 1992). Although serum calcium was in the normal reference limits in our patient on admission and after therapy, hypercalcemia was found in five patients (Alexander *et al*., 1992; Yoshitake *et al*., 1976; van Wijk *et al*., 1986; Gallango *et al*., 1988) and hypocalcemia in four patients with IgE myeloma (Vladutiu *et al*., 1976; Kimura *et al*., 1981; Koh *et al*., 1986). As with common immunoglobulin classes, renal insufficiency was also an indicator of poor prognosis in patients with IgE myeloma, although severe renal failure occurred in only three patients (Galton and Peto, 1973). Erythrocyte sedimentation rate (ESR) was found to be >20 mm/h in more than 90% of patients with IgE myeloma. Our patient had an ESR of 48 mm/h on admission and in normal range after therapy. As most patients with IgE myeloma had no detectable monoclonal protein, we did not discover the presence of monoclonal protein in our patient's serum by ordinary electrophoresis, either. However, immunohistochemical studies of our patient's bone marrow showed that the plasma cells were strongly positive for cytoplasmic IgE and κ light chain and negative for λ light chain. Several studies showed that patients with multiple myeloma might have reduced percentage of CD4 cells and increased percentage of CD8 cells, and the T4/T8 ratio remained decreased after therapy (San Miguel *et al*., 1985; de Rossi *et al*., 1987). The increase in T-suppressor cells may play a role in the suppression of polyclonal immunoglobulin synthesis. In our patient we detected decreased CD4 cells and normal CD8 cells.

As a mucin-like glycoprotein, although CA125 has been shown to be elevated in most women with ovarian cancer compared with a healthy population, it is also increased in hematologic malignancies such as Hodgkin's and non-Hodgkin's lymphomas (NHL) and is used as a marker to predict prognosis and to detect advanced disease (Russo *et al*., 2007). In NHL patients high levels of CA125 were observed to be correlated to the presence of abdominal and serosal involvement. The exact mechanism of CA125 elevation in these cases is unclear, but it has been proposed that cytokines such as interleukin (IL)-1β and tumor necrosis factor-α (TNF-α) secreted by lymphoma cells might lead to secretion of CA125 by mesothelial cells (Dilek *et al*., 2005). In our patient, although there were no abdominal involvement and serosal effusion, his CA125 level was extremely high on admission and dramatically decreased to normal limits after chemotherapy and never increased to higher than reference limits again. About the exact cause and clinical significance of CA125 elevation in our patient, we are not sure whether some cytokines abnormally synthesized by plasma cells stimulated the mesothelial cells to increase the secretion of CA125 or plasma cells themselves abnormally synthesized CA125, or whether the falling CA125 level after treatment could be used to confirm response to specific treatments and elevating CA125 level to signal recurrence? Despite an exhaustive search of the literature we could not find a single case of IgE myeloma reported, in which abnormal CA125 level was detected. Apparently, more similar cases are needed to evaluate the significance of CA125 in disease staging, prognosis, and relapse of IgE myeloma.

IgE myeloma is generally reported to be more aggressive than other forms of myeloma. The average survival from time of diagnosis in a review of 38 cases (Kairemo *et al*., 1999) was significantly shorter in patients with IgE myeloma (one year) than those with other forms of myeloma (30 months) (Yoshitake *et al*., 1976). Our patient is alive well and healthily with an 18-month complete remission up to now.

ACKNOWLEDGEMENT

We thank the Department of Hematology of Shanghai Changzheng Hospital, specifically, Prof. Hou Jian for allowing immunohistochemical study of bone marrow biopsy.

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