



Case Study

A rare and unique case of aggressive IgE- λ plasma cell myeloma in a 28-year-old woman presented initially as an orbital mass

Ke Li MD^a, Grace Ku MD^b, Min Yan MD^b, H. Elizabeth Broome MD^a,
Michael Kelner MD, MS^a, Huan-You Wang MD, PhD^{a,*}

^aDepartment of Pathology, University of California San Diego Health System, La Jolla, CA 92093–0987, USA

^bDepartment of Medicine, Division of Hematology/Oncology, University of California San Diego Health System, La Jolla, CA 92093–0960, USA

Received 30 March 2012; revised 13 June 2012; accepted 6 July 2012

Keywords:

IgE;
Plasma cell myeloma

Summary A 28-year-old African-American woman presented with new onset of left exophthalmos and diplopia. Computed tomography of the head showed a solitary mass in the left orbit. Excisional biopsy revealed a diffuse infiltrate composed of exclusively λ -restricted monotypic plasma cells based on morphology and immunohistochemistry, consistent with a plasma cell neoplasia. A subsequent staging bone marrow biopsy showed involvement of the bone marrow by λ -restricted monotypic plasma cells, consistent with a plasma cell myeloma. Serum protein electrophoresis and immunofixation studies on the peripheral blood showed a monoclonal band of IgE- λ ; thus, an IgE- λ plasma cell myeloma was established. Additional clinical and radiologic workups showed multiple lytic bone lesions, diffuse lymphadenopathy, a pelvic mass, multiple mesenteric soft tissue nodules, and multiple pulmonary nodules, although none of the aforementioned sites was biopsied. The patient was treated with a combination of multiple chemotherapeutic agents and localized radiation due to the aggressive nature of the disease. To the best of our knowledge, this is the first case of an IgE plasma cell myeloma in a patient under the age of 30 years old presenting as a mass in an extramedullary site.

© 2012 Elsevier Inc. All rights reserved.

1. Introduction

Plasma cell myeloma (PCM) is a bone marrow-based disease of the elderly that comprises 10% to 15% of all hematopoietic neoplasms. The disease is more commonly found in men and occurs twice as frequently in African Americans. More than 90% of the cases occur over the age of 50 with the median age of diagnosis of 70 years. Rarely has PCM been diagnosed in adults younger than 30 years. For instance, the incidence of PCM in patients younger than 30

years was estimated to be 0.3% [1]. PCM is further divided into symptomatic and asymptomatic types with the former presenting with signs and symptoms of end-organ damage, such as hypercalcemia, renal insufficiency, anemia, and bone lesions, in addition to clonal bone marrow plasma cell infiltrate and M-protein. The M-protein component, found in serum and/or urine, is most commonly IgG, followed by IgA, then κ or λ light chain. Although IgD and non-secretory PCM cases are uncommon, IgE and IgM PCM cases are extremely rare.

Since the first case of IgE PCM reported in 1967 [2], there have been only 47 cases of IgE PCM described in the English literature [2–10]. Aside from the typical clinical presentations of PCM, rare cases of IgE PCM involving the skin, breast, and

* Corresponding author.

E-mail address: hywang2@ucsd.edu (H. -Y. Wang).

orbit have also been reported [8,11,12]. Most of the cases with orbital involvement were a result of disease recurrence, rather than the initial presentation like this case, and proptosis was the major presenting symptom. Here, we report the first case of IgE PCM in a patient younger than 30 years, who presented with an orbital mass as her initial presentation. In addition, it appears that the IgE PCM in this patient had an aggressive clinical behavior owing to multiple organ/system involvement.

2. Materials and methods

2.1. Clinical history

A 28-year-old African-American female presented in October 2011 with two-week history of progressive left retro-orbital pain and exophthalmos. Her significant medical history included β -thalassemia trait and morbid obesity (BMI 60). Computed tomography (CT) of the orbit revealed a moderately enhancing mass abutting the left medial rectus muscle. After consulting with ophthalmology, she was started on prednisone 60 mg by mouth (PO) daily for a presumptive diagnosis of idiopathic orbital inflammation manifesting as left medial rectus myositis. Repeat CT of the orbit after three weeks of treatment revealed a left orbital mass measuring $3.7 \times 1.8 \times 2.1$ cm (Fig. 1) that abutted the left medial rectus muscle and the globe with resultant optic nerve displacement. Subsequently the patient underwent left orbitotomy with excisional biopsy of the mass. Soon after the operation, the patient developed abdominal pain. CT revealed a pelvic mass measuring 18×6 cm and numerous soft tissues nodules within the mesentery and subcutaneous tissues. There were also numerous bilateral pulmonary parenchymal nodules measuring up to 1 cm, large



Fig. 1 Radiologic findings of the orbital mass. CT scan of the head revealed a $3.7 \times 1.8 \times 2.1$ cm mass (arrow) in the left side of the orbit.

conglomerate mediastinal lymphadenopathy, and bilateral axillary lymphadenopathy. Skeletal survey showed multiple lytic bone lesions located to humerus, ulna, ileum, and sacrum.

After a λ -restricted plasma cell neoplasia was diagnosed from the orbital biopsy, a staging bone marrow biopsy was performed, which revealed a plasma cell myeloma with λ light chain restriction. Serum protein electrophoresis and immunofixation easy (IFE) confirmed IgE- λ para-protein; thus, an IgE λ PCM was established. The patient was soon treated, and her bone marrow showed no evidence of residual plasma cell myeloma after two cycles of VTDPAGE. Her complete blood count, quantitative serum immunoglobulins, and pertinent blood chemistry are summarized in the Table.

2.2. Flow cytometry

Detailed four-color flow cytometric analysis used in this study was published previously. The following fluoroconjugated monoclonal antibodies against CD19, CD20, CD38, CD45, CD56, surface κ , surface λ , cytoplasmic κ , and cytoplasmic λ were used, and all antibodies were purchased from Becton Dickinson (San Jose, CA).

Table Complete blood count (CBC) with differential count, quantitative serum immunoglobulin, and pertinent blood chemistry

CBC with differential count	Result	Reference limits
WBC (mm^3)	16,500	4,000-10,000
RBC (mm^3)	3,610,000	4,600,000-6,100,000
HgB (g/dL)	8.0	13.7-17.5
HCT (%)	26.3	40-50
MCV (fL)	72.9	79-95
MCH (pgm)	22.2	26-32
MCHC (%)	30.4	32-36
Platelet (mm^3)	485,000	140,000-370,000
Serum Immunoglobulin		
IgG (mg/dL)	714	700-1600
IgA (mg/dL)	283	70-400
IgM (mg/dL)	62	40-230
IgE (IU/mL)	22	0-99
κ light chain	2.07	N/A
λ light chain	103	N/A
Pertinent blood chemistry		
Total protein (g/dL)	9.5	6.0-8.0
Albumin (g/dL)	3.6	3.5-5.2
Creatinine (mg/dL)	0.6	0.67-1.17
Calcium (mg/dL)	10.4	8.6-10.5
Beta-2 microglobulin (mg/dL)	4.7	0.8-2.2
CA-125 (U/mL)	91	0-34

Abbreviations: CBC, complete blood count; WBC, white blood cells; RBC, red blood cells; HgB, hemoglobin; HCT, hematocrit; MCV, mean cell volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; Ig, immunoglobulin; N/A, not applicable.

2.3. Cytomorphologic assessments

The peripheral blood and bone marrow aspirate smears were stained with Wright-Giemsa. The clot section and decalcified bone marrow core biopsy were fixed in 10% formalin and acid zinc formalin and stained with hematoxylin and eosin (H&E) according to the standard protocol.

2.4. Immunohistochemistry

Immunohistochemistry was performed on Dako Auto-stainer using Envision (+) Detection Kit (Dako Inc, Carpinteria, CA). The antibodies and dilutions are as follows: BCL-1 (1:60; Biocare Medical, Concord, CA), CD19 (1:30; Epitomics Inc, Burlingame, CA), CD20 (1:250; Dako), CD56 (1:120; Cell Marque, Rocklin, CA), CD138 (1:60; abD Serotec, Taleigh, NC), κ (1:500; Biocare Medical), and λ (1:35; Biocare Medical).

2.5. Conventional karyotyping and fluorescence in situ hybridization (FISH)

Conventional karyotyping on bone marrow aspirate using G-banding was performed according the standard

protocol. FISH analysis using unenriched cell population was carried out on interphase nucleoli according to the manufacturer's instruction. The following probes were used: *EGR1* (5q31), *D7S486* (7q31), *D13S319* (13q14.3), *p53* (17p13), *CCND1/IGH* (translocation 11;14), *FGFR3/IGH* (translocation 4;14), *MAF/IGH* (translocation 14;16). All probes were purchased from Vysis (Abbott Molecular, Abbott Park, IL). *EGR1* (5q31), *D7S486* (7q31), *D13S319* (13q14.3), and *p53* (17p13) are locus specific probes, the rest are dual color, dual fusion probes sets.

2.6. Serum immunoglobulin measurement, serum protein electrophoresis (SPEP), and immunofixation (IFE)

Quantitative serum immunoglobulins levels (IgG, IgA, IgM, and IgE) were performed on a COBAS 6000 Immunochemical Analyzer using monoclonal antibodies obtained from the manufacturer (Roche Diagnostics Inc, Indianapolis, IN). SPEP and IFE were performed using a Helena SPIFE 2000 Electrophoresis System using an acid violet dye densitometry and polyclonal antibodies obtained from the manufacturer (Helena Laboratories, Beaumont, TX).

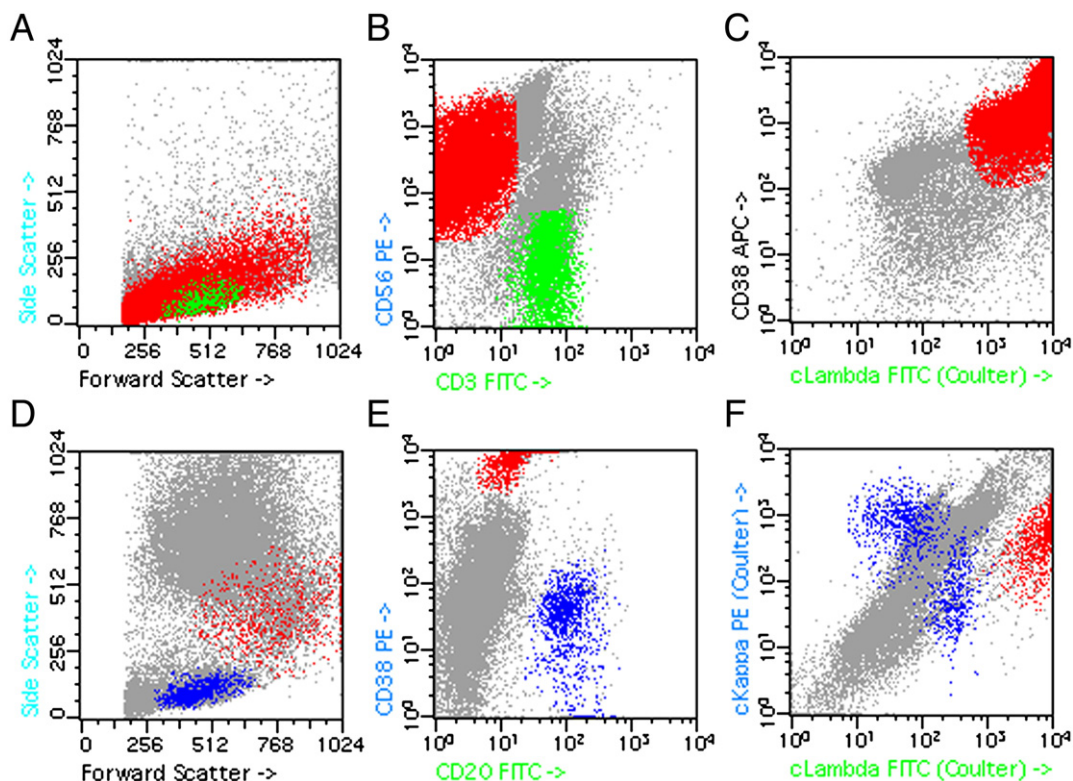


Fig. 2 Flow cytometric analysis of the orbital mass and bone marrow aspirate. A, The plasma cells (red) show variable size and low-orthogonal scatter property. B and C, The plasma cells are positive for CD56 (B) and bright positive for CD138 with λ -restriction (C). D, E and F, The plasma cells from the bone marrow aspirate are bright positive for CD38, negative for CD20 (E) with λ light chain restriction (F). Red, neoplastic plasma cells (A-F); green, normal T-cells (A and B); and blue, polytypic B-cells (D, E, and F).

3. Results

3.1. Flow cytometry

Four-color flow cytometry performed on the orbital mass revealed approximately 15% population of CD56 (+)

(Fig. 2B) and CD38 (bright +) and cytoplasmic λ -restricted plasma cells (Fig. 2C), which were negative for CD19, CD20, and CD45 (data not shown). Flow cytometric analysis of the bone marrow confirmed the presence of CD38 (bright +) (Fig. 2E) cytoplasmic λ -restricted (Fig. 2F) monotypic plasma cell population.

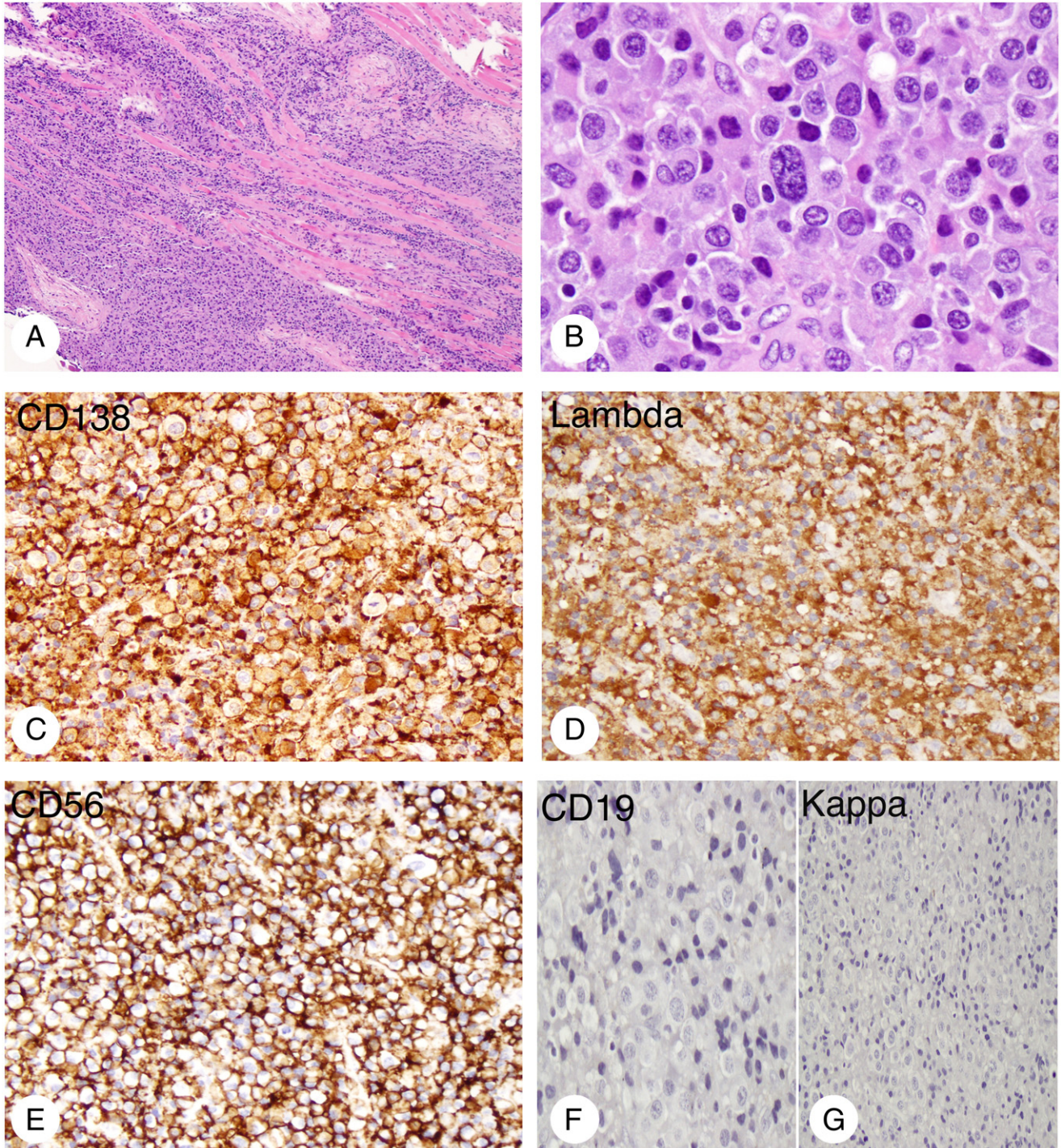


Fig. 3 Histopathology of the orbital mass. A, Sheets of plasma cells dissecting the skeletal muscles (A) with scattered cells showing cytologic atypia (B). (A, H&E, original magnification $\times 40$; B, H&E, original magnification $\times 400$). C-G, The plasma cells are diffusely and strongly positive for CD138 (C), λ (D), and CD56 (E), but negative for CD19 (F) and κ (G). (original magnification for C, D, E, F, and G are $\times 200$, $\times 200$, $\times 200$, $\times 200$, and $\times 400$, respectively).

3.2. Pathologic findings

3.2.1. Orbital mass

H&E sections of the biopsy showed a diffuse infiltrate of plasma cells dissecting skeletal muscle (Fig. 3A). The vast majority of the plasma cells exhibited eccentrically located

nuclei and abundant cytoplasm with peri-nuclear hof; however, occasional medium to large atypical forms were noted (Fig. 3B). These plasma cells were strongly and diffusely positive for CD138 (Fig. 3C), λ (Fig. 3D), and CD56 (Fig. 3E), but negative for CD19 (Fig. 3F) and κ (Fig. 3G), CD20 and CD45 (not shown). Ki-67 showed

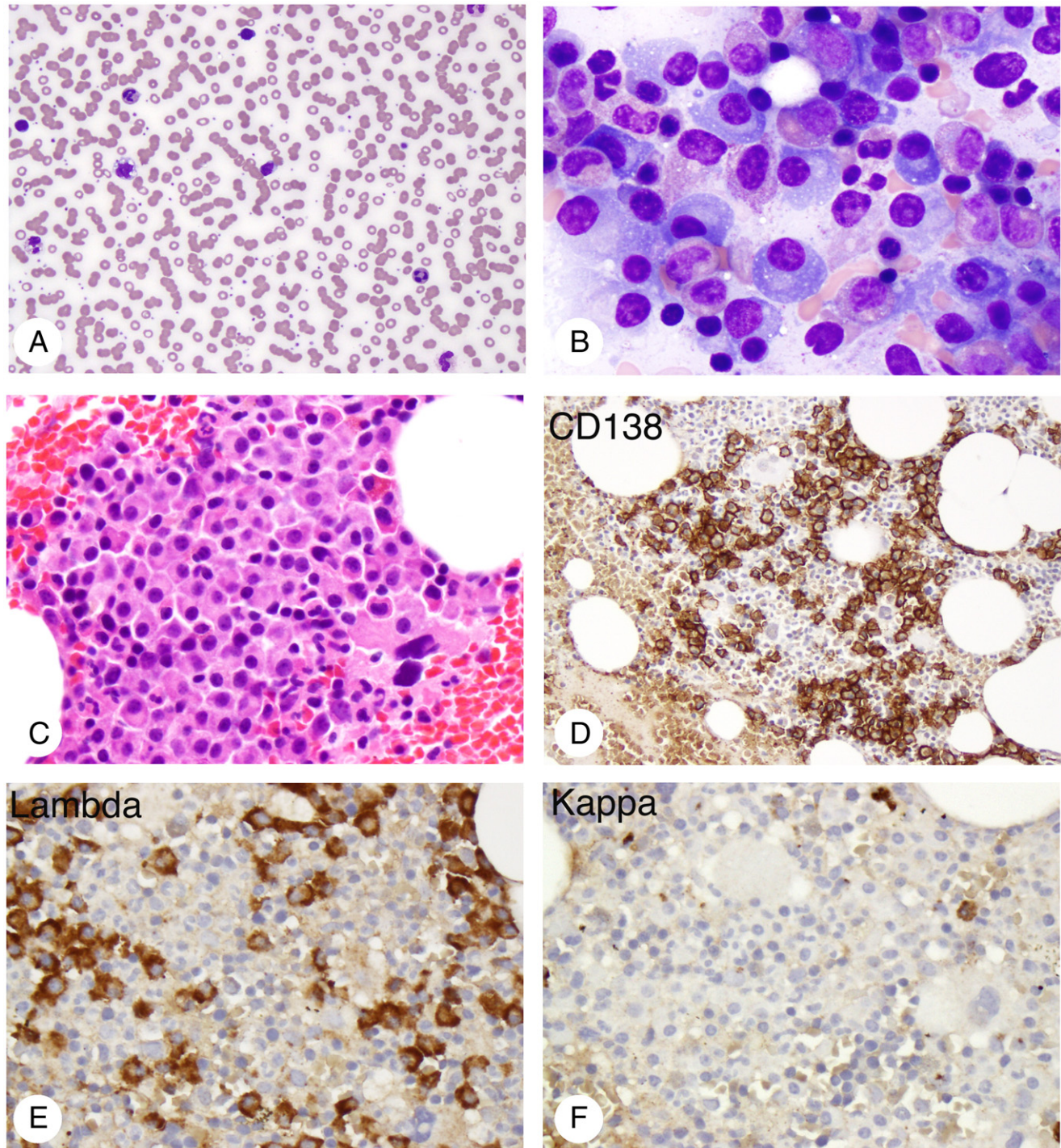


Fig. 4 Histopathology of peripheral blood and bone marrow. A, The peripheral blood showed Rouleaux formation. B, Frequent plasma cells were seen in the bone marrow aspirate. C, Focal sheets of plasma cells were easily appreciated in the clot section. D-F, The plasma cells were positive for CD138 (D), λ (E), but negative for κ (F). (A, Wright-Giemsa, original magnification $\times 200$; B, Wright-Giemsa, original magnification $\times 500$. C, H&E, original magnification $400\times$; D, E and F, original magnification $\times 200$, $\times 400$, and $\times 400$, respectively).

~5% proliferation index. In situ hybridization for EBV (EBER) is negative.

3.2.2. Peripheral blood and bone marrow

To investigate whether the plasma cell neoplasia identified in the orbital mass represented an extramedullary manifestation of a PCM or an isolated plasmacytoma, a bone marrow biopsy was performed. At the time of the bone marrow biopsy, as shown in the Table, the peripheral blood smear showed microcytic hypochromic moderate anemia with Rouleaux formation (Fig. 4A) and rare circulating plasma cells. The bone marrow aspirate smears contained cellular spicules with increased plasma cells with a 200-cell count of approximately 30% plasma cells (Fig. 4B). The core biopsy was small and fragmented, but the clot section showed ~60% overall cellularity with plasma cells comprising approximately 40% of total cellularity (Fig. 4C). The plasma cells were arranged in interstitial fashion and formed clusters (Fig. 4D). These plasma cells were positive for λ (Fig. 4E), but negative for CD19, CD20, cyclin D1, and κ (Fig. 4F).

3.3. Conventional karyotyping and FISH

Conventional karyotyping showed 46,XX in all 20 cells examined. FISH performed on an unenriched cell population using the following probes *D13S319* (13q14.3), *p53* (17p13), *CCND1/IGH* (translocation 11;14), *FGFR3/IGH* (translocation 4;14), *MAF/IGH* (translocation 14;16), and *EGR1* (5q31), *D7S486* (7q31) revealed no deletion of 13q14.3, p53, epidermal growth factor 1, or 7q31, there was no t(11;14), t(4;14) or t(14;16).

3.4. Quantitative immunoglobulins, SPEP, and IFE

The quantitative serum immunoglobulin values obtained using monoclonal antibodies and pertinent blood chemistry were summarized in the Table. The serum free κ to λ light chain ratio is 0.02.

To quantify the amount of M-protein and identify the isotype of the immunoglobulin heavy chain, SPEP and IFE were performed on the peripheral blood. As seen in Fig. 5A,

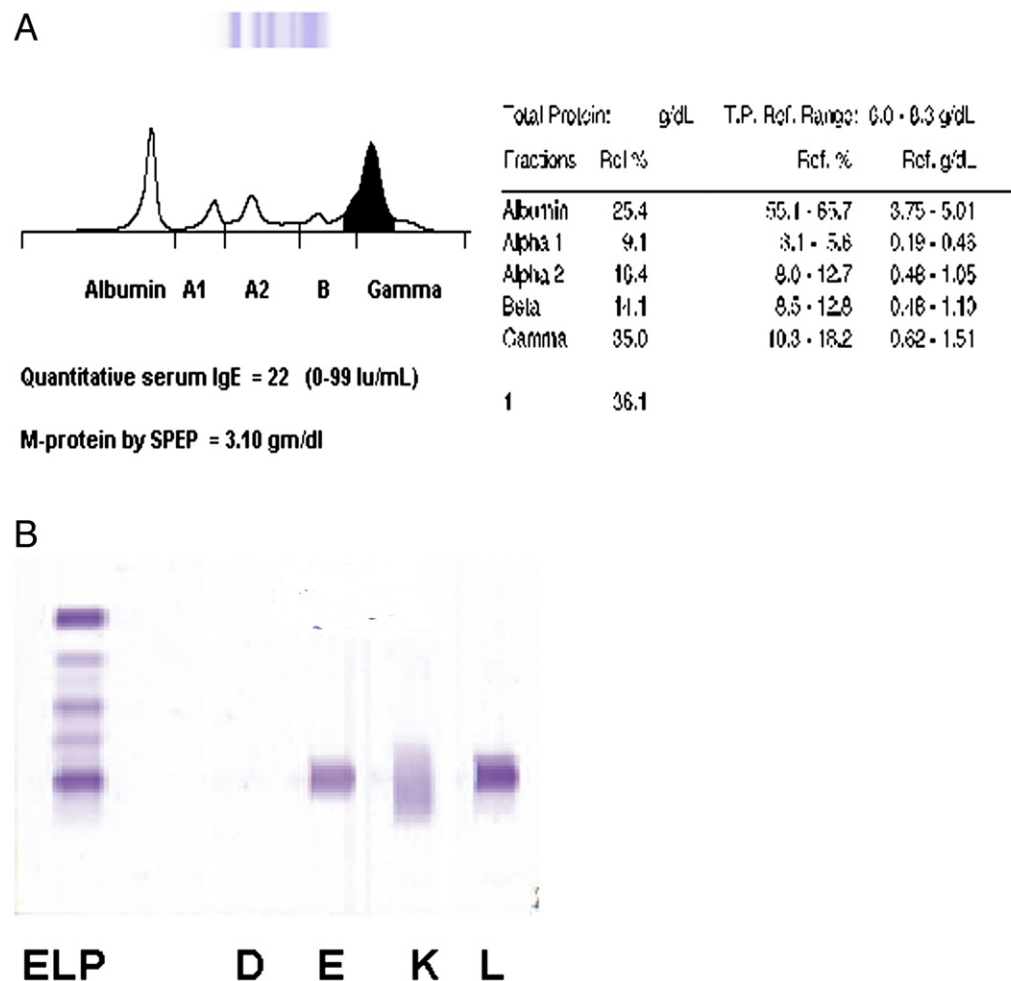


Fig. 5 Serum protein electrophoresis (SPEP) and immunofixation (IFE): SPEP (A) showed an IgE M-spike of 2.13 grams/dL, and the IgE clonal abnormality was confirmed by IFE (B) using polyclonal anti-IgE antibody done by nephelometry.

the M-protein was 31 g/L. IFE using IgG, IgA, and IgM yielded a monoclonal λ light chain with no heavy chain. Further testing for IgD and IgE using polyclonal anti-IgD and anti-IgE antibody, respectively, to our surprise, showed a distinct band in the IgE as well as the λ light chain (Fig. 5B), thus confirming the presence of an IgE- λ isotype M-protein.

3.5. Additional radiologic findings

After the diagnosis of this rare IgE- λ PCM was established, further work-ups for staging were conducted. PET/CT scans showed abnormal FDG uptakes in multiple areas including the bilateral neck (most prominently left level 2 nodal station with maximum SUV of 8), posterior neck soft tissues, bilateral retro-orbital regions, large lobulated area in the anterior mediastinum (maximum SUV 9.4), left hilum, foci in numerous ribs bilaterally, multiple subcutaneous nodules throughout the anterior and posterior thoracic wall, anterior and posterior abdominal wall, and soft tissues of the lower extremities bilaterally. Within the abdomen and pelvis, numerous FDG avid mesenteric, portal hepatis, retroperitoneal, and inguinal lymph nodes were present. The spleen contained multiple small focal areas of moderately increased FDG activity. In the pelvis, there was a multilobulated right adnexal mass (11 cm $\times$ 10 cm, max SUV 13.4). In addition, widespread osseous foci of abnormal radionuclide activity were seen scattered throughout the axial and appendicular skeleton including bilateral upper and lower extremities with concurrent CT images demonstrating a permeative lytic pattern throughout the osseous structures, most severe in the left sacrum with associated cortical disruption. The multiple small pulmonary nodules seen on chest CT did not demonstrate significant FDG activity.

3.6. Treatment and response to treatment

Given her multi-system end organ life-threatening disease, the patient was given a burst of dexamethasone 40 mg PO daily $\times$ 4 days and started 10 fractions of radiation to left orbit, sacrum, and left humerus. She was also treated with a bisphosphonate, which was continued on a monthly basis. Given the aggressive nature of her disease, after completion of radiation, the patient was initiated on combination chemotherapy containing velcade, thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide, and dexamethasone. Lovenox was used as prophylaxis. The chemotherapy course was complicated with neutropenic fever that responded well to broad-spectrum antibiotics. Chest CT on approximately Day 16 of treatment showed some response manifested by smaller left axillary and subpectoral lymph nodes now measuring up to 1 cm compared to previously (up to 1.7 cm), smaller right axillary and subpectoral lymph nodes measuring up to 1.4 cm compared to 2.3 cm previously. Anterior mediastinal soft

tissue abnormality in aggregate measures on the order of 3.1 $\times$ 4.4 cm compared to 4.5 $\times$ 7.3 cm previously. Scattered bilateral pulmonary nodules were generally smaller. Scattered subcutaneous nodules were grossly smaller (eg, 1.1 cm compared to 1.4 cm). Osseous lesions were unchanged.

SPEP done after cycle one showed a decrease in M-protein to 11.4 g/dL compared to the pre-treatment level of 31 g/L. CA-125 decreased to 23 IU/mL.

After recovery from the first cycle of chemotherapy and prior to the second cycle of chemotherapy, the patient underwent nail stabilization of the right femur, which was at extreme risk for pathologic fracture. The patient is now finishing her second cycle with no definitive evidence of residual plasma cell myeloma in the marrow. Depending on her response assessment, we hope to mobilize stem cells with plans for high-dose melphalan with autologous stem cell rescue.

Unfortunately, owing to lack of social supports and medical noncompliance, she was not a transplant candidate. She was next treated with lenalidomide, bortezomib, and dexamethasone. However, she did not tolerate the lenalidomide and was on it only for about a week before being admitted for nausea and vomiting. Abdomen/pelvis CT showed progression of disease. After her nausea and vomiting were controlled, she was discharged with plans for cyclophosphamide, bortezomib, and dexamethasone. The patient was readmitted shortly thereafter with altered mental status. CT of the head showed numerous masses throughout both cerebral and cerebellar hemispheres, and brain stem. There was associated vasogenic edema and she was started on steroids. Cerebrospinal fluid was obtained and showed numerous plasma cells (Fig. 6), which comprised 74% of the total cell count (21/mm³). Flow cytometry (data not shown) revealed these plasma cells were λ restricted. Discussion was held with family and the decision was to place patient on comfort care.

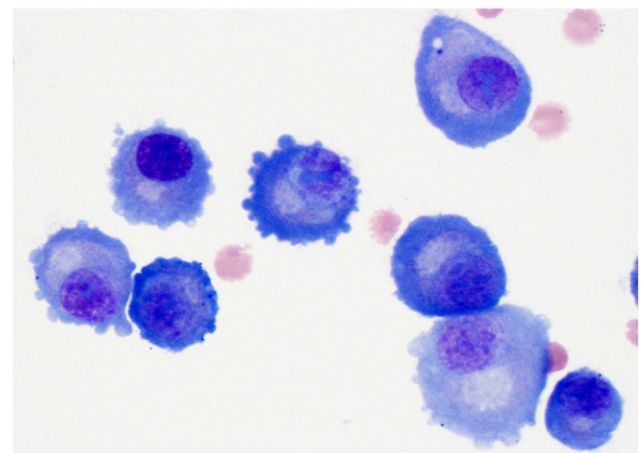


Fig. 6 Numerous plasma cells in CSF were easily appreciated (Wright-Giemsa, original magnification $\times$ 500).

4. Discussion

The case described here has several unique features. First, it occurred in a young age under 30 years old; secondly, it presented initially as an orbital mass; thirdly, it is an IgE PCM; fourthly, the patient's IgE PCM at the initial diagnosis involved multiple sites with at least one histologically and immunophenotypically proven extramedullary involvement; lastly, the myeloma is clinically aggressive with CNS involvement. To the best of our knowledge, this is the first reported IgE PCM with multiorgan/system involvement including CSF and under the age of 30. It is of interest to point out that while the quantitative serum immunoglobulin measurements using monoclonal antibody showed normal value of IgE (Table), which may well represent the normal IgE component, the presence of monoclonal IgE M-protein was only detected using polyclonal anti-IgE antibody in IFE (Fig. 5B), suggesting structural abnormality within the IgE molecules secreted by the neoplastic plasma cells.

PCM is typically a disease of the elderly with the median age of presentation at 70. Patients with PCM under the age of 30 have been rarely reported. For example, Blade et al reported 10 cases of PCM in patients younger than 30 years old [1]. In their study, the frequency of PCM in patients younger than 30 years old was 0.3% over a span of approximately 35 years [1]. Some studies have suggested that young and adolescent patients with PCM may have a longer survival but an atypical presentation [11], and others have showed a more aggressive disease process [13]. Similar to what has been previously reported [13], our patient's clinical presentation was atypical (orbital mass) and complex and showed clinical evidence of a far more aggressive form of PCM compared to older patients.

Among the previously reported cases of PCM in patients under 30 years old, a majority of them have been described to have extramedullary involvement at initial presentation. The extramedullary locations ranged from breast, orbit, nasopharyngeal, to liver and spleen [11,14-16]. In our patient, the initial presentation included orbital mass, soft tissue masses, lymphadenopathy, and multiple lytic bone lesions, although definitive involvement of soft tissue, lymph nodes and lytic bone lesions have not been confirmed due to lack of biopsy from these sites.

Generally speaking, the differential diagnosis for orbital lesions is diverse and can show similar appearances on imaging studies, therefore, anatomical location, clinical information such as age, duration of symptoms, and presence or absence of pain can often help narrow down the differential diagnosis. In children, the differential diagnosis of an orbital lesion includes retinoblastoma, rhabdomyosarcoma, metastasis of neuroblastoma and sarcoma, leukemia, and fibro-osseous lesion. The differential diagnosis in adults includes pseudotumor, thyroid orbitopathy, uveal melanoma, meningioma, metastasis of carcinoma, plasma cell myeloma, lymphoma, and fibro-osseous lesion. In our case, the patient

presented with an orbital mass abutting the left medial rectus muscle, which was initially thought to be a manifestation of idiopathic myositis. The top differential diagnosis of a mass in this location in an adult is pseudotumor, lymphoproliferative disorder, or thyroid orbitopathy. Pseudotumor, a diagnosis of exclusion, will usually present with non-specific inflammation, pain, edema, and respond to steroid treatment. Lymphoproliferative disorders, with 60% to 90% being non-Hodgkin lymphomas, will usually have predilection for the lacrimal gland and show enhancement on imaging. Lymphomas with muscle involvement can mimic thyroid orbitopathy, which is most commonly associated with Grave's disease, which is the most common cause of adult proptosis. Multiple myeloma involvement is exceeding rarely based on location, age, and radiological findings.

Orbital involvement in PCM is considered rare. Based on a literature review by Burkat et al, in 2009 [12], among the 52 cases of orbital involvement by PCM reported, the average age was 56.5, and only 7.7% (4/52) reported cases were in patients 30 years or younger. The most common clinical symptom was proptosis followed by other visual field disturbances. Three quarters of the cases showed predilection for the supero-temporal quadrant of the bony orbit. Of the cases with available immunoglobulin results, approximately half of the patients were IgG and no cases of IgE were ever reported [12]. Contrary to the common belief that orbital involvement is often the initial presentation of PCM [17,18], only close to one-third (35%, 18/52) of the cases had orbital symptoms being the initial presentation of PCM [12]. In our case, the patient came to the hospital with the complaint of visual disturbance and proptosis without a prior history of PCM, thus the orbital mass and symptoms are the initial presentation of our case.

Among the various immunoglobulin subtypes of PCMs, more than 90% of them are IgG, IgA, or light chains. IgD and non-secretory types are uncommon, but IgM and IgE are extremely rare, in fact, none of the 1027 newly diagnosed PCM was IgE [19]. IgE PCM was first published by Johansson et al in 1967 [2], and since then, only 47 cases have been reported. Almost all of the cases were in the form of a single case report with one study containing two cases of IgE PCM [20]. Clinical presentations and features of IgE PCM varied from a more aggressive form of myeloma with shorter overall survival, a higher frequency of plasma cell leukemia, to a high incidence of osteoblastic bone lesions [6,7]. A case of prolonged survival, on the other hand, has been documented as well [4]. Other rare clinical presentations included cutaneous manifestation, systemic amyloidosis, and elevated serum CA125 [8-10]. Our patient's clinical presentation also included lytic bone lesions and clinical evidence of involvement of the mesentery and lymph nodes, but she also presented with an orbital mass, which differed from what has been previously reported. The peripheral blood was involved by circulating plasma cells but was not considered leukemic (<20% circulating plasma cells). The serum CA125 level in our patient was indeed elevated initially (91 U/mL [reference limits 0-34 U/mL]) but decreased

to within normal range after the first cycle of treatment. It has been previously suggested that cytokines such as interleukin (IL)-1 β and tumor necrosis factor- α (TNF- α) secreted by myeloma cells might lead to secretion of CA125 by mesothelial cells [21]. Given the extent of peritoneal involvement in our patient; it does seem to confirm the correlation between elevated CA125 level and abdominal involvement.

Avet-Loiseau et al reported high incidence of translocation t(11;14) in rare PCMs including IgM, IgE, and non-secretory types [20]. t(11;14) was found in 7 of 8 IgM myelomas, 11 of 14 non-secretory myelomas, and 2 of 2 IgE myelomas. In later case reports of IgE myeloma, t(11;14) was present in two additional cases as well [6]. Among the more common types of PCM (IgG and IgA), the finding of t(11;14) involving the *BCL-1* gene is associated with a “lymphoplasmacytic” morphology and a more favorable prognosis. In our case, both the conventional karyotyping and FISH showed no genetic aberrancy including t(11;14). Due to the limited number of cases, the prognostic significance of t(11;14) involving IgH and *BCL-1* in IgE PCM needs further studies.

Optional treatment options and prognosis for rare types of PCM including IgE are little known. In comparing somewhat shorter survival in IgE PCM than in common types of PCM (IgG or IgA) by the standard therapy [22], the overall survival of patients with IgE PCM is also poor even following autologous transplantation but substantially better than that reported for patients who were not transplanted. In the cohort of 13 IgE myelomas [22], the median overall survival was the shortest of all groups, and the post-transplant non-relapse mortality rate was also higher. For our patient, the initial plan is to move her toward an autologous stem cell transplant with high-dose melphalan after the completion of chemotherapy.

In summary, we report the first case of IgE- λ PCM in a patient under the age of 30, with orbital mass as the initial presentation and subsequent discovery of systemic disease involvement. IgE PCM is by far the rarest subtype of PCM with variable clinical presentation and poor prognosis and treatment outcomes, therefore, multi-mortality approaches is needed to make the correct diagnosis in order to guide appropriate treatment options.

References

- [1] Blade J, Kyle RA, Greipp PR. Multiple myeloma in patients younger than 30 years. Report of 10 cases and review of the literature. *Arch Intern Med* 1996;156:1463-8.
- [2] Johansson SGO, Bennich H. Immunological studies of an atypical (myeloma) immunoglobulin. *Immunology* 1967;13:381-94.
- [3] Chiu W, Pullon H, Woon ST, Oei P, The R, Ameratunga R. IgE-type multiple myeloma with the late development of IgA2 kappa and plasma cell leukemia. *Pathology* 2010;42:82-4.
- [4] Hayes MJ, Carey JL, Krauss JC, Hedstrom DL, Gulbranson RL, Keren DF. Low IgE monoclonal gammopathy level in serum highlights 20-yr survival in a case of IgE multiple myeloma. *Eur J Haematol* 2007;78:353-7.
- [5] Kairemo KJ, Lindberg M, Prytz M. IgE myeloma: a case presentation and a review of the literature. *Scand J Clin Lab Invest* 1999;59:451-6.
- [6] Takemura Y, Ikeda M, Kobayashi K, et al. Plasma cell leukemia producing monoclonal immunoglobulin E. *Int J Hematol* 2009;90:402-6.
- [7] Macro M, Andre I, Comby E, et al. IgE multiple myeloma. *Leuk Lymphoma* 1999;32:597-603.
- [8] Wozney JL, Ahmed F, Bayerl MG, Ehmann WC, Talamo G. Skin involvement in immunoglobulin E multiple myeloma. *J Clin Oncol* 2009;27:637-8.
- [9] Hagihara M, Hua J, Inoue M, Michikawa N. An unusual case of IgE-multiple myeloma presenting with systemic amyloidosis 2 years after cervical plasmacytoma resection. *Int J Hematol* 2010;92:381-5.
- [10] Wang ML, Huang Q, Yang TX. IgE myeloma with elevated level of serum CA125. *J Zhejiang Univ Sci B* 2009;10:559-62.
- [11] Maeda K, Abesamis CM, Kuhn LM, Hyun BH. Multiple myeloma in childhood: report of a case with breast tumors as a presenting manifestation. *Am J Clin Pathol* 1973;60:552-8.
- [12] Burkat CN, Van Buren JJ, Lucarelli M. Characteristics of orbital multiple myeloma: a case report and literature review. *Surv Ophthalmol* 2009;54:694-704.
- [13] Clough V, Delamore IW, Whittaker JA. Multiple myeloma in a young woman. *Ann Intern Med* 1977;86:117-8.
- [14] Bernstein SC, Perez-Atayde AR, Weinstein HJ. Multiple myeloma in a child. *Cancer* 1985;56:2143-7.
- [15] Kaste SC, Ripps LG, Pedrosa F, Ribeiro RC. Multiple myeloma in an adolescent. *Pediatr Radiol* 1992;35:341-2.
- [16] Harster GA, Krause JR. Multiple myeloma in two young postpartum women. *Arch Pathol Lab Med* 1987;111:38-42.
- [17] Fay AM, Leib ML, Fountain KS. Multiple myeloma involving the orbit. *Ophthal Plast Reconstr Surg* 1998;14:67-71.
- [18] Rodman HI, Font RL. Orbital involvement in multiple myeloma. *Arch Ophthalmol* 1972;87:30-5.
- [19] Kyle RA, Gertz MA, Witzig TE, et al. Review of 1027 patients with newly diagnosed multiple myeloma. *Mayo Clin Proc* 2003;78:21-33.
- [20] Avet-Loiseau H, Garand R, Lode L, Harousseau JL, Bataille R. Translocation t(11;14)(q13;q32) is the hallmark of IgM, IgE, and nonsecretory multiple myeloma variants. *Blood* 2003;101:1570-1.
- [21] Dilek I, Ayakta H, Demir C, Meral C, Ozturk M. CA125 levels in patients with non-Hodgkin lymphoma and other hematologic malignancies. *Clin Lab Haematol* 2005;27:51-5.
- [22] Morris C, Drake M, Apperley J, et al. Efficacy and outcome of autologous transplantation in rare myelomas. *Haematologica* 2010;95:2126-33.