Open Journal of Pathology, **2012, 2, 155-158**
Published Online October 2012 (http://www.SciRP.org/journal/ojpathology)
http://dx.doi.org/10.4236/ojpathology.2012.24029

Rapid Disappearance of Testicular Plasmacytoma after Treatment with Lenalidomide plus Dexamethasone

Masao Hagihara[1*], Morihiro Inoue[1], Jian Hua[1], Nobuyasu Iwaki[1], Kosuke Yoshioka[2], Takeshi Kobayashi[2]

[1]Department of Hematology, Eiju General Hospital, Tokyo, Japan; [2]Hematology Division, Tokyo Metropolitan Cancer and Infectious Diseases Center, Komagome Hospital, Tokyo, Japan.
Email: *hagihara@eijuhp.com

Received June 2nd, 2012; revised July 6th, 2012; accepted July 18th, 2012

ABSTRACT

We describe a rare case of testicular plasmacytoma first manifesting as a relapse. The patient was initially diagnosed with IgG-λ-type multiple myeloma and treated with melphalan and prednisolone plus bortezomib, achieving a complete remission. Four months later, his left scrotum began to swell and pathological investigation of a needle biopsy specimen revealed proliferation of plasma cells expressing IgG-λ, confirming myeloma recurrence. However, bone marrow aspiration samples showed no significant increase in myeloma cells and there was no skewed deviation of the κ/λ ratio on flow-cytometric analysis. The extramedullary tumors disappeared completely soon after treatment with lenalidomide plus dexamethasone, and the patient was judged to be in very good partial remission based on negative M-protein results by serum immunoelectrophoresis. This is the first report, to our knowledge, describing complete disappearance of a testicular plasmacytoma after treatment with lenalidomide as the key-drug.

Keywords: Plasmacytoma; Testis; Lenalidomide

1. Introduction

Extramedullary plasmacytoma (EMP) is a plasma cell neoplasm that occurs as a solitary lesion or develops simultaneously or secondarily to multiple myeloma (MM). EMP can involve a wide variety of anatomical sites, but approximately 85% of all cases have disease in the head and neck region [1]. Testicular plasmacytoma is extremely uncommon and estimated to account for 0.03% - 0.1% of all testicular malignancies or around 2% of all plasma cell neoplasms [2-5]. In previous reports, the majority of testicular plasmacytoma cases had been diagnosed based on local manifestation of systemic plasma cell disorders rather than as having a solitary EMP [2,6-9].

Herein, we present a rare case in which testicular involvement without bone marrow invasion was observed 4 months after the first complete remission of MM had been achieved using a regimen that included bortezomib. Furthermore, the extramedullary tumor disappeared completely after treatment with another novel anti-myeloma reagent, lenalidomide.

2. Case Report

A 78-year-old man was admitted to our hospital in March 2011. Two years before (in 2009), the patient had complained of pain in multiple bones, which led to a diagnosis of IgG-λ-type MM, Durie-Salmon stage II, with multiple bone fractures (ribs, thoracic and lumbar vertebrae), elevated serum IgG (6075 mg/dL) and proliferation of plasma cells (18% of whole nucleated cells) in bone marrow. After receiving 10 cycles of melphalan and prednisolone plus bortezomib (MPV) treatment, he had achieved a complete remission in October 2010. In February 2011, swelling in his left scrotum manifested. Although there were no significant changes in laboratory data, his serum IgG level was slightly increased (1872 mg/dL) and a monoclonal band of IgG-λ was identified by immunoelectrophoresis. At that time, a needle biopsy of the left scrotum was performed, and the proliferation of plasma cells was revealed by pathological investigation. As shown in **Figure 1**, the plasma cells expressed the IgG-λ light chain and CD138 when examined immunohistochemically, confirming the tumor to be a myeloma recurrence.

On admission, magnetic resonance imaging (MRI) showed an enlarged mass in the left scrotum and chest computed tomography (CT) demonstrated a tumor in the right thoracic pleura (**Figures 2(a)** and **(c)**). However, bone marrow aspiration samples showed no significant

*Corresponding author.

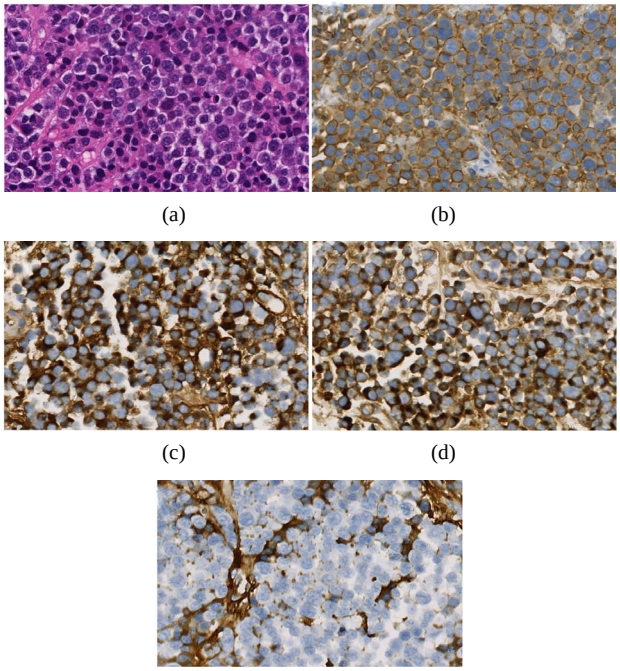

Figure 1. Proliferation of plasma cells in testicular tissue. The sections were stained with (a) Hematoxylin and eosin; (b) Anti-CD38; (c) Anti-IgG; (d) Anti-λ; (e) Anti-κ; Original magnification ×40.

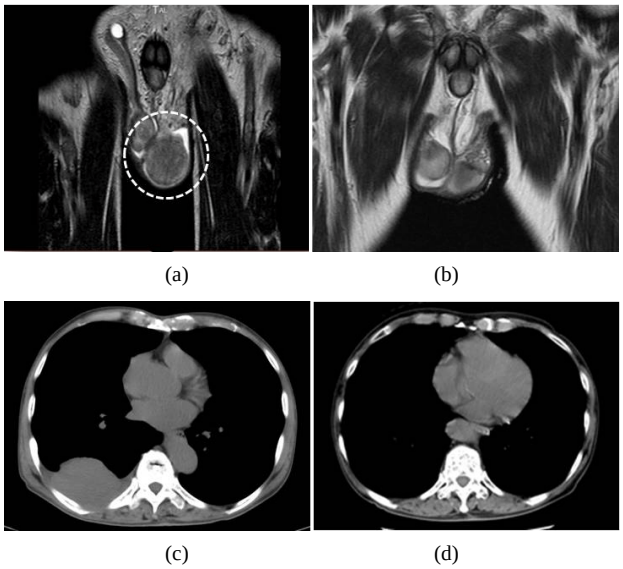

Figure 2. MRI and CT findings at disease onset ((a) and (c), respectively) and after treatment ((b) and (d), respectively). The masses in the left scrotum and right thoracic pleura disappeared completely after Ld treatment.

increase of myeloma cells, and flow-cytometric analysis did not reveal a skewed deviation of the κ/λ ratio. The patient was treated with lenalidomide (L: 25 mg/day × 21 days) plus dexamethasone (d: 20 mg on days 1, 8, and 15). After 3 cycles of this treatment, total IgG decreased to within normal range (less than half of the initial level) and the left testicular and right thoracic tumors both disappeared completely (**Figures 2(b)** and **(d)**). As of October 2011, the patient has continued to receive monthly Ld treatments and is thought to have entered a period of very good partial remission (VGPR) based on negative M-protein results obtained using serum immunoelectrophoresis. During these treatments, a moderate skin eruption transiently appeared but resolved rapidly with short-term application of an anti-allergic drug. The only other adverse reaction was grade 3 neutropenia, From December 2011 through April 2012, the patient has received maintenance therapy with low-dose lenalidomide therapy (10 mg/dL × 3 weeks per every 28-day cycle) and has remained in VGPR.

3. Discussion

EMP is a rare tumor that can appear at various anatomical sites but is most frequently found in the respiratory system or gastrointestinal tract as well as the lymph nodes or skin [5]. Although testicular plasmacytoma is a relatively rare disorder, more than 50 cases have been reported since its first description by Ulrich [10,11]. Anghel *et al*. reviewed 51 cases in 2002. According to their report, the median age of patients was 51 years and higher than that of testicular cancer [12]. Moreover, they mentioned that the occurrence of a solitary testicular plasmacytoma without MM was unusual [6]. In fact, 34 of the 51 cases had previous or simultaneous MM and/or EMP. Twenty of these 34 cases had a fatal clinical course with progressive disease with only 4 patients surviving. In one of Anghel's cases, the plasmacytoma showed a tendency to spread not only to the testis but also to other sites including multiple bones, the lung, skin, and pancreas [6].

EMP is widely regarded as being radiosensitive and can be successfully controlled with local radiotherapy [13]. For testicular EMP, an orchiectomy followed by chemotherapy or radiotherapy is considered to be a therapeutic option [14]. Turk *et al.* recently reported a case of MM that presented with a testicular plasmacytoma and multiple bone lesions [1]. The patient received chemotherapy consisting of melphalan and prednisolone and palliative radiotherapy after orchiectomy. In our case, as the patient had an extramedullary tumor not only in the testis but also in the thoracic wall, chemotherapy using lenalidomide plus low dose dexamethasone was selected as a salvage regimen without orchiectomy.

Since the first description by Krauth *et al.*, bortezomib has been recognized as an effective agent for EMP treatment [15,16]. However, thalidomide lacks efficacy against soft-tissue plasmacytoma [17]. Lenalidomide, an analogue of thalidomide, has much more potent anti-tumor activity [18] and the response is unaffected by

previous bortezomib treatment [19,20]. Rosenberg *et al.* presented a case of testicular plasmacytoma with previous MM in which regression of the mass was achieved using a combination of bortezomib and lenalidomide [21]. Furthermore, Carovo-Villas *et al*. recently reported that lenalidomide in combination with dexamethasone was effective against extramedullary plasmacytoma in patients with relapsed or refractory MM [22]. For their 18 reported cases, the overall response was 61%, including a complete disappearance in 44% of these cases. It was assumed that lenalidomide could have direct anti-proliferative mechanisms on myeloma cells irrespective of its existence in the bone marrow stroma or other tissue microenvironments [23]. Angiogenesis is promoted in plasmacytoma tissue, such that lenalidomide might exhibit anti-tumor activity especially through its anti-angiogenic effects [24]. Adams *et al.* reported that bortezomib did not penetrate into testicular tissue [25]. It might be the reason why plasmacytoma appeared especially in testis. Our experience might indicate that lenalidomide could possibly be distributed in testis.

Carovo-Villas *et al.* noted that 3 of 11 patients relapsed and new strategies were thus necessary to overcome treatment resistance of the disease [22]. Recently, abundant encouraging data have been accumulated regarding the clinical significance of maintenance therapy using lenalidomide [26]. Therefore, we are still now giving this patient low-dose lenalidomide alone, as maintenance therapy, even though attained VGPR.

In conclusion, we demonstrated an excellent clinical effect of lenalidomide on a rare type of testicular plasmacytoma in a patient with relapse after administration of bortezomib, the widely accepted first choice for the EMP treatment.

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