American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2019; 20: 1623-1629
DOI: 10.12659/AJCR.917670

Received: 2019.05.21
Accepted: 2019.08.23
Published: 2019.11.05

A Case of Multiple Myeloma in a 17-Year-Old Girl Treated with Autologous Hematopoietic Stem Cell Transplantation (ASCT)

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 17
Final Diagnosis: Multiple myeloma
Symptoms: Bone pain
Medication: —
Clinical Procedure: —
Specialty: Hematology

Objective: Unusual clinical course
Background: Multiple myeloma is mainly a disease of the elderly. The diagnosis of multiple myeloma in patients under 30 years of age is rare. A rare case is presented of a 17-year-old girl diagnosed with multiple myeloma who was successfully treated with autologous hematopoietic stem cell transplantation (ASCT).
Case Report: A 17-year-old Vietnamese girl presented with pain in the left hip and difficulty walking. She was diagnosed with stage IIIA IgG lambda (λ) multiple myeloma and was treated with a bortezomib-based chemotherapy regimen followed by ASCT. The patient showed a good response to treatment. At 14-month follow-up, her bone pain had resolved, and her ability to walk was improved.
Conclusions: A rare case of multiple myeloma is presented in a 17-year-old girl who responded well to ASCT.

MeSH Keywords: Multiple Myeloma • Plasmacytoma • Antineoplastic Agents

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/917670

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Background

Multiple myeloma, also known as plasma cell myeloma, myelomatosis, and Kahler's disease, arises from a clonal population of plasma cells [1]. Multiple myeloma accounts for approximately 10% of all hematologic malignancies [2]. According to recent data from the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) program, multiple myeloma is more common in men than women, and occurs more frequently between the ages of 65–74 years, with a median age at diagnosis of 69 years [3]. Between 2012–2016, the number of new cases per 100,000 persons was 8.7 for men and 5.6 for women [3]. The incidence of myeloma below 30 years of age is extremely low. SEER recently reported an incidence between 20–34 years, 35–44 years, 45–54 years, and 55–64 years of 0.5%, 2.7%, 10.6%, and 23.2%, respectively, with no reported cases in patients under 20 years of age [3].

Multiple myeloma is relatively uncommon in Vietnam, with an incidence of 530 new cases per year and a 5-year prevalence of 1,093 individuals [4]. A rare case is presented of a 17-year-old girl diagnosed with multiple myeloma who was successfully treated with autologous hematopoietic stem cell transplantation (ASCT).

Case Report

A 17-year-old girl presented to the department of orthopedics complaining of pain in the left hip joint that had been increasing for the previous month. She had no other significant personal or past medical history, and she had no significant family history. However, in the previous year, she had sustained injuries in a road traffic accident that left her with pain in the left hip joint. Although she had been treated at the time at a local hospital, no supporting documents were found for the diagnosis made or the treatment given, but she was not treated surgically.

On this admission to hospital, clinical examination showed limitation of movement in the left hip. Computed tomography (CT) imaging showed a lytic bone lesion in the wing (or ala) of the left ilium. The patient underwent a biopsy of the bone lesion. The histopathology of the bone biopsy was consistent with a diagnosis of plasmacytoma or multiple myeloma (Figure 1A, 1B).

She was then referred to the Blood Transfusion and Hematology Hospital, Ho Chi Minh City, Vietnam. At the time of hospitalization, the patient was dependent on crutches for walking. There were no signs and symptoms of hemorrhage, infection, splenomegaly, hepatomegaly, or lymphadenopathy. No abnormality was detected on cardiovascular or pulmonary examination, and her vital signs were normal.

The patient was further evaluated according to the protocol of the Blood Transfusion and Hematology Hospital and was diagnosed with IgG lambda (λ) multiple myeloma, stage IIIA, according to the Durie-Salmon staging system, or stage I disease according to the Revised International Staging System (R-ISS) for myeloma, and medium-risk disease [5,6]. The baseline disease characteristics of the patient are summarized in Table 1.

The patient underwent induction chemotherapy with bortezomib (1.3 mg/m^2 on days 1, 4, 8, and 11) and dexamethasone (40 mg on days 1–4 and days 8–11) every three weeks for four cycles followed by autologous stem cell transplant (ASCT)

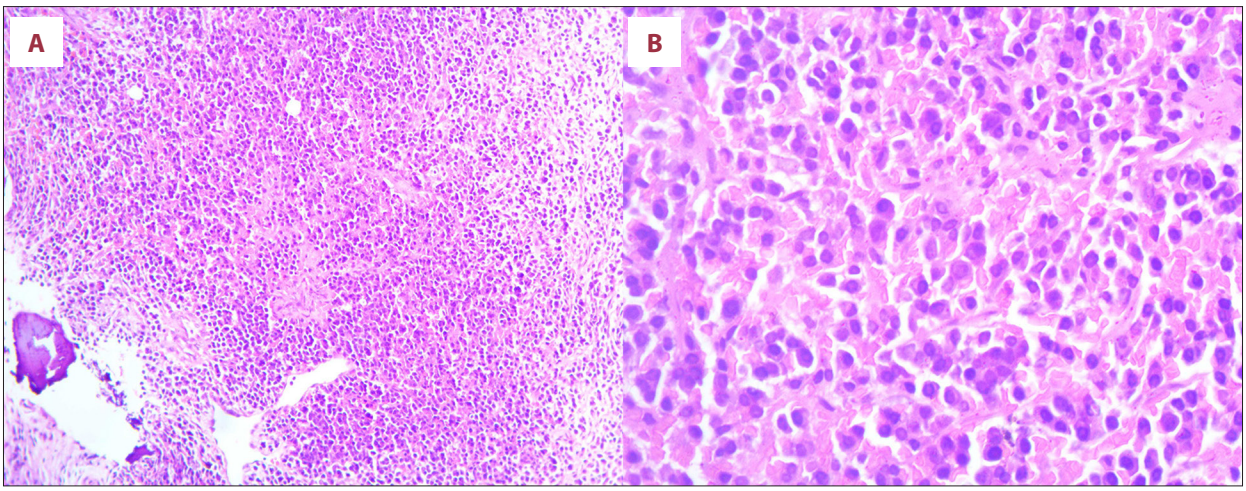

Figure 1. Photomicrographs of the histology of the bone biopsy in a 17-year-old girl with multiple myeloma. (**A**) The histology shows hypercellularity with a uniform population of plasma cells. Hematoxylin and eosin. (H&E). Magnification ×10. (**B**) Atypical plasma cells are seen at higher power, consistent with a diagnosis of plasmacytoma or multiple myeloma. H&E. Magnification ×40.

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Table 1. Baseline characteristics.

Performance status	ECOG: 2
Blood counts	Haemoglobin: 10.9 g/dl
	Platelet count: 214k/ul; White blood cell count: 5.54 k/ul
β2 microglobulin	1.49 mg/L
Serum quantitative Ig G	41.73 g/L (7–16)
Serum immunofixation electrophoresis	IgG, Lambda
Serum protein electrophoresis	Albumin/Globulin: 0.66
Proteinuria of Bence Jones in urine	Negative
Bone marrow aspirate	Plasma cell #7%
Bone marrow biopsy	Plasma cell <5%
Tumour biopsy	Plasmacytoma
Flow cytometry	Plasma cell #3%
Karyotype	46, XX
Fluorescence *in situ* hybridization	No abnormality detected
X-ray and computed tomography scan	Several lytic lesions of left pubis and wing of ilium
Positron emission tomography scan	Multiple lytic bone lesions, hyper attenuation of the femoral bone, increased metabolic activity

ECOG – Eastern Cooperative Oncology Group; Ig – immunoglobulin.

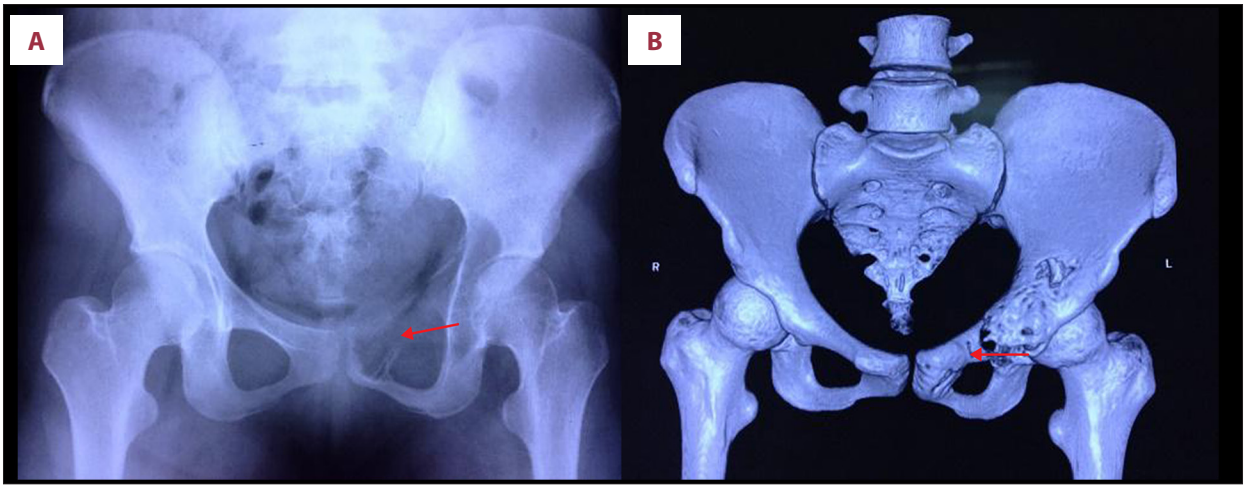

Figure 2. X-radiographs of the lytic bone lesions before and after treatment in a 17-year-old girl with multiple myeloma. (**A**) The bone lesion (arrow) in the wing (or ala) of the left ilium seen on X-ray before treatment. (**B**) The bone lesion (arrow) in the wing (or ala) of the left ilium seen on X-ray after autologous hematopoietic stem cell transplantation (ASCT).

with high-dose melphalan (200 mg/m^2 dose) followed by consolidation with bortezomib and dexamethasone for another two cycles.

Adjunctive treatment consisted of bisphosphonate at the beginning of every cycle and the use of analgesics. The patient was using crutches when walking and underwent physical therapy. Acyclovir and trimethoprim/sulfamethoxazole were given prophylactically. Observed adverse events included constipation reported during the first cycle of chemotherapy, which resolved without any medication or change in planned therapy.

At the end of induction therapy with four cycles of bortezomib and dexamethasone, her pain had completely subsided,

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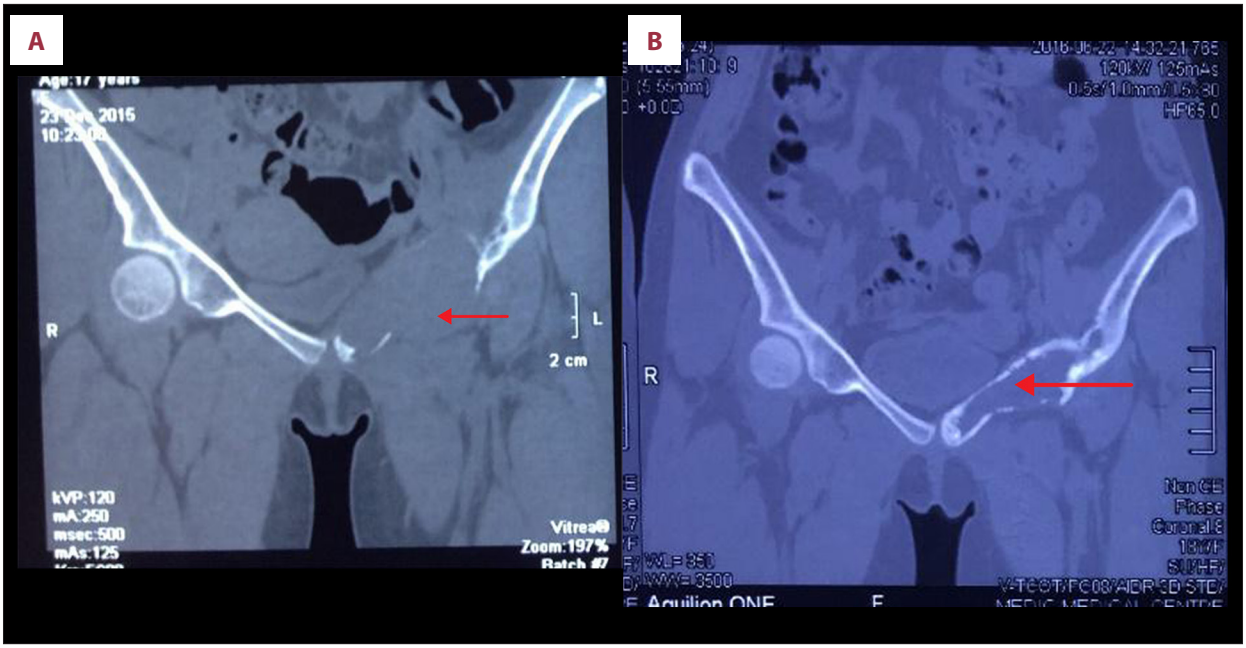
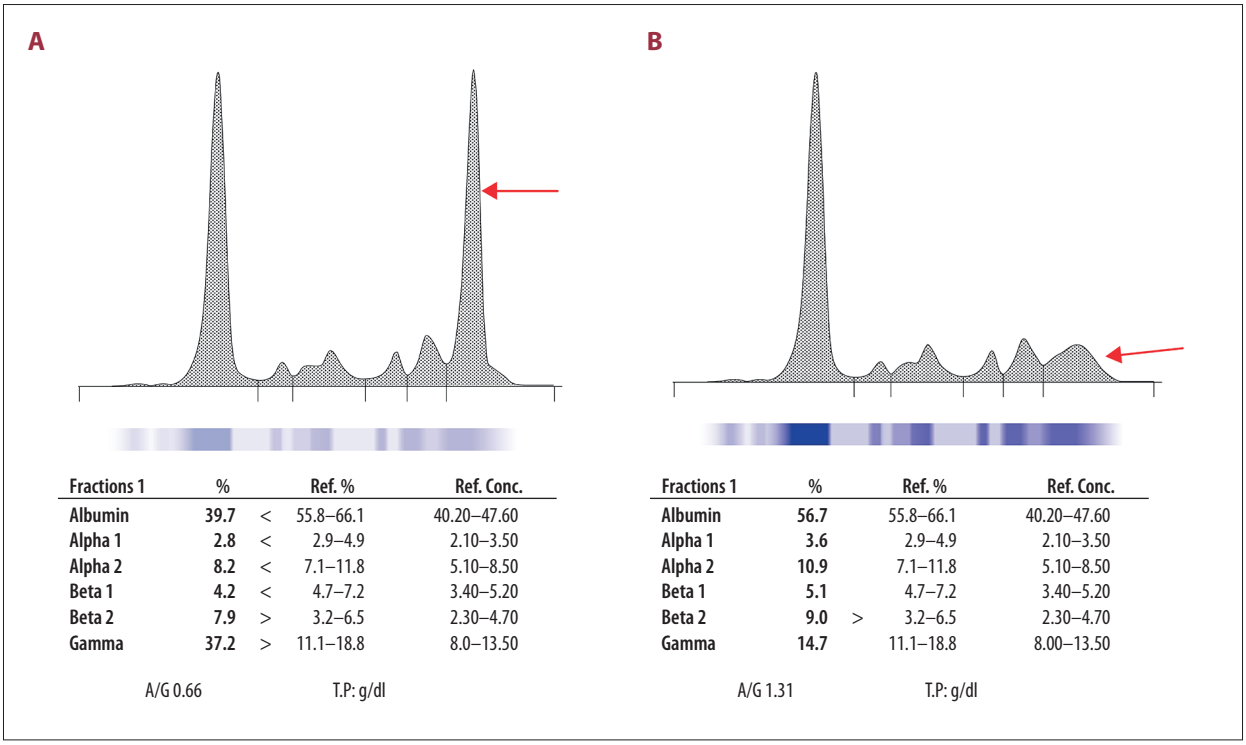


Figure 3. Computed tomography (CT) imaging of the lytic bone lesions before and after treatment in a 17-year-old girl with multiple myeloma. (**A**) The bone lesion in the wing (or ala) of the left ilium seen on CT before treatment. (**B**) The bone lesion in the wing (or ala) of the left ilium seen on CT after autologous hematopoietic stem cell transplantation (ASCT).



Fractions 1	%		Ref. %	Ref. Conc.
Albumin	39.7	<	55.8–66.1	40.20–47.60
Alpha 1	2.8	<	2.9–4.9	2.10–3.50
Alpha 2	8.2	<	7.1–11.8	5.10–8.50
Beta 1	4.2	<	4.7–7.2	3.40–5.20
Beta 2	7.9	>	3.2–6.5	2.30–4.70
Gamma	37.2	>	11.1–18.8	8.0–13.50

A/G 0.66 T.P: g/dl

Fractions 1	%		Ref. %	Ref. Conc.
Albumin	56.7		55.8–66.1	40.20–47.60
Alpha 1	3.6		2.9–4.9	2.10–3.50
Alpha 2	10.9		7.1–11.8	5.10–8.50
Beta 1	5.1		4.7–7.2	3.40–5.20
Beta 2	9.0	>	3.2–6.5	2.30–4.70
Gamma	14.7		11.1–18.8	8.00–13.50

A/G 1.31 T.P: g/dl

Figure 4. Protein electrophoresis for gamma globulin levels before and after treatment in a 17-year-old girl with multiple myeloma. (**A**) Protein electrophoresis for gamma globulin levels (red arrow) before treatment. (**B**) Protein electrophoresis for gamma globulin levels (red arrow) after autologous hematopoietic stem cell transplantation (ASCT).

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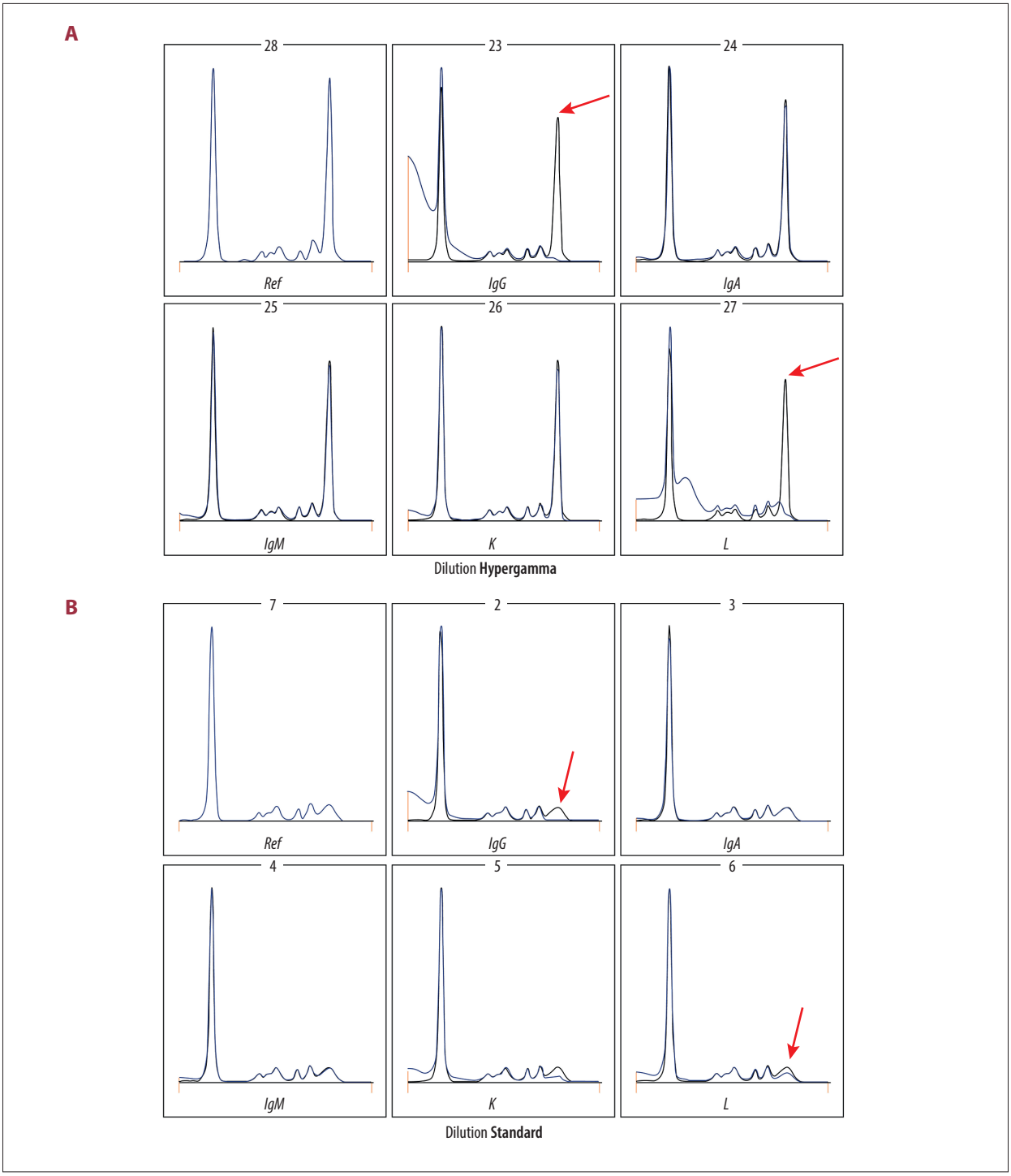

Figure 5. Immuno-electrophoresis for gamma globulin and free IgG lambda (λ) light chains before and after treatment in a 17-year-old girl with multiple myeloma. (**A**) Immuno-electrophoresis for gamma globulin (red arrow) and free IgG lambda (λ) light chains (red arrow) before treatment. (**B**) Immuno-electrophoresis for gamma globulin (red arrow) and free IgG lambda (λ) light chains (red arrow) after autologous hematopoietic stem cell transplantation (ASCT).

she began walking normally and achieved a very good partial response (VGPR) for multiple myeloma. X-ray confirmed that the bone mass had reduced in size following treatment (Figure 2A, 2B), and these findings were supported by computed tomography (CT) imaging (Figure 3A, 3B). The increased levels of gamma globulins that were detected before treatment

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Table 2. Clinical characteristics after induction and Post transplantation.

	After 4 cycles of induction	After stem cell transplantation
Performance status	ECOG: 0	ECOG: 0
Blood counts	Haemoglobin: 12 g/dl	Haemoglobin: 12.3 g/dl
	Platelet count: 192×10³/µl; White blood cell count: 8.36×10³/µl	Platelet count: 240×10³/µl; White blood cell count: 7.5×10³/µl
β2 microglobulin	1.3 mg/L	1.26 mg/L
Serum quantitative IgG	10.28 g/L	8.42 g/L
Serum immunofixation electrophoresis	Normal	Normal
Serum protein electrophoresis	Albumin/Globulin: 1.3	Albumin/Globulin: 1.31
Proteinuria of Bence Jones in urine	Negative	Negative
Bone marrow aspirate	Plasma cell #3%	Plasma cell #3%
Bone marrow biopsy	Plasma cell <5%	Plasma cell <5%
Tumour biopsy	–	–
Flow cytometry	–	–
Karyotype	46, XX	46, XX
X-ray and computed tomography scan	No increasing lesions	Recovery

ECOG – Eastern Cooperative Oncology Group; Ig – immunoglobulin.

returned to almost normal levels after treatment (Figure 4A, 4B), and immuno-electrophoresis showed that the IgG lambda (λ) component decreased after treatment (Figure 5A, 5B).

Following ASCT and consolidation therapy with two cycles of bortezomib and dexamethasone, the patient sustained the VGPR and was able to walk. Here clinical findings after induction treatment and ASCT are summarized in Table 2. The patient chose maintenance treatment with thalidomide (100 mg/day), and her clinical condition was stable at 14-month follow-up.

Discussion

This report is of an extremely rare clinical presentation of multiple myeloma in a 17-year-old girl. Multiple myeloma is very rare in people aged less than 30 years, accounting for about 0.3% of all cases. However, in this age group, the presenting clinical features and response to therapy are reported to be similar to that for patients of all ages who have multiple myeloma [7]. There have been previous sporadic reports in the literature of similar presentations of multiple myeloma in younger patients. Multiple myeloma has previously been reported involving the skull and ribs in a 23-year-old woman, as a solitary plasmacytoma of the tibia in a 21-year-old man, and a case of multiple myeloma has been previously reported in a 27-year-old man [8,9].

A study of 10,549 patients from the International Myeloma Working Group showed that the patients younger than 40 years of age were more likely to be male and to have more prolonged survival than patients older than 40 years [10]. In a multicenter retrospective study of 52 patients diagnosed with myeloma at the age of ≤30 years (age range, 8–30 years), the median overall survival was approximately 14 years. The prognosis of multiple myeloma in young patients was reported to be as good as if not better than that of myeloma patients overall, possibly because of the use of novel agents and hematopoietic stem cell transplantation (SCT) in younger patients [11]. The patient presented in this report showed a good response to treatment, which included autologous hematopoietic stem cell transplantation (ASCT), and this response was sustained for more than a year on clinical follow-up.

At the time this patient was being treated, antimyeloma agents available in Vietnam included bortezomib, dexamethasone, cyclophosphamide, and thalidomide. Common challenges for the management of myeloma in Vietnam include affordability of treatment, access to medicines, and patient compliance with treatment. Generic bortezomib was chosen in this case because of cost considerations. The use of bortezomib and thalidomide as part of the induction regimens can be associated with a risk of developing peripheral neuropathy, which can result in discontinuation of treatment. Because this patient was young and female, an effective and well-tolerated combination

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of bortezomib and dexamethasone was chosen as induction therapy [12]. The patient experienced one mild adverse event, which was constipation during the first treatment cycle, which resolved without the need for medical intervention.

After induction, the patient's symptoms improved, and she attained a very good partial response (VGPR). She underwent ASCT followed by consolidation maintenance treatment that extended the duration of response. The patient received consolidation therapy with bortezomib and dexamethasone for two cycles and still had a VGPR at the 14-month follow-up. The patient and her family were informed about the necessity of maintenance therapy, and the patient chose treatment with thalidomide in the maintenance phase. This decision was made due to financial and medical insurance issues and also to avoid the frequent hospital visits required for bortezomib injections. Adequate counseling was provided to the young girl regarding fetal teratogenicity associated with thalidomide. Her treatment response status remained stable at 14-month follow-up.

Conclusions

This case illustrates an atypical presentation of myeloma, however rare its incidence physicians should be aware of its possibility of occurrence and maintain a high degree of suspicion for achieving early diagnosis and optimum treatment. Treatment outcome of this case indicates that generic bortezomib based regimen coupled with stem cell transplantation is a good treatment option for MM with low cost. Availability of generics resulted in better access- Increase in usage of Bortezomib based regimen and treatment at lesser cost and in savings in overall Insurance budget of hospital.

Conflicts of interest

None.

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