Multiple Myeloma in Young pregnant Patient

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Abstract

Background: Multiple Myeloma (MM) is a relatively uncommon cancer that accounts for approximately 10 percent of all hematologic malignancies. It is an incurable disease and is behind about 20 percent of mortality from hematologic malignancy and 2 percent of mortality from all cancers. MM is usually characterized by the neoplastic proliferation of plasma cells producing a monoclonal immunoglobulin. The plasma cells proliferate in the bone marrow and can result in extensive skeletal destruction with osteolytic lesions, osteopenia, and /or pathologic fractures. MM is rarely seen in those younger than 35 years old. Despite those in the younger age group having been shown to have a more aggressive course, reportedly they have had similar responses to treatment compared to older patients.

Case: This case is about a young pregnant female who presented to the hospital with body ache and diplopia in her 30th week of pregnancy. Multiple Myeloma type IgA lambda was diagnosed. The baby was delivered prematurely but healthy. The patient was treated initially with bortezomib, cyclophosphamide, and dexamethasone (VCD) regimen along with radiation therapy and chemotherapy. The patient responded well to the treatment.

Conclusion: This case of Multiple Myeloma in a young pregnant female presented with unexplained symptoms and was diagnosed after presentation with neurological symptoms. Treatment with VCD regimen along with radiation therapy and chemotherapy showed excellent response. It highlights that multiple myeloma may present atypically in young patients and early diagnosis is important. The Case report is needed.to determine optimal treatment regimens for this subset of young patients.

Key words: Multiple Myeloma, young, pregnant, diplopia.

Introduction

Multiple Myeloma (MM) is a relatively uncommon cancer that accounts for approximately 10 percent of all hematologic malignancies. It is an incurable disease and is behind about 20 percent of mortality from hematologic malignancy and 2 percent of mortality from all cancers. The median age at diagnosis is 65 to 74 years; only 10 and 2 percent of patients are younger than 50 and 40 years, respectively. MM is also additionally slightly more frequent in men than in women (approximately 1.4:1) [1]. There are only 3 percent of cases that are reported have confirmed diagnosis before the age of 40. MM is extremely rare in people who are less than 35 years of age. The incidence is 0.02 to 0.03 percent. MM is not considered to be a genetic disorder, however, there are some rare cases where patients are affected on a familial basis [2-4]. Since having a pregnancy after 45 years of age is very uncommon, the association of pregnancy with multiple myeloma is very rare. Moreover, many of the signs of pregnancy such as back pain and anaemia can be very easily confused with signs and symptoms of multiple myeloma [5-7]. Multiple myeloma (MM) is usually characterized by the neoplastic proliferation of plasma cells producing a monoclonal immunoglobulin. The plasma cells proliferate in the bone marrow and can result in extensive skeletal destruction with osteolytic lesions, osteopenia, and/or pathologic fractures [8]. Most patients with MM present with signs or symptoms related to the infiltration of plasma cells into the bone or other organs or to kidney damage from immunoglobulin deposition. Common presentations include anemia, bone pain, elevated creatinine or serum protein, fatigue, and hypercalcemia. Another manifestation of multiple myeloma, Bence Jones proteinuria, is found to be more common (81%) in younger patients than in relatively older cases. The monoclonal antibodies produced by the neoplastic plasma cells are of 2 types, of which Bence Jones proteins are one. In myelomas, these protein bodies are secreted in the urine of the patient, thereby establishing the Bence Jones protein test as an effective diagnostic measure for myeloma [7&8]. Less common presentations that require urgent evaluation, rapid attention and intervention include spinal cord compression, acute kidney failure, severe hypercalcemia, and hyper viscosity. There is no cure, but treatments can slow its spread and sometimes allow the patient to get rid of the symptoms [9].

Case Presentation

A 35 years old married female patient previously healthy, presented on a few occasions with recurrent body ache in 2017. Both physical examination and laboratory test showed no abnormalities at that time. During pregnancy she had recurrent visits to the health centre due to back ache and weakness. Family history indicated diabetes mellitus and hypertension, with no incidence of any type of cancer. Later in her 30th week of pregnancy during her antenatal follow up, she was found to have intrauterine growth retardation and an incidental finding of anemia and hypercalcemia; also she was complaining of headache and left eye diplopia, and was then referred to the hospital April 2018. The laboratory analysis of the patient showed that she was suffering from anaemia. The calcium level was found to be 3.83 mmol/l, which is indicative of hypercalcemia. The renal function was also found to be disturbed with elevated creatinine levels of 109 mmol/l (Table 1). Imaging (MRI, CT on April 2018) showed: Widespread osteolytic lesions were seen involving the skull vault, skull base, mandible and visualized cervical vertebrae. Some lesions showed adjacent soft tissue component. At the skull base the soft tissue component was seen extending to the left cavernous sinus causing filling defect within the sinus. This soft tissue component was also extended to the left petrous apex and revealed multiple osteolysis; multiple myeloma disease was suspected however the patient's age is not typical. The baby could be delivered prematurely but healthy. The bone marrow biopsy showed 2 percent plasma cells by cytomorphology. Flow cytometry conducted on the biopsy indicated no monoclonal cells. Moreover, the immunohistochemistry analysis on the bone marrow showed that there was minor infiltration of plasma cell neoplasms with lambda light chain restrictions. The patient was diagnosed with Multiple myeloma IgA Lambda, with multiple osteolytic lesions in all skeletal segments. The Magnetic Resonance Imaging of the skull indicated a mass in the base of the skull impinging on the internal carotid artery and growth in the pituitary lobe. Significant corrosion of the wall of the sphenoidal sinus was also observed in the scan. (Figure 1). Diplopia was due to sella tumor with paresis of left M. abducens (cranial nerve VI involvement) and IgA 33.8 g/l Lambda -light chains 408 mg/l B2M 5. More importantly, the molecular pathology tests showed that there was no TP53 mutation. The bone CT scan conducted in June 2018 showed multiple osteolytic lesions in various areas, therefore indicating a greater possibility of bone fractures. Another scan was conducted in August 2018, which showed almost the same morphology of the osteolytic lesions as found in the scan conducted in June. Decreasing osteolysis was observed at the dorsolateral position of the left 9th rib. She was treated by radiotherapy; the first cycle according to the VCD scheme was administered without acute toxicities from 22.06.18 onwards. A cMRI showed a mass in the area of the base of the skull with compression of the internal carotid artery and growth in the pituitary lobe as well as corrosion of the wall of the sphenoid sinus. An irradiation of the skull base with a total of 30 Gy over two weeks was initiated. MRI of the entire spinal column additionally revealed osteolysis requiring radiation in the areas of BWK 4 BWK 7, LWK and the sacrum of the left side. The irradiation was accompanied by therapy with VCD, which produced an excellent serological response. Mobilization therapy and autologous blood stem cell transplantation followed from September to November 2018. Meanwhile, maintenance therapy with Revlimid 10 mg had been initiated as recommended in March 2019. The recent cycle of Revlimid was given with 5 mg due to leucopenia. MRI head with contrast 28th June 2020 showed re-demonstration of the multiple variable sized focal osseous lesions involving the calvarial bones, clivus and skull base which showed decrease in number and post therapeutic changes. There was regression of the

previously depicted left paraclival soft tissue intensity component (Figure 2). All medical assessment showed no disease activity with known and remaining osteolytic lesions in virtually all bones. Follow-up checks conducted in successive three months in 2019 & 2020 indicated that the patient recovered physically with no more diplopia. The bone disorders also subsided considerably, and the incidence of respiratory infections also decreased. Patient is doing well, no active symptoms with follow up serology (light chain, IgA) and MRI of brain planned to be done every six months.

Table 1: Laboratory results

	25/12/17	19/04/2018	22/04/2018	29/01/2019	21/04/2020	01/04/2021
WBC	4.2	6.70	7.10	1.6	L2.6	3.2
RBC	4.2	L 3.5	L2.9	3.3	L3.7	4.1
Hgb	11	L 9.9	8.0	10.4	11.9	12.5
HCT	35	L 29.3	24,3	36.6	35.2	36.6
MCV	84.4	83.8	83.9	92.5	94	89.9
MCHC	31.3	28.3	33.1	34.0	31.8	34.3
Platelet	258	184	154	136	191	233
ANC	1.72	1.7	1.4	L 0.7	0.9	1.4
Lymphocytes Auto	1.96	1.7	5.1	L 0.6	1.3	1.3
Monocyte Auto	0.32	0.3	0.5	0.2	0.3	0.3
Eosinophil Auto	0.20	0.1	0.1	0.0	0.1	0.1
Basophil Auto	0.02	L 0.00	L0.00	L0.00	0.02	0.10
Neutrophil Auto %	40.8	69.4	72.2	47.1	33.5	44.4
Lymphocyte Auto %	46.4	25.2	20.9	37.1	50.2	39.9
Monocyte Auto %	7.6	4.1	6.5	13.4	13.2	10.8
Eosinophil Auto	4.7	1.0	0.3	2.0	2.3	2.4
Basophil Auto%	0.5	0.3	0.1	0.4	0.8	2.5
Creatinine	77	103	H 113	60	72	80
Albumin	40	27	L 23	L34	35	36
Adjusted Calcium	2.39	3.81	H 3.05	2.42	2.28	2.35
Calcium	2.39	3.56	2.42	2.30	2.18	2.27
IgA		IgA 33.8 g/l Lambda - light chains 408 mg/l B2M 5			IgA :0.3 g/l Lambda - light chains :<1.3 mg/l	

Figure 1

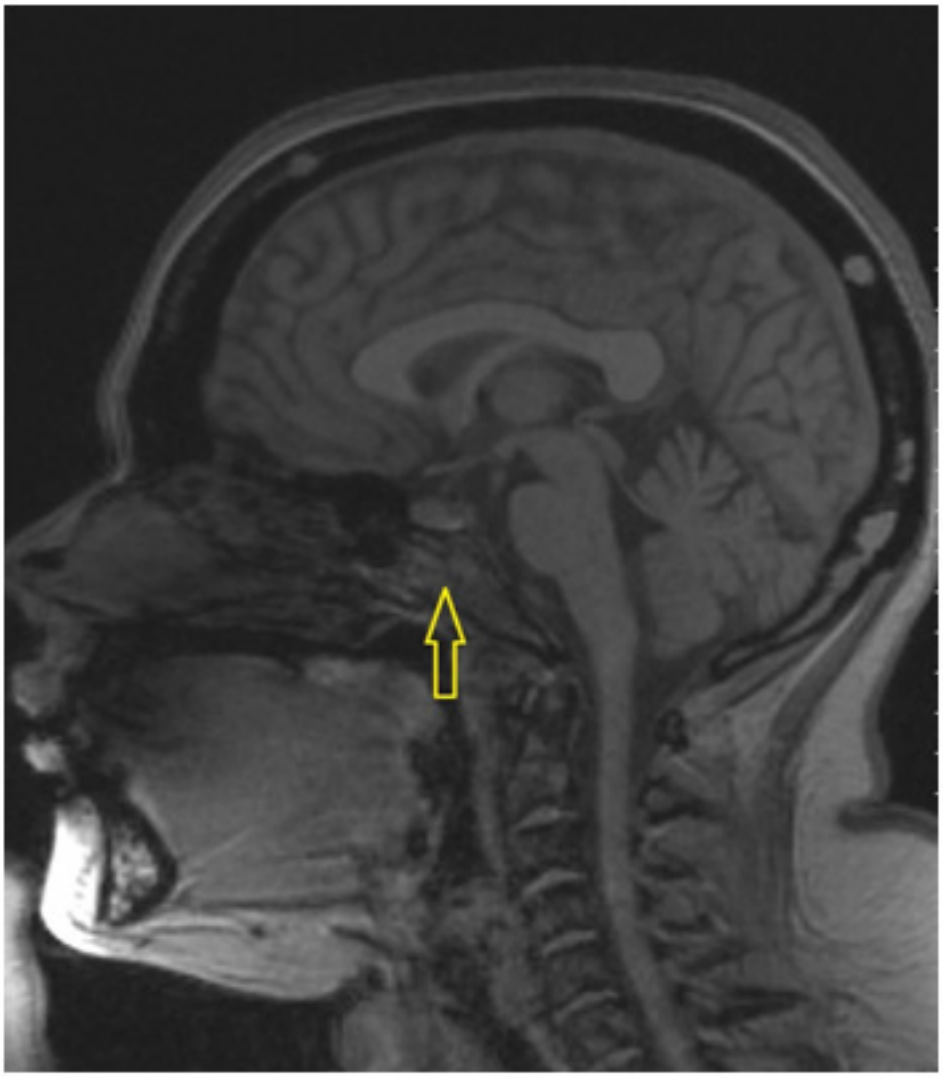
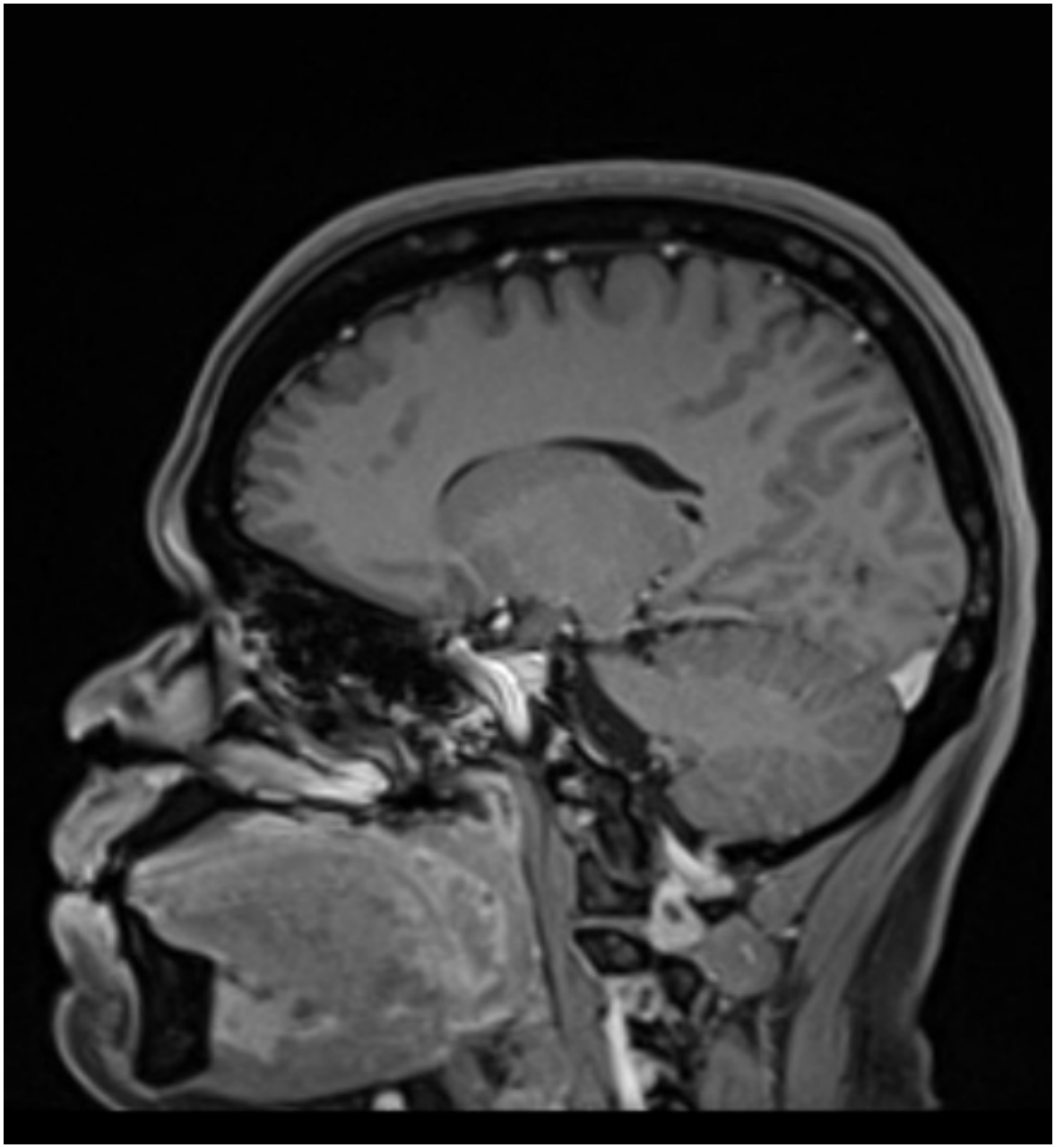


Figure 2



Discussion

This is a rare case of a young pregnant patient presenting with body ache and diplopia diagnosed with multiple myeloma, as the mean age of diagnosis of multiple myeloma is 69 years [10]. 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 [11]. The presenting clinical features in this case are reported to be similar to patients of all ages who have multiple myeloma [8&9]. This is the classic example of how the metastasis of myelomas can inflict damage on various tissues in the body. Osteolysis is due to the induction of osteoclasts, which act to dissolve the bony tissues. It has been found that more than 80 percent of the cases of multiple myelomas have osteolysis occurring in the bony tissues. Higher number and size of osteolytic lesions lead to poor prognosis [12]. In the bone diseases associated with myeloma, uncoupling of the osteoblast and osteoclast activity occurs, which disrupts the normal bone formation and resorption processes in the body. The diplopia in this case is due to the involvement of the 6th cranial nerve. This occurs primarily due to the occurrence of orbital plasmacytomas. The location of plasmacytomas resulted in these unusual neurologic findings which interfere with the mechanical functions of the muscles of the eye, and leads to diplopia [13&14]. The unique presentation of this case is the soft tissue extramedullary plasmacytomas, which have an incidence of 0.04 cases per 100,000 individuals and usually are solitary masses [15]. Bone lesions and abnormal laboratory results seen in this case are thought to be caused by increased activity of osteoclasts and inhibition of osteoblastic activity. Hence serum ALP levels are usually normal in MM. The increased activity of osteoclasts is thought to be mediated by increased RANKL on osteoblasts and decrease of OPG

(osteoprotegerin). Hypercalcemia ensues due to increased osteoclastic activity. Anemia is caused by overtake of the BM by the myeloma cells and disruption of the natural processes of hematopoiesis[16]. Furthermore, only 1-2% of patients at the time of initial diagnosis have extramedullary disease, and 8% develop extramedullary disease later [17]. Renal function impairment and hypercalcemia which were observed in this case were also reported in 30% and 20% of patients, respectively in the study conducted by Blade et al [6]. The most common induction regimens used today are thalidomide–dexamethasone, bortezomibbased regimens, and lenalidomide–dexamethasone; three to four courses are recommended before proceeding to stem cell collection [18]. The current patient showed a good response to treatment similar to many other cases which indicated that 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.

Conclusion

MM can present at a younger age less than 40 years and any patient with unexplained symptoms with hypercalcemia, anemia, and serum albumin-protein gap should be worked up for MM. This case is a rare case of multiple myelomas in young age, suffering from diplopia due to orbital plasmacytomas, treatment with VCD regimen along with radiation therapy which showed excellent patient response. The chemotherapy also manifested positive results in the treatment of osteolytic lesions. However, more research and case reports are needed to determine optimal treatment regimens for this subset of young patients. Therefore, case reports may be helpful in collecting data for future analysis and studies, so these patients would be most likely to benefit from a cure, given the young age and potential loss of life years.

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List of abbreviations

MM	Multiple myeloma
VCD	Bortezomib, Cyclophosphamide and Dexamethasone regimen
MRI	Magnetic resonance imaging
CMRI	Conventional neurology magnetic resonance imaging
CT	Computed tomography scan
B2M 5	Beta 2 microglobulin 5
TP 53	Tumor protein 53
GY	Gray (level of radiation)
ALP	Alkaline phosphatase
RANKL	Receptor activator of nuclear factor kappa beta
OPG	osteoprotegerin
BM	Bone marrow
SCT	Stem cell transplantation
IRB	Institutional Review Board

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