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The Unfortunate Event - Extramedullary Myeloma Of The Urinary Tract

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ORIGINAL

Introduction

Multiple myeloma is a type of haematological malignancy that arises from the abnormal proliferation of plasma cells leading to excessive production of monoclonal immunoglobulins (1). These antibody-secreting plasma cells are produced by the B-lymphocytes (2). They play an important role in humoral immune response due to their ability to produce antibodies. As important as the plasma cells are to the human body, they can be equally destructive in plasma cell neoplasms.

Multiple myeloma is the more commonly known name for plasma cell neoplasm which is an umbrella term for a host of other disorders that are associated with clonal proliferation of plasma cells which includes extramedullary myeloma. We would like to discuss a rare case of extramedullary myeloma of the urinary tract in a 65 years old gentleman.

Case Report

We present a 65-year-old man who was diagnosed with extramedullary plasmacytoma (involving the right buccal and retroperitoneal region) in 2015. He was treated with a cycle of induction chemotherapy with Hyper-CVAD A regimen (cyclophosphamide, vincristine, adriamycin, and dexamethasone) followed by 6 cycles of VCD regimen (bortezomib, cyclophosphamide, and dexamethasone) and was put on thalidomide maintenance. Upon completion of chemotherapy, he underwent radiotherapy and subsequently autologous stem cell transplantation.

He achieved remission for 5 years until he developed gross haematuria. A solid mass arising from the right ureteric orifice was seen on a flexible cystoscopic examination. Proceeded with computed tomography (CT) of the abdomen and pelvis showed a retroperitoneal tumour infiltrating into the lower pole of the right kidney with another lesion at the right distal ureter extending into the vesico-ureteric junction (VUJ) causing hydronephrosis. He underwent transurethral resection of the bladder tumour (TURBT) and histopathologic examination (HPE) revealed plasma cell neoplasm consistent with plasma cell myeloma. He was then started on 2 cycles of VCD (Bortezomib, cyclophosphamide, and dexamethasone) followed by 5 cycles of VTD (Bortezomib, thalidomide, and dexamethasone). The tumour responded to the treatment, evidenced by FDG-PET CT showing no abnormal tracer uptake.

Unfortunately, he developed another relapse in 2 years which was found during CT surveillance. The lesions over the right kidney and right VUJ increased in size extending to the lateral bladder wall and similar HPE findings on the second TURBT. He was not amendable for radiotherapy in view of the extensive tumour burden and he was not able to tolerate the subsequent chemotherapy, hence he was started on an immunomodulator (lenalidomide).

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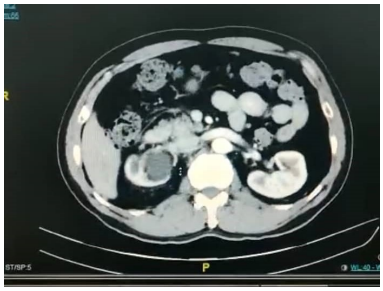

Figure 1. Relapse of EMM. A retroperitoneal lesion involving the right kidney causing hydronephrosis

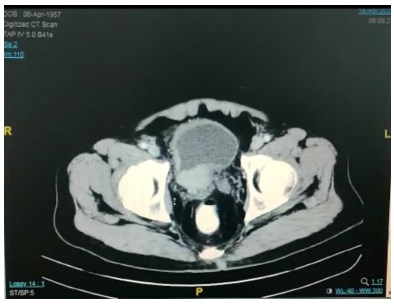

Figure 2. Right sided bladder mass involving the right vesico-ureteric junction

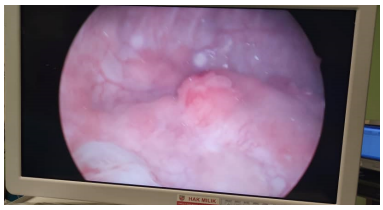

Figure 3. Intraoperative picture (cystoendoscopic view) showing the tumour involving the trigone of the bladder

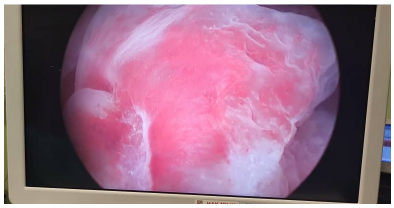

Figure 4. Cystoendoscopic view of the tumour involving the right lateral wall of the bladder

Discussion

EMM is an aggressive sub-entity of MM, characterized by the ability to thrive outside of the bone marrow microenvironment leading to a highly proliferative state and resistance to standard treatment (3).

The initial recognition of EMM was from the autopsies performed in the mid-20th century on multiple myeloma patients which showed extra-skeletal involvement (4). The total incidence of EMM was about 13% of the population of multiple myeloma patients (this includes the detection of EMM either at the time of diagnosis or relapse) and about 7% of the multiple myeloma patients develop de-novo EMM (5). Many studies have demonstrated that EMM has a higher predilection for male sex and the mean age of fifth decade of life (5; 6). This statement correlates with our patient who was first diagnosed with EMM of the right buccal and retroperitoneal region during the 5th decade of his life.

The common sites for EMM reported were the lymph nodes, breast, upper respiratory tract, and liver (6). EMM of the urinary tract is relatively rare (7), where only 19 cases of bladder plasmacytoma and 7 cases of renal involvement were reported in the literatures (8; 9; 10).

The clinical features of EMM are dependent on the location of the soft tissue tumours. For example, plasmacytoma of the lymph nodes may present with lymphadenopathy, the liver may result in jaundice or ascites, and the lungs may lead to pleural effusion. In this case, the gentleman presented with haematuria. A high index of suspicion for EMM is required although he was deemed to be in remission for multiple myeloma at the time of presentation.

The treatment of EMM involves local control and systemic therapy. Local control can be achieved by radiotherapy or surgery if the tumour is resectable. Due to the rarity of the disease, clinical data and therapeutic evidence of the available treatment modalities are scarce. However, the existing literature has shown that EMM responds well to local therapy and surgery renders high local control rates (11). That said, surgery or radiotherapy is beneficial for primary EMM confined to a single organ (12). Therefore it is imperative to differentiate solitary plasmacytomas from

multifocal EMM. Due to the aggressive nature of the latter, systemic therapy is the treatment of choice (13). This particular patient was deemed not suitable for surgery as he had an extensive retroperitoneal tumour involving the urinary tract.

In our case, there appeared to be multifocal involvement of the retroperitoneum, right kidney, right ureter, and bladder after a period of latency. Current approaches for systemic therapy include a combination of conventional chemotherapy with novel agents such as immunomodulator drugs (thalidomide and lenalidomide) and proteasome inhibitors (bortezomib and carfilzomib). Although the mean survival rate is prolonged with modern treatments, almost all patients eventually suffer a relapse (14) as with our patient.

Studies have suggested that patients with soft tissue-related EMM relapse have a statistically significant poorer survival rates than those with paraskeletal EMM relapse (30 vs 45 months) (15). The choice of drug in relapsed/ refractory EMM is dependent on a number of factors namely the refractoriness to the primary chemotherapy agents used and cross-refractoriness between drugs of the same pharmacological group. Our patient suffered a double relapse after a combination treatment with conventional chemotherapy (cyclophosphamide), bortezomib, and thalidomide. As he is intolerant to the adverse effect of chemotherapy and taking into consideration of refractoriness to the given drugs, he is currently on treatment with lenalidomide. Hernandez et al (16)elucidated that there should be a balance between achieving treatment response with quality of life, especially in the elderly patient.

Gaggelmann et al (17) have demonstrated an increase in median survival with autologous stem cell transplantation (ASCT). Also, ASCT was shown to be more effective in soft tissue EMM compared to paraskeletal EMM.17 Our patient suffered from relapse despite ASCT underpins the finding that less favourable outcomes in patients with EMM (18). It was also reported that EMM at diagnosis was associated with shorter overall survival in patients treated with conventional chemotherapy, although some studies showed there were no significant differences in progression-free survival in the presence or absence of EMD (5; 19).

Conclusion

EMM carries a poorer prognosis despite the advancement of treatment. Many important questions on EMM remained unanswered. There are several promising treatments were still under investigation. Prospective analysis focusing on drug sensitivity and resistance based on molecular genetic profiling should be encouraged for EMM with the aim to increase survival outcomes.

Conflict Of Interest

All authors declare no conflict of interest of any kind.

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