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Overview of Multiple Myeloma from Complicated Treatment Protocols to More Simplified its Management! A Radiation Oncologist Perspective

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Abstract: ***Incidence of multiple myeloma is 1/lac population and median age of presentation is around 62 years of age multiple myelomas is a malignant tumor of plasma cell origin, primarily characterized by wide spread flat bones osteolyticlesions often associated with refractory anemia with renal dysfunction and depressed ability to resist infection.***

Keywords: Plasma cell tumor, Multiple myeloma

1. Discussion

Multiple myeloma is a malignant proliferation of plasma cell, normal plasma cells derived by B cells lymphocytes which produces immunoglobulin's which contains heavy and light chain both , Normal immunoglobulin's are polyclonal in nature which means that the variety of light chains are produce and each may be of kappa or lambda light chains types, in myeloma plasma cells produce immunoglobulin's of single heavy and light chain immunoglobulin's, this monoclonal light chain proteins are known as M Paraproteins, in some case only light chain are produced called as Bencejhons proteins which is nothing but same M Para proteins. Frequency of different paraproteins found in multiple myeloma are IgG - 55% Most common, IgA - 21%, Only light chains - 22% and others like IgD and IgE are found only in 2% cases of multiple myeloma.

Presence of Bans john protein predicts poor outcome of disease however Bans john protein found also in case of, metastatic bone secondary, nephritis, leukemia's, in the the investigation part Bone scan $Tc^{99}M$ Phosphate isotope study is found inferior to conventional radiography, Due to immunological deficiency streptococcal pneumonia and gram negative organism causes frequent episode of infections, Amylodosis in multiple myeloma occurs in 10 to 15% cases which can result in Nephrotic syndrome.

Pathology: Although small numbers of malignant plasma cells are present in blood circulation but majorities are present mainly in bone marrow, malignant plasma cells produces cytokine's which stimulate osteoclast cells of bone leading bone absorption resulting in bone pain, lytic bone lesion, pathological fracture, hypercalcemia, over stretched bone marrow further leading in compromise in production of hemoglobin, healthy B cells in order to produces immunityfurther leading to Pancytopenia.

Clinical features: bone erosion by osteoclast cells leads to bone pain pathological fracture which causes severe localized bone pain, hypercalcemia leading to thirst, constipation etc, since this disease is oifprimarily bone marrow in origin thus leads to anemia, pancytopenia, infection etc, excessive production of light chain protein light chain immunoglobulin which get deposited on renal tubules further more leading to renal failure / involvement, 5% patients of multiple myeloma presents with paralysis secondary to spinal cord compression due to vertebral fracture or collapse.

Diagnosis of Multiple myeloma:
Diagnosis of multiple myelomas are based on three criteria's out of three two must be present to diagnosed the patient as given below

1) Bonemarriow Plasmacytosis normally plasma cells are present in bone morrow in less than 5% cells of all nucleated cells in bone marrow but if plasma cells present in bone marrow more than 10% of all nucleated cells we call it plasmacytosis.
2) Serum / Urinary Paraprotein present / detected. However 2% multiple myelomas are called **Non secretary multiple myeloma** in these patients you don't find serum or urinary M paraprotein, M protein considered measurable if it is more than 1gm/dl in serum or more than 200mg/day found in urine only then we considered it as positive test for multiple myeloma, so in case of non secretary multiple myeloma free light chain in seummesurment use to confirm diagnosis.
3) Multiple punch out skeletal lesions are present in flat bones.

Staging of multiple myeloma:

Stage 1: Hgb more than 10gm/dl, serum calcium less than 12mg/dl, IgG LEVEL LESS THAN 5GM/DL, IgA level less than 3gm/dl. Serum β_2 micro globulin level less than 3.5mg/dl

Stage 3: Hgb less than 8.5 gm/dl, serum calcium more than 12mg/dl, IgG level more than 7gm/dl, IgA level more than 5gm/dl. Serum β_2 micro globulin level more than 3.5mg/dl
Term A& B used depending upon renal involvement is present (stage - B) when no renal involvement (stage - A).

Major criteria[1]
- Marrow plasmacytosis >30%
- Plasmacytoma
- M-component
  - Serum IgG >3.5 g/dl or IgA >2 g/dl
- Urine Bence-Jones protein >1 g/24 h

Minor criteria[1]
- Marrow plasmacytosis of 10–30%
- M-component present
- Lytic bone lesions
- Immunoglobulin levels reduced to less than 50% of normal

Figure 1: Criteria's for diagnosis of multiple myeloma

Poor prognostic factors:
1) Hgb less than 7 gm
2) Severe hypo albumin level
3) Renal failure
4) Thrambocytopenea
5) High β_2 micro globulin level.
6) Benjhons protein detected.

Stage	Criteria	Survival (mo)
I	β_2-microglobulin <3.5 mg/L and albumin ≥3.5 g/dL	62
II	β_2-microglobulin <3.5 mg/L and albumin <3.5 g/dL OR β_2-microglobulin 3.5-5.5 mg/L regardless of albumin levels	44
III	β_2-microglobulin ≥5.5 mg/L regardless of albumin levels	29

Figure 2: International guidelines for predicting the disease out come on basis of β_2 Microglobuline level.

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2. Management of Multiple Myeloma

Investigation:
1) CBC Complete blood count, Hgb, ESR to be focused upon.
2) Renal function test & serum electrolytes especially serum calcium % serum createine level.
3) Bone narrow involvement or failure can be Picked up by looking reticulocite count and hemoglobin level.
4) Disease activity assess by finding out the value of serum $\beta_2$microglobulin level.

Multiple myeloma being disease originally from bone marrow must be considered as systemic disease requires systemic chemotherapy as well as local treatment in form of chemotherapy and radiotherapy.

Schedule - 1 Chemotherapy:
Bortiuzomib 1.3 mg/m^2 maximum up to 2mg/m^2 three times in a month by subcutaneous route/ intravenously, Cyclophosfamide 300mg/m^2 500mg/m^2 weekly intravenously along with injection Dexamethasone 40mg intravenously weekly, above regime given up to 8 weeks with response rate is 90%.

Schedule – 2 Chemotherapy: VAD
VAD Regime, Vincristine 1.4mg/m^2 D1 TO D4, maximum up to 2mg, along Doxorubicine 9mg/m^2 D1 TO D4, Dexamethasone 40mg D1 - D4, three weekly regime. Above schedule provides response rate of 70%.

Schedule - 3Chemotherapy:
Melphalan.15mg/kg body weight maximum up to 7mg D1TO D7 along Predenesolone 60 - 80mg/m^2 maximum 100mg dose D1 TO D7 given 6 weekly basis this regime produces response rate of 50%.

If patient do not respond above chemotherapy regime we can give same chemotherapy along with peripheral stem cell support or we can think of considering Bone marrow transplant.

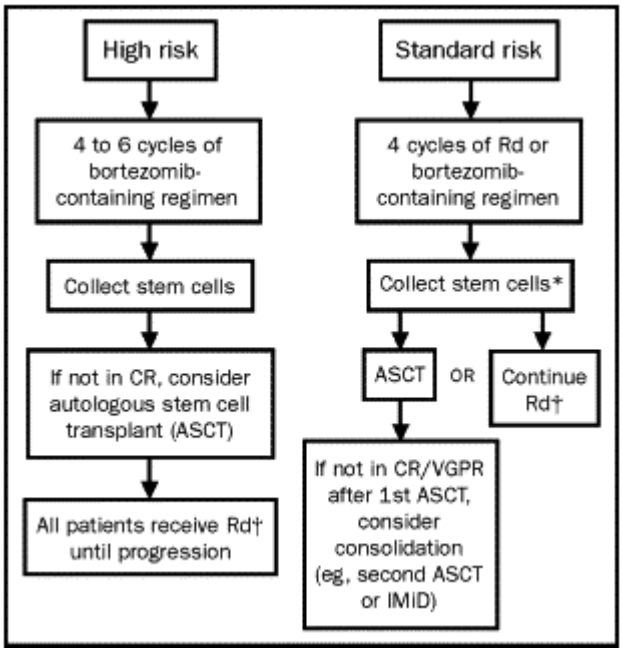

Figure 3: Treatment approach for Multiple Myeloma

Radiotherapy in Multiple myeloma: Radiotherapy used in form of curative or palliative radiotherapy in order to achieve pain and pressure relief usual dose is 40 to 50 Grey as radical curative intent radiotherapy. Radiotherapy produces 80% subjective response. Conventional treatment planning is sufficient for most of palliative treatments to long bones, usually with AP/PA field arrangement. In cases where there is soft tissue disease or nearby critical structures to be avoided, 3D CT – based treatment planning may be of use to more accurately define the treatment volume & Critical Structures Doses used for treatment of myeloma rarely exceed normal tissue tolerance, and normal structures are not routinely delineated.

3. Conclusion

a) Multiple myeloma is a malignant systemic hematological disease that arises from monoclonal plasma cells. It usually affects older patients and is characterized by the presence of monoclonal immunoproteins in the serum and/or urine.
b) The diagnostic work - up comprises mandatory analysis of blood and urine samples, bone marrow evaluation, and imaging procedures. In patients under 70 years of age without serious comorbidities, induction treatment should be followed by high - dose treatment with autologous stem - cell transplantation. Older patients can be managed with age - adjusted high - dose treatment and autologous stem - cell transplantation. Supportive measures such as pain therapy, administration of bisphosphonates, and irradiation of skeletal/extra medullary lesions are important accompaniments to the treatment of patients with multiple myeloma

Conflict of interest: None

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