

Neurological manifestations among Sudanese patients with multiple myeloma

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Abstract:

Background: Multiple myeloma may involve the nervous system at every level, including the neuromuscular junction, peripheral nerve, plexus, spinal nerve root, spinal cord, meninges, and brain. Such involvement may be primary or secondary, as well as non-invasive paraneoplastic effects.

Objective: To find out the prevalence and pattern of CNS manifestations in Sudanese patients with multiple myeloma seen in Al-Shaab Teaching Hospital and Khartoum Nuclear Hospital.

Methodology: This is a prospective descriptive cross sectional, hospital based study. It was conducted in Al-Shaab Teaching Hospital and Khartoum Nuclear Hospital in the period from June 2009 to June 2010. 50 patients with multiple myeloma were included in the study.

Results: Males were more than females with ratio of 2.8:1. The common (36%) age of presentation was between 55-64 years. There was increased incidence of multiple myeloma in patients from the west of Sudan. Farmers and free workers had high incidence of multiple myeloma (34% and 27% respectively). The study demonstrated that the most common non-neurological symptoms was locomotor symptoms (24%), while the most common neurological symptoms were backache and neck pain. The most common neurological findings were cord compression (8%) followed by peripheral neuropathy (2%) and CVA (2%). 22% of patients completed treatment with good response, 12% with partial response, 18% with no response and 48% are still on treatment.

Conclusion: CNS involvement among our studied group was not uncommon.

Keywords: neuromuscular, paraneoplastic, monoclonal immunoglobulin.

MULTIPLE myeloma (MM) is characterized by the neoplastic proliferation of a single clone of plasma cells in the bone marrow producing a monoclonal immunoglobulin^{1, 2}. This proliferate results in bone abnormalities that may lead to pathologic fractures^{3, 4}. Anemia and hypercalcemia ending with renal insufficiency; are among the common clinical findings. However, patients are predisposed to bacterial infections and bleeding tendency^{5, 6}. MM may involve the nervous system at every level, including the neuromuscular junction, peripheral nerves, spinal nerves roots, spinal cord, meninges and brain^{7, 8}. Common neurological complications in patients with MM include radiculopathy and spinal cord compression, usually in the thoracic or lumbosacral area, resulting from compression by plasmacytoma or collapsed bone. Peripheral neuropathy is

uncommon and intracranial plasmacytomas are rare^{9,10}.

Objective:

To describe the pattern of CNS manifestations of MM among Sudanese patients seen in Al-Shaab Teaching Hospital and Khartoum Nuclear Hospital in period from June 2009 to June 2010.

Methodology:

This is a prospective, descriptive, cross-sectional, hospital-based study. It was conducted in Al-Shaab Teaching Hospital and Khartoum Nuclear Hospital in the period from June 2009 to June 2010. Al-Shaab Teaching Hospital is a tertiary hospital, located in the centre of Khartoum town. There are two neurological units with 43 beds and two neurosurgical units with 50 beds, there are three intensive care units, two neurology referred clinics and three neurosurgery

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referred clinics each week. Khartoum Nuclear Hospital is a tertiary hospital, located in the centre of Khartoum town. It is the biggest center in Sudan for chemotherapy, radiotherapy and management of cancer related diseases.

Inclusion criteria: (1) Sudanese patients admitted during that time and diagnosed as multiple myeloma. (2) Those who agreed to participate in the study.

All patients gave verbal or written consent to participate in this study. The study was approved by the local ethics committee.

Exclusion criteria: patients with multiple myeloma and HIV.

Data collection and analysis: Data were retrieved from the patients or close relatives using anonymous questionnaire. Detailed history was taken and through clinical examination was performed for each patient. Investigations done for patients include: urine analysis, hemoglobin, TWBC, ESR, urine for Bence Jones protein, renal function test, serum protein, serum calcium, X-rays (skull, vertebrae, ribs), bone marrow aspiration and biopsy, plasma protein electrophoresis, brain CT, MRI spine and if needed EMG and NCS. The data were analyzed and the results were expressed.

Results

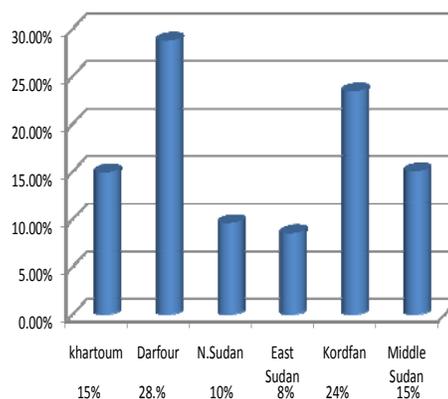
Fifty patients fulfilled inclusion criteria and were enrolled in the study. The common age (36%) of presentation was between 55-64 years (Table1).

Table 1: Showed age distribution among 50 Sudanese patients with multiple myeloma.

age	Frequency (%)
35-44	3 (6)
45-54	9 (18)
55-64	18 (36)
65-74	13 (26)
>75	7 (14)

Males (74%) were more than females (26%) (ratio2.8:1). They were coming from different parts of Sudan (Figure1).

Fig.1 shows residence by state among 50 Sudanese patients with multiple myeloma seen in Alshab teaching hospital and Khartoum nuclear hospital in study done in period from June 2009 to June 2010



The study showed that farmers and free workers had higher incidence of multiple myeloma (61%).

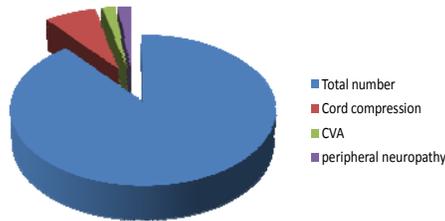
Non neurological symptoms involved the skin and locomotor symptoms that constituted 24% each, renal symptoms 20%, GIT symptoms 12% and cardiovascular symptoms 12%.

Table 2 shows distribution of neurological symptoms. It was found that backache and neck pain were the common presenting symptoms (38%). The neurological diagnoses were illustrated in figure 2.

Table2: Distribution of neurological symptoms.

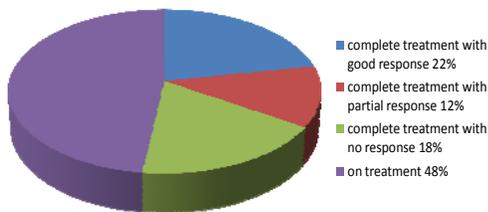
symptom	Frequency (%)
Head ache	8 (16)
Convulsions	0 (0)
Loss of consciousness	0 (0)
Limb weakness+ numbness	6 (12)
Back ache + neck pain	19 (38)
Sphincteric disturbances	2 (4)
Muscle pain	7 (14)

Fig. 2 shows distribution of neurological diagnosis among 50 Sudanese patients with multiple myeloma seen in Alshab teaching hospital and Khartoum nuclear hospital in study done in period from June 2009 to June 2010



It was found that 29% of the patients had low haemoglobin, 22% had high ESR, 70% had high serum calcium, 20% had high renal function test and 62% had high serum protein. It did appear that 24% (14% with neurological manifestations) of the patients had Bence Jones protein in their urine. It was found that 62% had high total serum protein. It did appear that 22% of patients with neurological manifestations had high serum protein while 40% of patients without neurological manifestations had high serum protein. X-ray (skull, vertebrae, ribs) abnormalities among the patients showed that 66% had lytic lesions. It was noticed that 24% of patients with neurological manifestations had lytic lesions while 42% of patients without neurological manifestations had lytic lesions. The study showed that 22% of the patients complete treatment with good response (Figure3).

Fig.3 shows the outcome of treatment among 50 Sudanese patients with multiple myeloma seen in Alshab teaching hospital and Khartoum nuclear hospital in study done in period from June 2009 to June 2010



Discussion

Similar to what was reported by other researchers; word wide the study showed that males were affected more than females¹¹⁻¹³. Like others it was found that the common age of presentation was between 55-64 years and it is rare below 35years and above 74 years^{14, 15}. The increased incidence of MM among patients from West of Sudan (Darfur and Kurdfan) can be attributed to environmental, social and genetic factors. The study demonstrated that the farmers and patients with free work had high incidence of MM. This may be explained by prolong exposure and contact to chemicals that have been linked to development of multiple myeloma including a variety of pesticides and herbicides (e.g., organophosphates), and wood preservatives. A population-based case-control study in Japan identified numerous occupations associated with significant increased risk of multiple myeloma, including architects, engineers and related technicians, cooks, waiters, bartenders and others, also increased risk of MM had been noted in atomic bomb survivors in Japan exposed to more than 50rad¹⁶.

Although cerebral disorders, cranial nerves are the most frequent neurological manifestations¹⁷, none of our patients had cerebral disorders or cranial nerves involvement. Low backache and neck pain were the common presenting symptoms (38%). As in literature spinal cord compression, radiculopathy, and peripheral neuropathy were seen in our patients^{17, 18}.

Our data showed that, low backache, headache, bone pain and weight loss were common presenting symptoms among patients with multiple myeloma reflecting what was mentioned in the literature¹⁹⁻²¹.

Among our studied group the renal system was the most common system involved by MM, followed by locomotor system and this is related to the infiltration of plasma cells into the kidneys and bones by excess light chains^{22, 23}.

Central particularly cerebral disorders and peripheral nervous systems were affected by MM and these may manifest clinically. Pathological fracture resulting in spinal cord compression can be a presenting feature of MM^{17, 18}.

Hyperviscosity syndrome affects 8% to 39% of patients with MM and may present clinically with headache, dizziness, vertigo and on occasions can end with severe ischemia^{24, 25}.

A considerable number of our patients had low haemoglobin and high ESR, this is similar to what was reported by other researchers.^{26,27} Chronicity of the disease and bone marrow involvement especially in late stages of the disease, like in our patients, may explain low haemoglobin results. About 62% of our patients had high serum protein and 24% had Bence Jones protein, so the correlation between the disease extension and progression is not so clear.

Conclusion

Multiple myeloma affects males more than females in our studied group. West of Sudan has higher incidence of multiple myeloma than other states of Sudan with no clear cause. The most common presenting symptoms were lower backache, bone pain, weight loss and lower limbs weakness and numbness, while paraplegia was found to be the most common neurological presentation in our patients. Further researches are needed to demonstrate exact incidence and prevalence of multiple myeloma in Sudan.

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