Polymyositis associated with non-secretory myeloma – a case report

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CASE REPORT

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Abstract

Idiopathic inflammatory myopathies, a heterogeneous group of disorders characterised by weakness and inflammation of skeletal muscle, are often associated with malignancies. This association has been infrequently reported in Asian countries. We report a case of an Indian patient who presented with polymyositis in conjunction with non-secretory myeloma, hypercalcaemia and renal failure.

Key Words
Polymyositis, dermatomyositis, non-secretory myeloma

Background

Polymyositis (PM) and dermatomyositis (DM) are classified as idiopathic inflammatory myopathies (IIM), with these conditions predominantly affecting adults. [1] Their aetiology is undetermined and they present with characteristic muscle and cutaneous manifestations. Dermatomyositis, and to a lesser extent PM, carry a higher risk of cancer than that of the general population as demonstrated by several studies.[2,3] The mechanism underlying the association between IIM and malignancies remains unclear. The most common cancers associated with IIM are cancers of the ovary, nasopharynx, lung, pancreas, stomach, urinary bladder and haematologic malignancies including non-Hodgkin's and Hodgkin's lymphoma.[2,3] Cancers associated with PM and DM are diverse and very few reports are available. [2.3] The most common tumours associated with DM are cancers of the ovaries, lungs, stomach, colon and pancreas, along with non-Hodgkin's lymphoma. The most significant associations are with cancers of the bladder, breast and uterus[2]. The epidemiological data on IIM – associated cancer types, however are scarce and varied in the Asian population. Breast cancer, stomach and nasopharyngeal cancers have been reported to be more commonly associated with DM in Korea[4], whereas studies in Singapore, Hong Kong, southeastern China, and Taiwan revealed that nasopharyngeal carcinoma was 6–10 fold more commonly associated with IIM.[5,6,7]

Case details

A 47-year-old male patient from Kerala (a state of south India) presented with a four-month history of both knees giving way while walking. This was associated with frequent falls and swelling above both knees. He needed support while walking, and reported difficulty in getting up from a squatting position and with putting his legs on a bed. He also complained of neck pain and constant low backache. There was no history of any sensory disturbances, weakness of the upper limbs, or bladder or bowel disturbances.

On examination there was grade 3 power of both knee extensors, with patellar jerks absent bilaterally. There was bilateral swelling of the knee at the insertion of the quadriceps tendon. No fasciculations were observed. Examination of the skull and spine was normal.

Laboratory investigations revealed the following: haemoglobin 11 gm%, total leukocyte count 9900 cells/cumm, ESR 48 mm in 1 hour, blood urea 121 mg/dl, serum creatinine 5.6 mg/dl, sodium 135 mg/dl, and

potassium 5.0 mg/dl. Liver function tests showed a mild increase in liver enzymes with normal bilirubin. The level of creatine kinase was 1343, and urinanalysis showed 2+ protein with granular casts. Serum calcium levels were 14.2 mg/dl. The serum intact parathyroid hormone (PTH) level was low <2.5 pg/ml (Normal range: 14-72 pg/ml).

In view of anaemia, renal failure, and hypercalcaemia with low PTH levels, an ectopic source of calcium was suspected and a bone marrow examination performed. This revealed 16% plasma cells with atypical forms, a few cells with immature nuclear chromatin, and binucleate forms suggestive of myeloma (Figure 1).

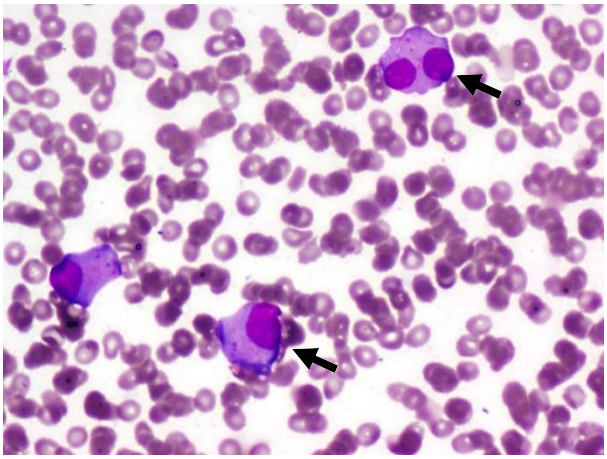

Figure 1: Photomicrograph of bone marrow aspiration showing plasma cells, atypical forms, few with immature nuclear chromatin, binucleate forms (indicated by arrows) suggestive of myeloma (H &E stain x 40)

However, protein electrophoresis did not reveal any M band. Serum immunoglobulin IgA was < 46 (200-280 mg/dl), IgG 949 (1200-1480 mg/dl), IgM was <40 (110-136 mg/dl) and urinalysis for the existence of Bence-Jones protein was negative. Thyroid function tests were within normal limits. Skeletal survey (consisting of plain X-rays of the skull, spine, pelvis and long bones) did not reveal any lytic bone lesions, and bone marrow immuno-histochemistry of plasma cells with CD138 showed strong linear staining of cytoplasmic membrane (a specific marker for plasma cells), thereby confirming myeloma cells (Figure 2).

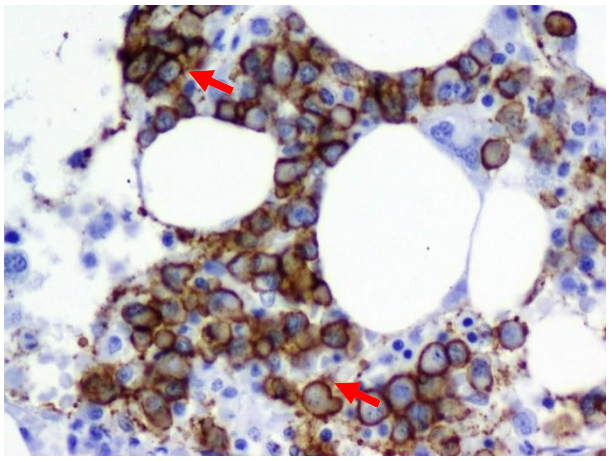

Figure 2: Photomicrograph of immuno-histochemistry of plasma cells showing CD138 membrane positivity (indicated by arrows) (H &E stain x 40)

Muscle biopsy revealed normal perimyseal and endomyseal components, polygonal fibers with peripherally placed nuclei, and an occasional regenerating fibre. There were few foci of perimyseal perivascular inflammation involving small vessels which was suggestive of PM. Electromyography of the quadriceps showed sharp positive waves and polyphasic motor unit potentials of low amplitude and short duration. Both findings were consistent with myopathy.

In this patient the initial clinical diagnosis was inclusion body myositis in view of the predominant involvement of the quadriceps muscles and the early loss of patellar reflexes, however the final diagnosis was PM. This was made in accordance with the Bohan and Peter classification[8], with symmetric proximal muscle involvement, elevated creatinine kinase, electromyography suggestive of myopathy and muscle biopsy showing inflammatory infiltration of non-necrotic muscles.

Non-secretory myeloma was diagnosed according to the classification criteria of the International Myeloma Group 2003[9], with absence of M band on serum electrophoresis, normal to lower levels of immunoglobulins, bone marrow infiltration with >16% plasma cells, evidence of organ or tissue impairment (renal failure), and immuno-histochemistry of plasma cells with CD138 showing strong membrane positivity confirming myeloma cells. Therefore, a case of PM with non-secretory myeloma of Salmon-Durie IIIB classification (Table 1) was diagnosed. The patient refused chemotherapy, and was managed symptomatically for hypercalcaemia and renal failure.

Table 1: Salmon-Durie staging classification of multiple myeloma

Stage I (all the following criteria are present)
• Haemoglobin > 10 gm/dl
• Normal calcium levels (≤ 120 mg/l)
• Isolated plasmacytoma or normal bone
• Low level of monoclonal immunoglobulins (IgG < 50 g/l, IgA < 30 g/l, urine Ig < 4 g/24 hrs)
• Estimated low level of myeloma cells (< 0.6 x $10^{12}/m^2$)
Stage II (none of the criteria of stage III and most of the criteria for stage I)
• Intermediate level of myeloma cells (0.6 - 1.2 x $10^{12}/m^2$)
Stage III (at least one of the following criteria)
• Haemoglobin < 8.5 gm/dl
• Hypercalcaemia > 120 mg/l (> 3 mmol/l)
• Multiple osteolytic lesions with or without bone fractures
• High level of immunoglobulins (IgG > 70 g/l, IgA > 50 g/l, urine Ig ≥ 12 g/24 hrs)
Sub-classification: A: Normal renal function (creatinine < 20 mg/l) B: Abnormal renal function (creatinine ≥ 20 mg/l)

Note: The subject of this case report was classified as Stage III-B

Patient consent

Written, informed consent was taken from the patient for the publication of all patient-related material including but not limited to clinical photographs, histopathological slide photographs and clinical details.

Discussion

Several studies[2,3,11] have reported on the prevalence of malignancies in inflammatory myositis. Prevalence ranged between 4 and 42%, presenting more frequently with DM than with PM. According to the cohort study conducted in Sweden, Denmark and Finland by Hill and colleagues[2] malignancies were found in 198 out of 618 patients with the prevalence being 32% and 15% for DM and PM respectively with a standardised incidence ratio (SIR) of 3.0 for DM and 1.4 for PM. Polymyositis was seen to have the highest association with non-Hodgkin's lymphoma, lung and bladder cancers. The risk of malignancy in patients with inflammatory myositis was reported to be highest in the first year after diagnosis of IIMs with the most common cancer being adenocarcinoma (70%). The risk of malignancy was shown to decrease over time and became minimal beyond five years.

Although the mechanism of association between IIM and malignancy remains unclear, a model of crossover immunity between tumour cells and myofibroblasts explains the parallel clinical course and the diagnostic utility of detection of myositis autoantibody in predicting the risk of malignancy.[12] Meta–analysis of four reports in 1994, by Zantos and colleagues, showed that in a total of 1078 myositis patients (565 patients with DM, 513 patients with PM) odds ratios of 4.4 (95% CI 3-6.6) of DM with malignancies and PM group odds ratio was 2.1 (95% CI1.4-3.3).[13] Very few cases of myositis associated with multiple myeloma were reported.[14] One case of non-secretory myeloma associated with hypercalcaemia and acute renal failure was reported in 2002[15], however we believe this report is the first published description of PM associated with non-secretory myeloma.

Multiple myeloma accounts for 10–15% of all blood cancers and 1–2% of all malignancies[16]. Its presentation may be varied with 10–40% of patients asymptomatic, and 50–70% having back pain, lytic lesion or pathological fracture[16]. Non-secretory myeloma is characterised by the absence of detectable monoclonal (M) protein in both serum and urine, accounting for 1–5% of all patients with multiple myeloma[17]. In 85% of patients with non-secretory myeloma, cytoplasmic M protein can be identified by immuno-peroxidase or immuno-florescence studies on plasma cells whereas in 15% it is truly non-secretory without M protein in cytoplasm of plasma cells but their prognostic significance is yet to be proved[18]. The mechanism of non-secretion is not known. Possible mechanisms for non-secretion include reduced protein synthesis, increased breakdown of abnormal immunoglobulin chains (intracellular or extracellular), the possibility that immunoglobulin may be synthesised but not secreted due to decreased permeability or absence and alteration of intracellular transport of light chains, or there may be intermittent excretion of immunoglobulin evading detection [18]. Patients with non-secretory myeloma seem to have less incidence of renal insufficiency presumably because light chains are not being secreted in urine.[19] There may be delay in diagnosis as patients do not produce paraprotein in serum or urine; therefore their chance of survival is reduced. This poses a diagnostic dilemma as other conditions such as, osteoporosis or hyperparathyroidism can present with similar clinical presentations. Occasionally secondaries can pose similar diagnostic dilemmas.[20] Nephelometric serum free light chain assay shows that only about one-quarter of non-secretory plasma cell myeloma cases may be truly non-secretory.[21] Our patient did not undergo serum free light chain assay, since this is useful

only in monitoring and does not seem to be recommended as a screening method for non-secretory myeloma.[17] Amongst the symptoms of myeloma, our patient had constant low backache that did not fit in to any local pathology, neck pain, bone tenderness, and feeling weak and very tired. However, in this instance the patient did not have lytic lesions commonly associated with myeloma.

Once diagnosed, treatment of non-secretory myeloma is the same as secretory myeloma. The response to treatment is also the same – with treatment the median survival of both secretory and non-secretory myeloma is 62 months for stage 1 disease, 45 months for stage 2, and 29 months for stage 3 disease[10,18]. A large cohort study of patients undergoing autologous stem cell transplantation between non-secretory and secretory multiple myeloma indicated no significant difference in terms of progression free survival or overall survival[22].

This case represents an unusual presentation, with the patient presenting with PM in conjunction with non-secretory myeloma, renal failure, and severe hypercalcaemia without lytic bone lesions. With the diagnosis of PM, physicians should be aware of the possibility of associated malignancy. In addition, non-secretory myeloma should be kept in mind when patients present with clinical features of multiple myeloma and the absence of M component.

References

1. Dalakas MC, Hohlfeld R. Polymyositis and dermatomyositis. Lancet 2003;362(9388):971-82.
2. Hill CL, Zhang Y, Sigurgeirsson B, Pukkala E, Mellemkjaer L, Airio A, Evans SR, Felson DT.Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. Lancet 2001;357(9250):96-100.
3. Stockton D, Doherty VR, Brewster DH. Risk of cancer in patients with dermatomyositis or polymyositis, and follow-up implications: a Scottish population- based cohort study. Br J Cancer 2001;85(1):41-45.
4. Lee SW, Jung SY, Park MC, Park YB, Lee SK. Malignancies in Korean patients with inflammatory myopathy. Yonsei Med J 2006; 47:519-523.
5. Peng JC, Sheen TS, Hsu MM: Nasopharyngeal carcinoma with DM. Analysis of 12 cases. Arch Otolaryngol Head Neck Surg 1995; 121:1298-1301.
6. Chan HL. DM and cancer in Singapore. Int J Dermatol 1985; 24:447-450.
7. Chen YJ, Wu CY, Shen JL. Predicting factors of malignancy in DM and PM: a case-control study. Br J Dermatol 2001, 144:825-831.
8. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). N Engl J Med 1975;292(7):344-347.
9. The International Myeloma Working Group. Criteria for the diagnosis of monoclonal gammopathies, multiple myeloma and related disorders: A report of the International Myeloma working group. Br J Haematol 2003;121(5);749-57.
10. Chen YJ, Wu CY, Huang YL Wang CB, Shen JL, Chang YT. Cancer risks of dermatomyositis and polymyositis: a nationwide cohort study in Taiwan. Arthritis Res Ther 2010;12(2):R70.
11. Chinoy H, Fertig N, Oddis CV, Ollier WE, Cooper RG. The diagnostic utility of myositis autoantibody testing for predicting the risk of cancer- associated myositis. Ann Rheum Dis 2007;66(10):1345-1349.
12. Zantos D, Zhang Y, Felson D. The overall and temporal association of cancer with polymyositis and dermatomyositis. J Rheumatol 1994;21:1855-59.
13. Colombo I, Fruguglietti ME, Napoli L, Sciacco M, Tagliaferri E, Della Volpe A, Crugnola V, Bresolin N, Moggio M, Prelle A.. IgD multiple myeloma paraproteinemia as a cause of myositis. Neurol Res Int volume 2010; Article ID 808474:3pages.
14. Prakash MS, Baliga KV, Singh AP, Mishra DK. Non secretory multiple myeloma with hypercalcemic acute renal failure. J Assoc Physicians India 2002;50:1330-1.
15. Winterbottom AP, Shaw AS. Imaging patients with myeloma. Clin Radiol 2009;64;1-11.
16. International Myeloma Working Group. International myeloma working group guidelines for serum- light chain analysis in multiple myeloma and related disorders. Leukemia 2009;23:215-24.
17. Blade J, Kyle R. Non secretory myeloma, IgD myeloma and Plasma cell leukemia. Haematol Oncol Clin North Am 1999;13:1259-72.
18. Smith DB, Harris M, Gowland E, Chang J, Scarffe JH. Non-secretory multiple myeloma: report of 13 cases with review of literature. Haematol Oncol 1986;4:307-13
19. Middela S, Kanse P. Non secretory multiple myeloma. IJO Indian J Orthop 2009;43(4):408-11.
20. Shaw GR. Non secretory plasma cell myeloma - Becoming even more rare with serum free light chain assay: A brief review. Arch Pathol Lab Med 2006;130(8):1212-15.
21. Kumar S, Pérez WS, Zhang MJ, Ballen K, Bashey A, To LB, Bredeson CN, Cairo MS, Elfenbein

GJ, Freytes CO, Gale RP, Gibson J, Kyle RA, Lacy MQ,Lazarus HM, McCarthy PL, Milone GA, Moreb JS, Pavlovsky S, Reece DE, Vesole DH, Wiernik PH, Hari P. Comparable outcomes in non secretory and secretory multiple myeloma after autologous stem cell transplantation. Biol Blood Marrow Transplant 2008;14(10):1134-40.

PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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CONSENT

The authors declare that

1. They have obtained informed consent for the publication of the details relating to the patient(s) in this report.
2. All possible steps have been taken to safeguard the identity of the patient(s).
3. This submission is compliant with the requirements of local research ethics committees.