Pseudoerythrocytosis in myeloma with associated peripheral neuropathy

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Summary

A number of unusual features have been described in patients who have peripheral neuropathy in association with plasma cell neoplasia. Amongst these features are raised haemoglobins and increased platelet counts. We have measured the red cell mass in one such patient and have shown that the raised haemoglobin was due to a pseudoerythrocytosis. Our patient is also of interest because of his youth being only 19 years old at presentation.

KEY WORDS: pseudoerythrocytosis, myeloma, neuropathy.

Introduction

The association of monoclonal plasma cell proliferation with peripheral neuropathy and other abnormalities including polycythaemia, thrombocytosis, lymphadenopathy, hyperpigmentation and endocrine disorders has recently been reviewed (Driedger and Pruzanski, 1980). We report a case of myeloma and peripheral neuropathy with a raised haemoglobin and thrombocytosis in which the 'polycythaemia' has been shown to be a pseudoerythrocytosis.

Case report

A 19-year-old male of Indian parentage presented with a symmetrical sensorimotor peripheral neuropathy. Symptoms, which had been present for 6 months, included numbness below the knees and clumsiness in the legs. Examination showed distal motor weakness in the legs with areflexia and a high steppage gait. There was also moderate quadriceps weakness. There was no objective sensory loss. At the age of 9, he had been treated for pulmonary tuberculosis with rifampicin, isoniazid and para-aminosalicylic acid. He was on no medication. Investigations included haemoglobin 17.2 g/dl, mean cell volume 85 fl, white cell count 10×10^9 /litre, erythrocyte sedimentation rate 0 mm/hr. Cerebrospinal fluid was clear with no cells and protein 0.98

g/litre, of which 6% was IgG. The following were normal: glucose tolerance test, blood urea electrolytes, calcium, liver function tests, lipids, thyroxine and urinary culture. Sensory nerve action potentials were present but reduced (right median nerve less than 10 μ V amplitude, right ulnar nerve less than 7 μ V amplitude). Motor conduction velocities were reduced (right median nerve 38 m/s, right ulnar nerve 41 m/s). Muscle biopsy showed changes consistent with denervation and partial reinnervation, with atrophied fibres of both types, a tendency to fibre-type grouping and core-targetoid fibres. Sural nerve biopsy was normal under light and electron microscopy with no evidence of amyloid. The patient was given a course of prednisolone starting at 60 mg per day for one week and reducing to zero over the next 8 months, with little effect.

Four months after presentation, his neuropathy had progressed. He now had bilateral footdrop with loss of deep tendon reflexes in all limbs. There was loss of light touch and pain sensation distally in both upper and lower limbs with impaired proprioception and vibration sensation in the ankles and feet.

An abdominal radiograph was performed because of a transient episode of loin pain and vomiting. An asymptomatic cyst in the right upper femur was noted. This was multilocular and clearly demarcated with minimal periosteal reaction laterally. Three months later, he had become generally unwell with weight loss of 2 kg and frequent sweats. His neuropathy had progressed further with marked loss of power and hypotonia in all limbs. All deep tendon reflexes were absent and little change had occurred in his sensory signs. His haemoglobin was 18.6 g/dl, red blood cells (RBC) 6.29×10^{12} /litre, platelets 867×10^9 /litre. Red cell mass measured by the chromium method was 31.6 ml/kg (normal 25-35 ml/kg) with a derived plasma volume of 33 ml/kg (normal 40-50 ml/kg). White cell count was 15.5×10^9 /litre with 91% neutrophils, though this soon returned to normal. Radiography showed that the bone cyst was enlarging. Isotope bone scan showed no other lesions. Open biopsy of the lesion

showed it to be a plasmacytoma. Sternal marrow aspirate showed 2–3% plasma cells with some clumping and occasional binucleate cells. Megakaryocytes were increased. Erythroid and myeloid series were normal. Serum IgG was 28 g/litre with normal IgA and IgM levels. Immunoelectrophoresis showed a monoclonal IgG λ band in serum and small amounts of λ light chain in 100-fold concentrated urine.

Over a period of 20 days, he was given a total of 4000 rads to the plasmacytoma and in addition he received a single 5 day course of melphalan with a course of prednisolone reducing over one month. After a further 3 months, the IgG had fallen to 18.7 g/litre, haemoglobin to 15.8 g/dl and platelets to 320×10^9 /litre. There was slight improvement in his neuropathy with increased power in proximal leg muscles. Ankle oedema developed at this stage despite a normal albumin and the absence of cardiac failure. Two hyperpigmented patches were noted on his buttocks. A pathological fracture developed at the site of the plasmacytoma.

Eight months after radiotherapy his haemoglobin had risen to 18.2 g/dl and the platelets to 480×10^9 /litre. A marrow aspirate showed the same findings as before. He was commenced on pulsed cyclophosphamide and prednisolone. After 6 months, haemoglobin had fallen to 15.5 g/dl and platelets to 226×10^9 /litre. His neuropathy had improved significantly so that he could stand with support. Treatment continues.

Discussion

The association of plasma cell neoplasia and peripheral neuropathy has long been recognised (Crow, 1956). The nature of the plasma cell neoplasia varies along a spectrum including monoclonal gammopathy without bone lesions or marrow infiltration, solitary plasmacytoma and multiple myeloma (Driedger and Pruzanski, 1980) in which tumour mass is usually low (Delauche, Clauvel and Seligman, 1981). The patients are predominantly male and are young compared to those with typical myeloma. The low tumour mass and young age may reflect early presentation due to the neuropathy. When a paraprotein can be demonstrated, it is commonly IgG λ . Amyloid deposition is not prominent and is unlikely to be of significance to the pathogenesis of this condition (Delauche *et al.*, 1981).

Many other features have been described in patients with plasma cell neoplasia and peripheral neuropathy. These include raised haemoglobin and platelet counts, skin thickening and oedema, hyperpigmentation, ascites and pleural effusions, hepatosplenomegaly and lymphadenopathy, papilloedema, clubbing, sclerotic bone lesions, endocrine abnormalities (including diabetes mellitus, gynaecomastia,

amenorrhoea and hirsutism) and excessive sweating. Whilst the combination of many of these abnormalities with plasma cell neoplasia and peripheral neuropathy has been given the name Takatsuki syndrome, it is becoming clear that many more cases demonstrate just a few of these additional features (Driedger and Pruzanski, 1980; Delauche *et al.*, 1981). Our patient was a 19-year-old male and presented with a peripheral neuropathy associated with what was initially a solitary plasmacytoma, secreting IgG λ . He also had a raised haemoglobin, raised platelet counts and oedema. Although plasma cell neoplasia and neuropathy has been reported from many countries, this is only the second recorded case in an Indian (Gupta and Prabhakar, 1965).

Polycythaemia defined as a haemoglobin greater than 18 g/dl has been reported in 9 out of 51 patients with plasma cell neoplasia and peripheral neuropathy (Driedger and Pruzanski, 1980; Delauche *et al.*, 1981). The typical finding in myeloma is pancytopenia. We have shown that the 'polycythaemia' is, in fact, a pseudoerythrocytosis, with a reduced plasma volume and a normal red cell mass. The mechanism is unknown. Plasma volume has typically been shown to be raised in patients with monoclonal gammopathies, rather than reduced (Alexanian, 1977).

A case has been reported in a 41-year-old female in which many features of Takatsuki syndrome were present, but in which there was a 6% plasma cell population in the bone marrow without evidence of a para-protein or plasmacytoma (Meshkinpour, Myung and Kramer, 1977). The authors showed that the red cell mass was raised and the plasma volume was normal.

Platelet counts were raised in 10 out of 31 patients with plasma cell neoplasia and peripheral neuropathy (Driedger and Pruzanski, 1980; Delauche *et al.*, 1981). In our case, this was associated with increased megakaryocytes in the bone marrow. Increased platelet counts are also seen in the more usual presentation of myeloma, when anaemia rather than polycythaemia is seen (Zimelman, 1973), though thrombocytopenia is more common.

Dramatic improvement of the neuropathy has been reported after treatment of the plasma cell neoplasia (Delauche *et al.*, 1981; Moya-Mir *et al.*, 1980). Although our patient showed some improvement, it was not dramatic.

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