CASE REPORT

Pure red cell aplasia and myasthenia gravis: a patient having both autoimmune conditions in the absence of thymoma

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Accepted 10 August 2017

SUMMARY

This is a patient who was presented initially with symptoms of malaise, tiredness and exertional dyspnoea and found to have a severe normocytic normochromic anaemia with low reticulocyte counts. Bone marrow confirmed the diagnosis of pure red cell aplasia (PRCA) and at the time serology for recent parvovirus infection was positive. He was successfully treated with transfusions and intravenous Ig. Six years later, he had a mild relapse of his PRCA and subsequently developed severe dysphagia and dysarthria which were fatigable. Positive antiacetylcholine receptor antibodies confirmed the diagnosis of myasthenia gravis. The two conditions are both known to be associated with thymoma. Imaging and resection of the thymus gland showed only the presence of a thymic cyst. Treatment with pyridostigmine and intravenous Ig have kept the patient asymptomatic and in remission. The rare association of the two autoimmune conditions associated in the same patient without thymoma is discussed.

(PRCA). After treatment, on one occasion with high-dose intravenous Ig, he remained stable for 6 years, but then suffered a mild relapse with no symptoms. This relapse resolved spontaneously with no treatment after a 2-month period of observation, during which he required one transfusion initially. He did, however, after about 8 weeks, start complaining of difficulty with tongue movements and chewing and a sensation of food sticking at the back of the throat. Over a number of weeks, these symptoms progressed rapidly to the point of being unable to swallow liquids and developing slurring of speech. Symptoms were better on awakening in the morning. There was no double vision and no other symptoms of fatigue. On examination, he was found to be severely dysarthric with inability to swallow his own saliva. There was no ptosis or diplopia, no weakness of neck flexion and no fatigability of other muscles. His bulbar symptoms were on clinical grounds diagnosed to result from MG, although other conditions were to be excluded.

BACKGROUND

Pure red cell aplasia (PRCA) is an uncommon cause of anaemia and was originally described in 1922.¹ Red cell precursors in the bone marrow are absent resulting in a normocytic, normochromic anaemia. The condition may be congenital but is usually acquired and associated with haematological disorders including leukaemia.² It has also been associated with viral infections such as parvovirus B19 infection, autoimmune conditions and as an adverse effect of some medications.³ Thymoma has been found in about 10% of cases with PRCA.^{2,3} Myasthenia gravis (MG) is characterised by fatigability of skeletal muscle and associated with antibodies to acetylcholine receptors at the neuromuscular junction. Thymic hyperplasia is present in 65% and thymoma in 10% of patients.⁴ Case reports of the occurrence of both PRCA and MG in patients with thymoma are found in the literature.^{5,6} We report a case of PRCA and MG in the absence of thymoma.

CASE PRESENTATION

A 65-year-old male presented with symptoms of malaise, tiredness and shortness of breath on exertion and found clinically to be pale with no other signs on physical examination. He was confirmed to be anaemic at the time and on further investigation diagnosed to have pure red cell aplasia

INVESTIGATIONS

On investigation with his first presentation, a complete blood count revealed a haemoglobin of 6.0 (13–18 g/dL). Red cell count was 1.80 ($4.5\text{--}6.5 \times 10^{12}/\text{L}$). Haematocrit was 17.3 (40–54%) and mean cell volume was 95.1 (76–100 fL). Reticulocytes were initially high at 218.60 ($20\text{--}130 \times 10^9/\text{L}$), but dropped within 2 weeks to 7.00. White cell count was 6.10 ($3.5\text{--}11.0 \times 10^9/\text{L}$) and platelets were 378 ($140\text{--}400 \times 10^9/\text{L}$). Liver function, renal function and thyroid functions tests were normal. Serum B12 was 329.0 (142–725 pmol/L), serum ferritin 455.0 (28–365 ng/mL) and serum folate 7.40 (1.72–17.1 umol/L). Erythrocyte sedimentation rate was 38 (12–16 mm in first hour). C-reactive protein was <6 (0–10 mg/L). Tumour markers which included serum CA19.9, carcinoembryonic antigen and prostate specific antigen were within normal limits. Antitissue transglutaminase IgG and IgA were normal. Serum antineutrophil cytoplasmic antibody, antinuclear antibody and rheumatoid factor IgM were negative. Serum lactate dehydrogenase was 246 (135–220 u/L). Faecal occult blood was negative.

Imaging included chest X-ray and abdominal X-ray which were normal. Ultrasound of the abdomen was normal. CT scan of the thorax, abdomen and pelvis showed a homogenous lesion

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To cite: Aquilina A, Camilleri DJ, Aquilina J. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-220188

of low attenuation in the anterior mediastinum with features consistent with a thymic cyst, likely to be secondary to thymus involution or congenital.

A bone marrow trephine biopsy taken from the posterior iliac crest showed hypercellular marrow with marked reduction of erythroid precursor, myeloid hyperplasia and a normal megakaryocytic component. There was no obvious infiltrate on immunostaining, including CD3, CD20, CD5 and CD56. In conclusion, the findings were compatible with red cell aplasia. Parvovirus IgM antibodies in the blood were found to be positive. Direct antiglobulin test (Coombs) was initially positive but then repeatedly negative. Flow cytometry markers showed positive CD55/CD59 on RBC and WBC analyses, paroxysmal nocturnal haemoglobinuria negative. Serum protein electrophoresis was normal.

Haemoglobin at the time of the mild relapse 6 years after the initial presentation was 9.3 g/dL and reticulocyte count $9.40 \times 10^9/L$. A repeat bone marrow trephine biopsy confirmed relapsed PRCA. Viral screen for cytomegalovirus, rubella, toxoplasma, herpes simplex, Epstein Barr virus was negative. A repeat CT of the trunk showed only the thymic cyst unchanged as compared with the previous scan. Recovery from the PRCA was documented after about 8 weeks with a haemoglobin of 11.9 g/dL and polychromasia.

After a further 12 weeks, investigation for his bulbar symptoms included antiacetylcholine receptor antibodies which were positive at 15+ (<0.25 nmol/L). Antimuscle specific receptor tyrosine kinase (MUSK) antibodies were negative at <0.01 (<0.05 nmol/L). A repeat CT scan showed an unchanged thymic cyst and a positron emission tomography scan was negative.

Histology of the resected thymus gland showed a thin walled cyst with condensed proteinaceous content with few layers of bland squamoid cells in the wall and adjacent involutinal thymic tissue, compatible with thymic cyst.

TREATMENT

The patient was treated with repeated packed cell blood transfusions at his first presentation. He was subsequently given intravenous Ig after a diagnosis of PRCA was made with good response and a prolonged remission of about 6 years. On presenting with his mild relapse, further therapeutic options were being considered which included ciclosporin. However, the patient was reluctant to take this and his anaemia improved spontaneously. After about 8 weeks, he, however, presented with the bulbar symptoms of MG and responded to therapy with pyridostigmine 60 mg every 3 hours. He also received intravenous Ig at a dose of 0.4 g/kg/day for 5 days with subsequent improvement. In view of the common association of PRCA and MG with the presence of thymoma, it was decided to refer him for thymectomy. He underwent this surgery within a month without complications and has subsequently remained very stable and asymptomatic on treatment with pyridostigmine 60 mg every 3 hours, and regular intravenous Ig ever 4–6 weeks. He is reluctant to take steroids or other immunosuppressant medication and considers decreasing his present medications should symptoms remain in remission.

OUTCOME AND FOLLOW-UP

The patient remains stable and in remission on maintenance treatment with pyridostigmine and intravenous Ig with a view to tailing down the latter.

DISCUSSION

This case illustrates the occurrence of both PRCA and subsequently MG in the same patient. Acute infection with parvovirus was thought to have triggered the initial episode of PRCA in view of a positive serology IgM titre. Subsequent development of a mild relapse and shortly afterwards the development of MG with severe bulbar features indicate an association of these autoimmune conditions in this patient. The literature describes the rare association of PRCA with MG in patients having a thymoma.^{5 6} However, in our patient, only a thymic cyst was evident on repeated imaging and confirmed on histology after surgical resection. An association of the two autoimmune conditions therefore remains as the more probable explanation in this patient without thymoma. Parvovirus B19 infection has been implicated as a cause of PRCA in the literature with viral inclusions found in the bone marrow.⁷ However, the documented recent infection with parvovirus in our patient at the time of his initial presentation remains unexplained or may be postulated as having been the trigger for the autoimmune process.

Learning points

- ▶ This represents yet another case report of the rare association of pure red cell aplasia (PRCA) and myasthenia gravis, which should alert physicians to investigate appropriately when patients present with bulbar or other neurological features in patients with anaemia from PRCA.
- ▶ Thymoma can be associated with both conditions, but was not present in our patient.
- ▶ The role of the recent parvovirus infection at the time of the first presentation with PRCA is unexplained or may be postulated as the trigger for the autoimmune process.

Contributors AA encountered this interesting case and written it up for submission to BMJ Case Reports. The patient was under the care of DJC, Consultant Haematologist, for his pure red cell aplasia, and also under the care of JA, Consultant Neurologist, for his myasthenia gravis. Under their guidance, the data of the patient were compiled through information gained from the hospital interface as well as from the patient's medical notes. Both senior authors contributed equally to the case report and the discussion.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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