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Guillain – barre syndrome in a haemoglobin S patient

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Summary
A 43 year old female sickle cell anaemia patient who had a mild clinical course of the disease developed ascending paralysis, areflexia, sensory disturbance and bulbar affectation while on therapy with vitamin B_{12} for neurological complications of megalobalstic anaemia. She had initially presented with a history of paresthesia involving all extremities and moderate pain in both feet. Blood smear picture revealed macro-ovalocytosis and hyper-segmented neutrophils. Cerebrospinal fluid analysis revealed protein of >200mg %, WBC <5/mm^3-predominatly lymphocytes and was negative for cytology and Gram stain. This is the first case report of Guillain- Barre syndrome in a sickle cell anaemia patient.

Keyword: *Guillain–barre syndrome sickle cell anaemia*

Résumé
Une drépanocytaire anémie de 43 ans avait de symptome clinique legére de la maldaie développée une paralysie croissante, un réflexe des problémes sensoriel et bulbare alorsque qu'un traitement en vitamine B 12 contre des complications neurologiques d'anémie mégaloblastiques. Elle avait initialement une histoire de paresthésie des extremités et des douleurs moderées aux pieds. La microscopie de sang relévait la macro-ovalocytosie et les neutrophiles hyper-segmentés. L'analyse du fluide cérebrospinale revélait des proteins >200mg%, des globules blanc <5/ mm3- predominés par les lymphocytes et était négative a la cytologie et au gramme teinté. C'est le premier cas de syndrome de Guillain-Barre reporté chez un patient drépanocytaire.

Introduction

Guillain–Barre syndrome encompasses the spectrum of rapidly progressive demylinating polyneuropathies of the peripheral nervous system. This group includes acute inflammatory demylinating polyneuropathy (AIDP), acute motor-sensory axonal neuropathy, acute motor-axonal neuropathy and the Miller-Fisher variant. A similar syndrome that is more chronic and sometimes relapsing has been called chronic inflammatory demylinating polyneuropathy [1].

Guillain- Barre syndrome has been linked to several haematological disorders including the leukaemias [2,3,4]. To our knowledge this is the first report in a sickle cell disease patient in whom ascending paralysis, areflexia, sensory disturbance and bulbar affectation, signifying Guillain-Barre syndrome, occurred in the presence of megaloblastic blood smear changes.

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Case report

A 43-year-old woman, a known patient with sickle cell anaemia (homozygous haemoglobin S) diagnosed over 30 years ago. She had a mild clinical course of the disease; she was on omnivorous diet, receiving routine folate and vitamin B complex supplementation. She presented at the day care clinic where she gave a one-week history of paresthesia affecting all extremities with moderate pain in both feet. No antecedent history of diarrhoea. She denied use of medications outside routine drugs inclusive of sodium cyanate. On examination, she was not in painful crises, not febrile, not in distress. She had increased pigmentation of the palms and soles of the feet, hypopigmentation of the upper and lower lips and smoothening of the papillae of the tongue. Power was grade 5/5 globally, reflexes were normal, sensations were normal, and gait was normal.

Haematocrit was 24% (steady state 22 to 25%), platelets: 409,200/mm^3. Blood smear revealed anisocytosis, poikilocytosis, polychromasia, numerous sickled erythrocytes, macro-ovalocytosis and hyper segmented neutrophils. Serum Vitamin B_{12} and folate were not assayed because of the lack of necessary facilities. On the basis of history and peripheral blood smear appearance, vitamin B_{12} therapy was commenced- IM Hydroxycobalamin at 1mg alternate days times 6 doses, and routine folate supplementation was also continued.

On day 3 after admission and therapy, power in the lower limbs was grade 4/5, power in the upper limbs remained grade 5/5, reflexes were diminished globally, vibration sense reduced in the lower limbs and gait was ataxic. On day 12, the condition of the patient worsened abruptly; she complained of inability to sit up independently and she was unable to use her hands to eat. Power in the lower limbs was grade 1/5, there was global areflexia and impaired joint position and vibration sense; light touch and pain remained intact. Upper limb power was grade 2/5, weakness was worse in the fine muscles of the hand. She also had bilateral facial paresis, worse on the left than the right.

On day 13 she complained of difficulty with swallowing, worse with fluid and associated with coughing. She also began experiencing episodic difficulty with breathing and speaking. She also complained of constipation. A lumbar puncture revealed cerebro-spinal fluid protein of >200mg%, WBC <5/mm3- predominantly lymphocytes. Finding of cytological examination and gram stain were negative.

Guillain-Barre syndrome was diagnosed. Patient had modified plasmapheresis and a course of steroids therapy; prednisolone at a dose of 15mg 8 hourly was given. She made an initial mild clinical progress with improvement of muscle power to grade 2/5.

On day 33 she developed a febrile illness. There was associated haematuria and deep jaundice, packed cell volume was 18%. She was transfused with 2 units of packed cells at one unit daily and empirical antibiotic therapy was commenced. Clinical condition however deteriorated and she expired on day 36 of admission.

Discussion

This patient showed unusual associations of sickle cell disease in the presence of megaloblastic blood smear changes, and the Guillian-Barre syndrome. An association between sickle cell disease and neurological syndromes was first describes by Sydenstricker *et al* in 1923 [5]. An association with Guillain- Barre syndrome has however never been described. Impairment of various arms of the immune system has been demonstrated in sickle cell disease [5]. The weight of evidence in Guillain- Barre syndrome indicates that it is immune mediated, although the exact immunopathogenesis remains obscure [6].

Guillain – Barre syndrome is thought to be a single response of the nerve to a variety of infective processes. It can occur at any age and the clinical findings may be variable [7].

This patient had sickle cell disease that was diagnosed over 30 years before this presentation and she had been regular at clinic-visits every 3 months. She had a mild clinical course of the disease; she however developed symptoms signs and blood smear findings consistent with vitamin B_{12} deficiency.

It has been shown that patients with severe sickle cell disease may suffer from unrecognized vitamin B_{12} deficiency. Sinow *et al* [8], also described a case of unsuspected pernicious anaemia in a patient with sickle cell disease receiving routine folate supplementation while Dharmarajal *et al* [9] reported a case of life threatening vitamin B_{12} deficiency in a patient that had sickle cell trait [10]. Guillain–Barre syndrome was not associated with any of the above reported cases.

Clinical improvement in sickle cell disease associated with Vitamin B_{12} deficiency as in the case reported by Dharmarajal *et al* [10] is usually dramatic. This patient we report developed ascending paralysis during the course of therapy (there has not been previous documentation of an association between intramuscular vitamin B_{12} therapy and Guillain – Barre syndrome) and her presenting symptoms of paresthesia affecting all extremities and moderate pain affecting both feet may have indeed been prodromal symptoms of Guillain – Barren syndrome. It is also worth – noting that at presentation there was a history of pain in both feet which was of moderate intensity

Pain as a primary complaint in Guillain – Barre syndrome often-preceding onset of motor paralysis has been reported [11]. This is particularly important in this case in whom pain as a result of vaso-occulusive crises would tend to be the more common cause of pain. She was however not in vaso-occulusive crises at presentation. In the cases of sickle cell disease and sickle cell trait associated with Vitamin B_{12} deficiency reported by Sinow *et al* [9] and Dharmarajal *et al* [10] respectively, pernicious anaemia an autoimmune based disease was implicated as the cause of the vitamin B_{12} deficiency. In our report a case for possible autoimmune-based vitamin B_{12} deficiency is also plausible as.

1. The patient's diet was omnivorous she was also on routine vitamin B_{12} supplementation thus a dietary aetiology from inadequate consumption was most unlikely
2. There was the absence of intestinal surgery, chronic pancreatitis and Crohn's disease-pathological conditions known to precipitate vitamin B_{12} deficiency.
3. She had dermatological lesions (Hypo pigmentation of the lips and hyper pigmentation of the palms and sole of the feet), which are pointers to a possible autoimmune disease.

The occurrence of Guillain – Barre syndrome in association with another immune based disease has been documented in the literature. Emsley *et al* reported a case of inflammatory demylinating polyradiculopathy associated with membranous glomerulonephritis and thrombocytopenia [12] while Niclai A *et al* reported a case of opsoclonus, a rare eye movement disorder with an immune pathogenesis, in a patient with Guillain – Barre syndrome[13] Sinardi D *et al* also reported a case of autoimmune mediated central nervous system vasculitis related to an episode of Guillain – Barre Syndrome [14]. There has also been a report of an association of chronic inflammatory demylinating polyradiculopathy with membranous glomerulonephritis [15].

While Guillain – Barre syndrome includes several pathological subtypes the most common is a multifocal demylinating disorder of the peripheral nerve in close association with macrophages. There is also evidence to suggest that there is involvement of both cell mediated and humoral mechanisms, and immunological studies suggest that one third of patients have antibodies against nerve gangliosides [16].

Sickle cell anaemia and the Guillain – Barre syndrome are both disorders in which there is disruption of the immune system. The association between these two conditions in this case report although interesting may however have been co-incidental.

Conclusion

We report a patient with sickle cell anaemia who developed megalobalstic changes. She had intramuscular vitamin B_{12} with minimal improvement. She however developed ascending paralysis, areflexia, sensory disturbance

and bulbar affectation (features consistent with the guillain-barre syndrome) while on therapy, her clinical state worsened gradually and she finally expired.

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