PRACTICE REVIEW

Sydenham's chorea – clinical and therapeutic update 320 years down the line

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Post-streptococcal neuropsychiatric movement disorders (PNM) were first described in the Middle Ages, but today more than 300 years later, confusion remains surrounding the terminology, treatment and monitoring of these conditions.

Rheumatic fever is currently the major cause of acquired heart disease among children in South Africa.[1] The incidence of acute rheumatic fever (ARF) and rheumatic heart disease (RHD) is not declining. Recent figures quote the incidence of rheumatic fever as 0.6 - 0.7/1 000 population in the USA and Japan compared with 15 - 21/1 000 population in Asia and Africa.[2] In a study conducted in 1975 in Soweto, South Africa, 12 050 schoolchildren were examined and 19.2/1 000 had rheumatic heart disease.[3] A 2002 report from a cardiology workshop highlighted the belief among clinicians that South Africa is currently in the midst of a rheumatic fever epidemic.[4,5] Sydenham's chorea (SC) is a major manifestation of ARF. Accordingly, in the South African context when PNMs are diagnosed, treatment strategies must always include the prevention of RHD.

History

The term chorea originates from the Greek word 'khoreia', which translates as 'the act of dancing'. Paracelsus (1416) used the term chorea to describe the frenzied, hysterical movements of religious fanatics who visited healing shrines of St Vitus during the Middle Ages (St Vitus dance/chorea major), 'the emphasis here is hysterical'. In 1686 (320 years ago) Thomas Sydenham noted that chorea was occasionally associated with arthritis. He realised that chorea was organ-based and used the term chorea minor or Sydenham's chorea (SC).

In 1894, William Osler noted the behavioural component that has features of obsessive-compulsive disorder (OCD). He observed that some patients with chorea minor had a certain 'perseverativeness of behaviour'.

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In 1980, Susan Swedo described the first 50 cases of paediatric auto-immune neuropyschiatric disorders associated with streptococcus (PANDAS).[6]

In 2003 Dale *et al*.[7] described a spectrum of poststreptococcal auto-immune basal ganglia disorders. Group A beta-haemolytic streptococcus (GABHS) is linked to a number of autoimmune conditions (Table I).[7, 8]

Pathogenesis of the auto-immune response

A GABHS infection in a susceptible host leads to an abnormal immune response. A marker called the D8/17 marker is a monoclonal antibody, directed against a polymorphic protein on the surface of B-lymphocytes. This marker is present in over 90% of patients with ARF and in 85% of patients with PANDAS, but it is not found in healthy controls.[9,10] A single (limited) study has been performed in South Africa to establish the usefulness of this marker to identify susceptible hosts and its expression in South African populations *per se*.[11] It was postulated that these susceptible hosts produced abnormal antibodies, which attached to epitopes in the heart, leading to a pancarditis, or in the basal ganglia, resulting in conditions such as SC and PANDAS.[9,10]

Clinical features of Sydenham's chorea (SC)

SC is a neuropsychiatric disorder; the clinical features include both neurological abnormalities (choreatic movements,

Table I. Conditions associated with poststreptococcal autoimmune disorders

- SC
- PANDAS
- Tourette's disorder
- Chronic tic disorder
- ADEM
- Dystonia
- Myoclonus
- Anorexia nervosa

SC = Sydenham's chorea; PANDAS = paediatric auto-immune neuropsychiatric disorders associated with sttreptococcus; ADEM = acute disseminated encephalomyelitis.

weakness and hypotonia) and psychiatric disorders (such as emotional lability, hyperactivity, distractibility, obsessions and compulsions).[12] These abnormalities lead to inability to perform normal activities of daily living (ADL) including eating, talking, dressing, writing, walking, learning and socialising, and thus impact negatively on the child's quality of life. Although SC is typically described as benign and self-limiting,[13] our experience at the Rheumatic Fever Clinic (RFC) at Red Cross Children's Hospital (RCCH) is that at best it lasts for 6 months but more usually it has a relapsing course for up to 2 years, or at worst it may evolve into a chronic movement disorder.[14] The hypotonia and weakness range in severity from mild to severe, where it is termed chorea mollis[15] and may be confused with a stroke.

The clinical features of chorea were classified by Aaron *et al*.[16] as minimal, mild, moderate and severe: minimal – elicited on examination; mild – patient aware of chorea but no ADL affected; moderate – can ambulate and some ADL limited; severe – cannot ambulate, many ADL limited. This classification while useful does not take into account the impact of the psychiatric component on daily functioning. (We are currently formulating a rating scale which will include these parameters.)

SC abounds with a variety of clinical signs such as hippus, milkmaids, grip, piano-playing movements, pronator sign and many more. These too should be harnessed into a standardised scale, which would facilitate objective monitoring of the progression of the illness.

Results of studies performed during the first half of the 20th century established the tenet that only pharyngeal infection with group A streptococcus causes ARF.[13] Carapetis *et al*.[13] have recently challenged this concept. They have hypothesised that 'in tropical countries with a high prevalence of both pyoderma and rheumatic heart disease, skin infections caused by group A streptococcus have a priming role or even cause acute rheumatic fever, either directly or by subsequent infection of the throat'.[13] We must take cognisance of this; treatment of streptococcal skin infections at a primary health care level is recommended.

Physiology of poststreptococcal neuropyschiatric movement disorders

Motor movements, attention and emotions all result from a complex interaction of neurotransmitters in the basal ganglia, limbic systems and pre-frontal cortex.[17] Gamma-amino butyric acid, dopamine, noradrenaline and serotonin all play a role. Dopamine is particularly important in the control of motor movements. Excess dopamine results in hyperactivity, jerks and stereotyped movements.

Medications that act on the dopamine system include haloperidol and pimozide which block dopamine receptors, clonidine which increases pre-frontal lobe dopamine, L-dopa which increases dopamine levels and methylphenidate which stimulates dopamine neurones.

Explanation of clinical features of SC

The clinical presentation of SC consists of two syndromes in one disorder: (*i*) a tic or movement syndrome which results from overactivity of dopamine neurones; and (*ii*) a pre-frontal lobe syndrome which results from underactivity of dopamine neurones and which is also influenced by serotonin and nor-adrenaline. The pre-frontal lobe syndrome manifests as inability to pay attention, emotional lability, impulsivity and thoughtless actions.[17]

Neuropsychiatric movement disorders are influenced by dopamine, nor-adrenaline and serotonin. A dopamine-driven system would function as follows: Antibodies attach to epitopes in the basal ganglia, which results in decreased dopamine activity in the ventral tegmental area. This in turn results in decreased dopamine activity in the frontal lobe. This leads to disinhibition of subcortical structures, which leads to attention deficit disorder (ADD), impulsivity, learning difficulties and hyperactivity.

The decreased dopamine in the ventral tegmental area also leads to increased sensitivity of dopamine receptors in the striatum, leading to abnormal motor movements. In addition, the disinhibition effect leads to increased sensitivity of dopamine receptors. This concept of disinhibition is a key factor.[17]

Greater understanding of these behaviour trends in SC should follow from current studies being undertaken by the Department of Psychiatry, University of Stellenbosch and Rheumatic Fever Clinic, University of Cape Town, reviewing neuropyschiatric sequelae of affected patients early (at 6 months) and long term (2 - 12 years).

The Rheumatic Fever Clinic (RFC)

This clinic was established in the early 1970s by Dr Hyam Joffe (then head of cardiology at RCCH), housed in the pre-fab buildings of the old outpatient department. Currently 10 - 12 'old' cases are booked weekly and an average of 3 - 4 new referrals are received per month. These figures have not changed over the years, but the attendance rate has improved with patients keeping appointments and often phoning to reschedule when necessary. The goals of the clinic include empowering these young people to understand and take charge of their own illness, and facilitating transfer to an adult unit when indicated. With this end in mind a special Adolescent Rheumatic Fever Clinic will operate once-monthly from May 2006. It is hoped that these young people will become advocates and counsellors to create an awareness of rheumatic fever and its consequences. A database of attendees at the RFC is kept to facilitate improved data collection from developing countries.[13]