

HIV AND SICKLE CELL DISEASE

EPIDEMIOLOGY

Sickle cell disease (SCD) is a genetic disorder that is characterised by a chronic anaemia occurring almost exclusively in individuals of African descent. Individuals afflicted with SCD are homozygous for a key mutation in haemoglobin, whereas individuals who are heterozygous for this mutation are generally asymptomatic and are said to have *sickle cell trait*. SCD is relatively common throughout the Caribbean and could present some unique clinical management issues as a co-morbidity with chronic HIV infection.

CLINICAL MANIFESTATIONS

The clinical manifestations of SCD are due to both anaemia and vaso-occlusive events that result in tissue ischemia and infarction. SCD patients suffering from painful vaso-occlusive events are said to be in *sickle cell crisis*. Common causes of death for individuals with SCD are intercurrent infections, multiple pulmonary emboli, occlusion of a vessel supplying a major organ, and renal failure. The average life span of SCD patients is age forty to forty-five years.

Anaemia in SCD is usually stable but acute exacerbation of anaemia occurs in the setting of aplastic crisis, in which marrow red blood cell (RBC) production abruptly slows down. Aplastic crisis is usually the result of an acute infection; hence immunocompromised patients may be at higher risk for this complication. Individuals with sickle cell trait who are also HIV-infected are not expected to have significant worsening of any manifestations of their HIV disease or of their sickle cell trait.

MANAGEMENT OF THE PATIENT WITH CO-MORBID SCD AND HIV INFECTION

General Principles of Management

Infection with encapsulated organisms is more common in SCD patients with functional asplenia. HIV co-infection also appears to increase susceptibility to these infections, especially in children. Prophylactic antibiotics, pneumococcal vaccine, and early identification and treatment of serious bacterial infections are therefore critical.

The use of hydroxyurea (HU) in SCD is well established, and its use for treatment of HIV disease has been investigated. However, data from controlled clinical trials have revealed high rates of toxicity (e.g. pancreatitis, neuropathy, hepatotoxicity, and cytopenias) and blunted CD4+ T cell count responses in patients receiving HU with antiretroviral therapy (ART). Current guidelines therefore suggest that HU should generally not be offered as adjunctive therapy for HIV infection. Unfortunately, no data exist from controlled clinical trials involving patients with SCD who receive HU with ART. Clinicians considering the use of HU for HIV-infected patients with SCD should be aware of the potential additional toxicity of this agent when administered with nucleoside reverse transcriptase inhibitors (NRTIs).

Management of Anaemia

Anaemia is a common consequence of SCD, HIV disease, and some antiretroviral (ARV) agents, especially zidovudine (AZT). Therefore:

- ✓ Patients should be screened for anaemia prior to initiation of ART;
- ✓ The design of ARV regimens for patients at risk for anaemia should take into account the potential of individual agents to induce or exacerbate anaemia;
- ✓ Monitoring of haemoglobin levels is warranted after initiation of therapy, especially for patients with SCD or other risk factors for anaemia;
- ✓ ARV-induced anaemia typically improves once the offending agent is discontinued. Thus, appropriate modification of a patient's ARV regimen is advisable in the case of anaemia that is attributable to one or more of the prescribed ARV agents.

Management of Sickle Cell Crisis

Therapy is largely symptomatic for the sickle cell crisis. Standard interventions include rehydration, analgesics, and oxygen therapy. The presence of HIV infection in a patient suffering from a sickle cell crisis does not alter this general approach.

PAEDIATRIC CONSIDERATIONS

Splenic malfunction is common in both SCD and HIV infection. Therefore, several of the common infections seen in SCD also occur in HIV-infected children. However, while these two patient populations are not uncommon in the Caribbean, none of the publications on cohorts of children with HIV disease or sickle cell anaemia have described children afflicted with both disorders. Caribbean studies of pneumococcal and/or *Haemophilus influenzae* Type B infections have similarly failed to document outcomes involving children with both SCD and HIV infection.