A rare and insidious brain vessel disorder in children with HIV infection

Over the last decade children who acquire HIV infection from their mothers are surviving longer due to improved access to health care, nutritional support and antiretroviral therapies (ART). As they live longer, complications which were previously not recognised in this age group are becoming apparent. Stroke may result from direct invasion of the blood vessels in the brain by the HIV virus or opportunistic pathogens, or indirectly from clots, cardiac abnormalities or side effects of some antiretroviral therapy. Affected children may present with overt limb and/or facial weakness or “silent” events affecting behaviour and cognition without obvious weakness. There are reports of patients who have progressed silently to moyamoya syndrome.

Moyamoya disease is a rare disorder of the blood vessels of the brain leading to occlusion or narrowing of the vessels associated with the development of collateral network around the blocked vessels to compensate for the blockade. The collateral vessels are small, weak and prone to haemorrhage, dilatations and clots formation, and thus may present with recurrent strokes with diverse clinical signs including headache, seizures, motor, sensory, speech and visual deficits, personality changes, involuntary movements, disturbances of consciousness, and intellectual disability. On brain radiograph, the disease has a characteristic picture from which it derives its name “moyamoya”, a Japanese term which translates as a “puff of smoke”.

The origin of moyamoya disease is unknown. However, in some genetic, haematological and neoplastic (malignant) conditions a similar radiographic picture referred to as moyamoya syndrome occurs.

In the medical literature, though there are several reports of HIV-infected children presenting with strokes, only 2 cases of moyamoya syndrome had been reported. This report describes the South African experience of HIV-infected children presenting with cerebral blood vessel disorders and delineates a sub-group with moyamoya syndrome.

Between 2000 and 2015, 17 children with HIV-1 infection presented with cerebral blood vessel abnormalities at the 7 tertiary paediatric neurology centres in South Africa. Of these, 5 had moyamoya syndrome, 10 had isolated stroke which did not progress to moyamoya, and 2 had dissections of the carotid artery (Tab. 1).

Type of vascular disorder	Number of children	Sex (M:F)	Median age at presentation (age range)	Impaired viral suppression	Indirect cause and other aetiologies (number of cases)
Moyamoya syndrome	5	1:4	5.8 years (2.2 – 11)	**5/5**	Down syndrome (n=1)
Isolated strokes (without moyamoya syndrome)	10	7:3	7 years (2.3 – 11)	7/10	Post-chicken pox (4) Raised triglyceride and cholesterol (3) Decreased protein S levels (2) Increased C3 complement levels (1) Immune reconstituted inflammatory syndrome (1)
Arterial dissection	2	2:0	(1.4 -7 years)	1/2	Epidermal naevus syndrome (1)
Total	**17**	**10:7**	**6.3 years (1.4 – 11)**	**13/17**	

Tab. 1. Summary of the study cohort of children with HIV-associated cerebral blood vessel abnormalities referred to paediatric neurology services in South Africa between 2000 and 2015

The 5 children who presented with moyamoya syndrome were all of indigenous African ancestry and acquired HIV-1 infection through vertical transmission. The median age at presentation was 5.8 years (range 2.2 – 11 years). Four presented between 2002 and 2010, and one in 2015, when their HIV infection was inadequately suppressed, because either HIV infection was not diagnosed or treatment with ART was sub-optimal. Four of the children had no evidence of another cause for their vascular complications, the fifth had Down syndrome in addition to HIV infection.

In all 5 children, there were brain imaging evidence of preceding vascular events which appeared to be silent until they finally presented to neurology services with strokes or cognitive regression. The children did not have other HIV-related factors which could have predisposed them to stroke. Their main common factor was poor viral suppression which was evident as low CD4 counts or high viral loads. Following initiation of ART leading to viral suppression, 4 patients showed improvement in their clinical cause. One patient who presented in 2002 did not receive ART as her parents declined enrolment. With the improved availability of ART drugs in the public health sector, only 1 patient (with an additional risk factor of Down syndrome) has presented with this progressive vascular disorder in the last 5 years.

Conclusion

Findings from this study suggest that moyamoya syndrome in HIV-infected children can progress “silently”, and manifest with misleading phenotypes such as cognitive delay or regression. Improve viral suppression may prevent the progression of this rare vascular disorder. Where moyamoya syndrome is identified, it is important to follow-up with serial brain imaging. In sub-Saharan Africa where access to neuroimaging is limited, affected children may be under-diagnosed.

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