Cerebroretinal Microangiopathy with Calcification and Cysts in a Young Man—A Recently Described Syndrome

Pari Shams², Ata Siddiqui¹, Lisa Scoppetuolo¹, Dominic Parvour¹, Moin Mohamed¹, Gordon Plant¹
¹The Guys and St. Thomas’ Hospital NHS Foundation Trust, London, United Kingdom, ²Moorfields Eye Hospital, London, United Kingdom

HISTORY & EXAM:
A 24 year old Caucasian man presented with a 2 month history of floaters affecting the left eye. He was noted to have evidence of a retinal occlusive disease, telangiectasia and left vitreous haze. He was a myope. Two years earlier he was incidentally found to have evidence of chronic, inactive bilateral retinal vasculitis.

His past medical history consisted of intrauterine growth retardation and speech therapy at age 3. Age 7 he was diagnosed with osteopenia and Perthes disease and underwent a right femoral osteotomy. Age 13 he was found to have a pancytopenia, a hypocellular bone marrow and a thrombocytopenia of 50 which did not respond to immunoglobulin or steroids. Age 15 he developed an asymmetric upper limb intension tremor. He had migraine headaches since childhood. Twice per year there were episodes of dysarthria and deviation of eyes to the left, lasting 5–15 minutes. He did not complete his studies at university and there was concern over recent cognitive decline. There was no family history of consanguinity.

On examination he was found to be of short stature with clubbing of his finger nails. There was leuconychia, smooth hairless skin, generalised cutis marmorata and upper body telangiectatic vessels and hypopigmentation.

Ocular movement showed slow voluntary saccades. There was bilateral hypertonia and hyper-reflexia of the upper and lower limbs and bilateral intension tremor worse on the right and normal planar responses. Irregular jerky dystonia and a postural tremor were noted. His cardiovascular, respiratory and abdominal examination was within normal limits. His visual acuity was 6/6 left and 6/4 in the right eye. Fundoscopy revealed evidence of an ischaemic retinopathy and left vitreous haze.

He is currently under investigation for weight loss, epigastric pain and a macrocytic anaemia.

FINANCIAL DISCLOSURE: NONE
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Answer

FINAL DIAGNOSIS:
Cerebroretinal Microangiopathy with Calcification and Cysts

SUMMARY OF CASE INCLUDING PATHOLOGY:
We report a young man with bilateral occlusive retinal microangiopathy associated with intracranial calcification, cysts and leucoencephalopathy. He has been under medical care since birth but not diagnosed until the age of twenty four. He manifests many of the clinical features of two rare disorders; leucoencephalopathy with calcification and cysts (LCC)\textsuperscript{1,2} and so-called “Coats plus” syndrome\textsuperscript{3,4} including intrauterine growth retardation, bilateral retinal telengectasia and ischaemia, sparse hair, hypertonia and hyper-reflexia, dystonia, skeletal defects, pancytopenia, with a hypocellular bone marrow, hepatosplenomegaly, and gastrointestinal symptoms. CT and MRI brain scans demonstrated coarse calcification of the basal ganglia, pons and temporal lobe white matter with extensive and diffuse white matter signal abnormality and patchy contrast enhancement. There were associated cysts, particularly in the parietal white matter. Fundoscopy revealed evidence of an ischaemic retinopathy, right macular telangiectatic vessels and left vitreous haemorrhage and fluorescein angiography confirmed bilateral extensive areas, including the macula, of capillary non perfusion vascular anomalies but no neovascularisation. A left superior visual field defect was found on Goldmann and Humphrey visual fields showed. A skin biopsy showed atrophy with marked decrease of hair follicles and other adnexal structures whilst his muscle biopsy showed pronounced course granularity of the mitochondria with gomori stain and marked subsarcolemmal deposition of reaction product on the MADH preparation, with absence of ragged red fibers. His cytogenetic studies including chromosomal and mitochondrial DNA analysis have not shown any known defect.

Recent evidence suggests that LCC and Coats plus syndrome represent the same clinical entity\textsuperscript{2,5-11} with a common pathogenesis involving a small vessel obliterative microangiopathy now known as “cerebroretinal microangiopathy, calcification and cysts”. The presence of Coats-like retinopathy in a child without neurological symptoms or the discovery of cerebral calcification in the absence of an ophthalmic complaint should prompt a search for the other clinical features of this syndrome which are now thought to be manifestations of the same disorder.

The 24 year old patient, born with intrauterine growth retardation, slowly developed over many years, a constellation of skeletal, haematological, dermatological, neurological and ophthalmological signs and symptoms which at the time were difficult to fit to any single known disease entity. The two conditions which best fit his clinical manifestations were leucoencephalopathy with calcification and cysts (LCC) and a Coats plus–like syndrome, now thought to be part of a spectrum of disorders caused by a cerebral microangiopathy.

KEYWORDS: Cerebroretinal microangiopathy, Ischaemic/occlusive retinopathy, Intracranial calcification and cysts, Coats plus syndrome, Leukoencephalopathy

REFERENCES: