Paediatric Pearls

by Dr Julia Thomson, Paediatrician

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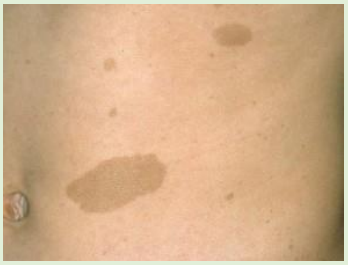
Monthly paediatric update newsletter for all health professionals working with children – put together by Dr Julia Thomson, Paediatric Consultant at Homerton University Hospital, London, UK. Housed at www.paediatricpearls.co.uk where comments and requests are welcome!

Dermatological manifestations of systemic disease - Neurofibromatosis type I

by Dr Anusuya Kawsar, dermatology registrar at Barts Health NHS Trust.

Last month, the axillary freckling seen in children from about 5 years old with NFI featured in the "What's in an armpit?" quiz. Here are some other dermatological findings in this autosomal dominant phakomatous* disease:

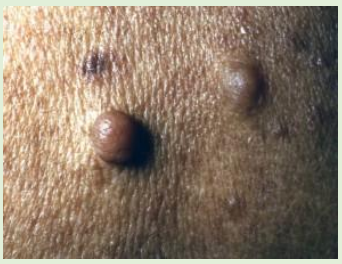


Café-au-lait macule

- Hyperpigmented light brown patch, evenly distributed pigment
- Well demarcated, round or oval
- Present at birth or early infancy

Multiple (more than 6) café-au-lait macules over 5mm are related to several genetic syndromes:

Neurofibromatosis type 1 (NF1)
Neurofibromatosis type 2
Legius syndrome
McCune Albright syndrome
Noonan syndrome with multiple lentigines
Watson syndrome
Bloom syndrome
Silver-Russell syndrome



Neurofibromas

- Soft brown, pink or skin-coloured nodules – pea-sized bumps on skin
- Usually appear during puberty and continue appearing in adulthood
- Usually benign tumours which grow along nerves anywhere in the body. May become malignant in 10% of people.
- May recur if surgically removed.

NF1 is not rare! Birth incidence is 1 in 2500 to 1 in 3000.

There should be 2 or more of the following 7 DIAGNOSTIC CRITERIA:

1. ≥ 6 café-au-lait patches (>0.5cm in children, >1.5cm in adults)
2. ≥ 2 neurofibromas or 1 plexiform neurofibroma
3. Axillary or groin freckling
4. Optic pathway glioma
5. ≥ 2 Lisch nodules (iris hamartomas seen on slit lamp examination)
6. Bony dysplasia (sphenoid wing dysplasia, bowing of long bone)
7. First degree relative with NF1

By the age of 8, most children with NF1 will meet the diagnostic criteria
95% of children with 6 café-au-lait patches alone will develop NF1
De novo mutations are common; half of cases have no family history of NF
(NF2 and Schwannatamosis are different and present outside of childhood)

Children with NF1 should have an annual assessment:

There is a good article on diagnosis and management of people with NF1 from *J Med Genet* here.

Table 3 Assessment of children with neurofibromatosis 1

The following should be recorded at each annual visit
• Development and progress at school
• Visual symptoms, visual acuity and fundoscopy until age 7 years (optic pathway glioma*, glaucoma)
• Head circumference (rapid increase might indicate tumour or hydrocephalus)
• Height (abnormal pubertal development)
• Weight (abnormal pubertal development)
• Pubertal development (delayed/precocious puberty due to pituitary/hypothalamic lesion)
• Blood pressure (consider renal artery stenosis, phaeochromocytoma)
• Cardiovascular examination (congenital heart disease, especially pulmonary stenosis)
• Evaluation of spine (scoliosis ± underlying plexiform neurofibromas)
• Evaluation of the skin (cutaneous, subcutaneous and plexiform neurofibromas)
• System examination if specific symptoms

*Asymptomatic children should also have one baseline assessment of colour vision and visual fields at the appropriate developmental age.

*phakomatoses refers to a group of neuro-oculo-cutaneous syndromes involving structures arising from the embryonic ectoderm. They include neurofibromatosis, tuberous sclerosis, Sturge-Weber syndrome, von Hippel-Lindau disease and ataxia-telangiectasia.

LESSONS FROM THE FRONT LINE Dr Lucy Walker (GPST2)

A 14 year old boy presented with acute dizziness, headache and vomiting 3 days into a chicken pox infection. Afebrile now, full house of cerebellar ataxia clinical signs – slurred speech, past-pointing, ataxic gait, nystagmus.

DIFFERENTIAL FOR ACUTE ATAXIA

- Post-infectious
- Toxins
- Tumours
- Trauma
- Metabolic
- Infections
- Vascular (stroke)
- Immune incl ADEM
- Conversion disorder

Further reading: **https://www.rch.org.au/clinicalguide/guideline_index/Ataxia/**

VARICELLA CEREBRITIS

- Onset over few hours to few days
- Follows prodromal illness (not only varicella) within days up to 3 weeks
- LP only indicated if fever, meningism, seizures/altered mental state
- Consider neuroimaging (MRI)
- Acyclovir unlikely to help
- Lack of evidence re IVIG and steroids
- Resolves 2-3 weeks later in 90% cases

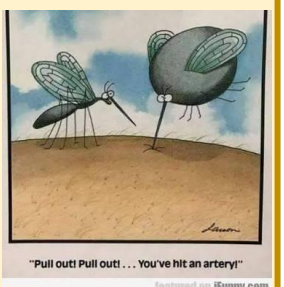
Restless legs syndrome (https://www.rls-uk.org/what-is-rls) is characterised by an irresistible urge to move to stop uncomfortable or odd sensations. Affects up to 10% of people in UK, F > M. Children get it too. Can be mistaken for ADHD if the child keeps fidgeting in class. Associated with Periodic Limb Movements (PLM) or limb jerking in sleep. Usually idiopathic but can be secondary to iron deficiency anaemia, renal and some autoimmune diseases. Refer children to a neurologist.

https://www.rls-uk.org/self-management has lifestyle advice for people with RLS.
Resources: https://www.nhs.uk/conditions/restless-legs-syndrome/diagnosis/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4961894/pdf/tre-06-401-7522-1.pdf

Dr Neaha Patel's Coca-cola urine story continued……

HAEMOGLOBINURIA causes intravascular haemolysis. There is excessive destruction of red blood cells, resulting in free haemoglobin in the plasma. Excess haemoglobin is subsequently filtered by the kidney and excreted into the urine which looks like "coca-cola". Acute haemoglobinuria indicates massive intravascular haemolysis.

Causes
Infections: Malaria – Blackwater fever
Drug-related: Post-artemisinin delayed haemolysis
Inherited: Paroxysmal nocturnal haemoglobinuria
G6PD deficiency
Sickle cell anaemia
Transfusion reactions



Our patient (see June 2019 newsletter) had been treated for *Plasmodium falciparum* malaria. Had it been only partially treated and now, 2 weeks later, she was presenting with Blackwater Fever? She seemed rather too well for that.

Malaria is a notifiable disease in the United Kingdom, with cases being imported by overseas travellers or visitors to the country. 10% of all cases in the UK are in children under 18 years. Most cases are caused by *Plasmodium falciparum* (81%), with a smaller number by *Plasmodium vivax* (9.2%) and *Plasmodium ovale* (6%). In severe cases, children can develop shock, hypoglycaemia, metabolic acidosis, jaundice, severe anaemia and renal failure. Every patient with suspected malaria must also be tested for G6PD deficiency. Treatment guidelines recommend oral Riamet (artemether with lumefantrine) for uncomplicated cases of falciparum malaria and parenteral artesunate in severe cases.

Blackwater Fever is an uncommon but severe complication of malaria and occurs almost exclusively with *Plasmodium falciparum* malaria. It is characterised by intravascular haemolysis, acute renal failure and the passage of black/"coca-cola" urine in severe *Plasmodium falciparum* infection when treated with amino-alcohol drugs including quinine, mefloquine and halofantrine. Whilst it is predominantly associated with Plasmodium falciparum infection (and quinine treatment), cases have been documented in association with *Plasmodium vivax*, *Plasmodium knowlesi* and *Plasmodium malariae*. Sufferers are extremely unwell with minimal or absent parasitaemia on peripheral blood smear. Mortality is high and secondary to renal failure. Chloroquine resistance and the use of quinine again has led to a recent global increase in incidence.

Post-artemisinin delayed haemolysis in *P. falciparum* malaria – the reason everyone treated with artesunate must have a repeat FBC 2 weeks later. Artesunate is the first-line treatment for severe malaria in the UK and has fewer side effects when compared to quinine. However, patients treated with IV artesunate for severe falciparum malaria can occasionally experience a delayed haemolytic episode. Artesunate functions by inducing pitting of red blood cells (dead parasites are expelled from the erythrocytes in the spleen) – these once infected erythrocytes then return to the circulation, and are then cleared a few weeks later, resulting in haemolysis.

This delayed haemolysis can occur in 20-25% of patients treated with IV artesunate, and up to 60% of those may require a blood transfusion. They will present approximately 2 weeks after treatment with fatigue, pallor, jaundice and "coca-cola" urine. Our patient had been given an appointment for a repeat FBC but presented with her coca cola urine a few days before the appointed date.

Jauréguiberry S et al. Post-artesunate delayed hemolysis is a predictable event related to the lifesaving effect of artemisinins. *Blood*. 2014 Jul 10; **124**(2): 167–175. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4093678/)