Shropshire Community Health NHS Trust

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2	V2 July 2022	Updated
3	V3 July 2024	General review and included links for measurements
4		
5		

Contents

1 Introduction

The measurement of head circumference (also called occipitofrontal circumference [OFC]), a direct reflection of head growth, is a crucial step in the evaluation of childhood growth and development. Deviations from normal head growth may be the first indication of an underlying congenital, genetic, or acqu ired problem (e.g. congenital infection, genetic syndrome).

The earlier these conditions are detected, the earlier appropriate treatment, services and genetic counselling can be provided.

This guideline applies to children and young people up to the age of 18 years.

2 Purpose

This guidance covers the assessment and investigation of macrocephaly. The guidance also covers the management of macrocephaly.

3 Definitions

The term ‘macrocephaly’ is a clinical finding and should not be used as a disease designation.

Macrocephaly is defined as an occipitofrontal circumference (OFC) more than 2 standard deviations (SD) above the mean for a given age, sex, and gestation (or above the 98th percentile). 2.3% of the general population would be considered macrocephalic even though many of these individuals are simply at the upper end of the population distribution. It is therefore essential to measure the OFC of the parents before considering further investigations.

Macrocephaly is mild when the OFC is between 2 and 3 SD above the mean and severe when the OFC is greater than 3 SD above the mean.

OFC is determined by measuring the greatest occipitofrontal circumference (from the occipital prominence to the frontal prominence- taking the biggest measurement of 3).

AVM- arteriovenous malformation

CNS-Central Nervous System

CSF-cerbrospinal fluid

CT- computerized axial tomography scan

FBC- Full Blood Count

GAG- Glycosaminoglycans

IVH- Intraventricular Haemorrhage

ICP- Intracranial pressure

NAI- Non accidental Injury

MRI- Magnetic resonance imaging

OFC –occipito-frontal circumference of head

SD-standard deviations

U&E- Blood urine and electrolytes

WHO- World Health Organisation

4 Duties

4.1 Chief executive

Should ensure that all clinical staff working with children and young people have access to this guideline.

Should ensure that appropriate training and updates are provided to all relevant staff groups.

Should ensure that staff have access to appropriate equipment that complies with safety and maintenance requirements.

4.2 Managers

Managers should ensure that staff are aware of and have access to policy guidelines.

Staff training needs should be highlighted and addressed.

Appropriate education, supervision and mechanisms are in place to ensure good practice.

4.3 All clinicians working with children and young people.

If the child has macrocephaly they should be referred to a community paediatrician for further management.

5 Classification

Macrocephaly is classified in a number of ways:

- By the time of onset – Congenital versus Acquired

Congenital macrocephaly is present at birth or by 36 weeks' gestation. It is sometimes called "primary macrocephaly".

Postnatal (acquired) macrocephaly can occur as either a static condition or as a result of progressive head growth. Therefore, obtaining serial measurements over time yields more comprehensive and enlightening data. Premature infants have faster head growth, so it is important to monitor them with growth charts designed for premature babies.

- By aetiology – Genetic, pathological, or environmental.

- By the relation to other growth parameters – Symmetric or Asymmetric.

Macrocephaly is considered symmetric (or proportionate) when the OFC is more than 2 to 3 SD above the mean but proportionate to weight and length (or height) which also are above the mean.

Asymmetric is when head size is disproportionate to weight or height.

6 Pathogenesis

Head size and cranial volume.

The head grows rapidly antenatally and in the first 3 months of life. The increase in head circumference during this period is 3cms per month. Between the ages of 4-6 years the head circumference increases by 1cm per year. The anterior fontanelle closes between 9-18 months.

The skull contains three compartments: CSF, blood, and brain. Expansion of one of these compartments is at the expense of the other.

The thickness of the skull bones also affects head size.

Head Circumference

All children attending community outpatient paediatric clinics should have their head circumference measured.

Measuring a child's head circumference is an important part of checking for neurological issues. Deviations from the expected head growth can be the first sign of underlying problems such as genetic disorders, infections, or brain conditions like hydrocephalus. The size of the head reflects the size and growth of the brain. It's important to measure the largest circumference, and it's better to measure the head more than once over time to get a clearer picture.

OFC is a direct reflection of brain size and brain growth. The accuracy of measurement is influenced by the presence of fluid beneath the scalp i.e. oedema, blood cephalhaematoma, thick hair and by the head shape.

Tracking measurements over time provides more valuable insights than a single measurement. It's crucial to plot the occipitofrontal circumference (OFC) on the appropriate WHO chart based on age and sex. For detailed instructions on measuring Head circumference and using the appropriate parameters, please refer to the provided link for the UK-WHO Growth Charts - Fact Sheet 3 Measuring and Plotting, created by the Royal College of Paediatrics and Child Health. It offers essential information on measuring and plotting children's growth, emphasizing the importance of proper training or supervision for those involved in this process. Topics covered include measuring weight, length, height, and head circumference, plotting measurements on a chart, calculating age, and understanding centile position.

From NICE Guideline-For all children aged under 4 years with suspected abnormal head shape or size:

- take 3 consecutive measurements of the child's head circumference at the same appointment, using a disposable paper tape measure.
- plot the longest of the 3 measurements on a standardised growth chart, corrected for gestational age.
- For children with a head circumference measurement that differs by 2 or more centile lines from a previous measurement on a standardised growth chart (for example, an increase from the 25th to the 75th centile, or a decrease from the 50th to the 9th centile):
    - refer to paediatric services for assessment and cranial imaging to exclude progressive hydrocephalus or microcephaly or
    - refer immediately to paediatric services if the child also has any of the following signs or symptoms of raised intracranial pressure:
        - tense fontanelle.
        - sixth nerve palsy
        - failure of upward gaze ('sunsetting')
        - vomiting
        - unsteadiness (ataxia)
        - headache.

7 Aetiology/Causes

Macrocephaly can be due to hydrocephalus (increased Cerebrospinal fluid), megancephaly (enlargement of the brain parenchyma) or thickening of the skull.

See Appendix 1 –Causes of Macrocephaly

Hydrocephalus

Increasing OCF, crossing centiles, is frequently the presenting sign of hydrocephalus. Other signs of increasing intracranial pressure are lethargy, poor feeding, vomiting, irritability, and delayed development. Hydrocephalus occurs when the cerebral ventricular system contains an excessive amount of CSF resulting in increased pressure and dilatation. Hydrocephalus may be caused by increased production, decreased absorption (communicating hydrocephalus) or obstruction to CSF (non-communicating hydrocephalus).

In a Child or Young person with macrocephaly and a history or examinations findings suggestive of hydrocephalus- urgent neuroimaging and discussion with neurosurgeon should be undertaken. Appendix 1

Benign enlargement of subarachnoid space.

This benign condition is also known as, external hydrocephalus, extra ventricular hydrocephalus, and benign subdural effusions. It is a self-limiting disorder of unknown aetiology. It is relatively common occurring in approximately 16% of infants. It is more common in males and a large head is the only feature. Macrocephaly may or may not be present at birth, rapid head growth occurs in the first 6 months of life. The anterior fontanelle is large but soft. Neurological examination is normal.

Neuro imaging reveals an enlarged sub arachnoid space, widening of the sylvan fissure and normal ventricular size. The normal ventricular size distinguishes it from cerebral atrophy.

Patients with this condition do not require any intervention or repeat scans once diagnosis is made. The head growth velocity should slow to normal after 6 months of age. The OFC should be monitored which should follow the 98th centile.

Increased intracranial blood volume.

Increased intracranial blood volume may be caused by haemorrhage (intraventricular, subdural, epidural) or arteriovenous malformation (AVM).

Increased OFC is rarely the sole manifestation of intracranial haemorrhage. Patients usually present with irritability seizures, nausea/vomiting, fatigue/drowsiness, collapse, or paresis.

If intracranial haemorrhage is suspected urgent neuroimaging and a referral to a neurosurgeon is required.

Megalencephaly

Familial megalencephaly

Also known as benign familial megalencephaly, or genetic megalencephaly is the most common cause of megalencephaly. These children are born with a large head but normal body size. During infancy, the OFC increases typically 2-4cms above but parallel to the 98th centile. The OFC may increase by 0.6-1cm per week compared to the normal 0.4cms per week. The head growth velocity slows to normal rate by approximately 6 months.

Diagnosis is made clinically only if all the criteria below are fulfilled.

- Normal neurological examination
- Normal development
- No clinical feature suggestive of a specific syndrome
- No family history of neurological problems or developmental delay
- First degree relative (parent or sibling) with macrocephaly

An infant with a rapidly increasing OFC with a normal examination will require neuroimaging to exclude serious pathology before the diagnosis of familial megalencephaly can be made.

Once the diagnosis has been made no further investigations or follow up are required.

Other causes of Anatomic Megalencephaly include:

- **Neurocutaneous disorders**

  E.g. Neurofibromatosis type 1, Tuberous sclerosis, complex linear sebaceous nevus syndrome, hypomelanosis of Ito.
- **Autistic Spectrum disorder**

  Accelerated head growth in the first year of life.
- **Achondroplasia**

  In addition to megalencephaly, they may also have hydrocephalus.
- **Cerebral gigantism (Soto's Syndrome)**

  This is an overgrowth syndrome with a prenatal onset, they may also have hydrocephalus.
- **Fragile X Syndrome**

  OFC large compared to weight and height but may not be more than 2 standard deviations above the mean.
- **Cowden Syndrome**

  This is an autosomal dominant cancer predisposing condition caused by mutation in the PTEN gene. Affected individuals have an increased risk of thyroid malignancy and females for breast cancer.
- **Nevoid basal cell carcinoma syndrome (Gorlin Syndrome)**

  This is an autosomal dominant condition on PTCH1 gene, which predisposes to basal cell carcinomas during adolescence and early childhood. Affected individuals have large OFC, heavy features, jaw cysts and palmar/plantar pits.

Metabolic megalencephaly

The deposit of metabolic products in the brain tissue causes metabolic megalencephaly. The OFC of affected children is normal at birth but increases during the neonatal period. These conditions include Alexander disease, Canavan disease, Metachromatic Leukodystrophy, Galactosaemia, Tay-Sachs, Gangliosidosis, Glutaric aciduria1 and Mucopolysaccharidoses.

Thickened skull

Bone thickening is a rare cause of macrocephaly. This can occur from bone marrow hyperplasia e.g. Thalassemia Major, or primary bone disorders e.g. skeletal and cranial dysplasia.

Mass Lesions

Increased OFC is rarely the sole manifestation of, intracranial cysts, tumours, or abscesses. More common presentations include nausea, vomiting, unsteadiness, headaches, fatigue, torticollis, irritability, or seizures.

Increased ICP

Increased ICP may be idiopathic (i.e. pseudo tumour cerebri) or caused by increased volume of intracranial contents (e.g. brain, CSF, Blood or mass lesions.), infection, inflammation, toxic and metabolic abnormalities(e.g. lead poisoning, vitamin A deficiency or excess, galactosaemia.

8 Assessment of Macrocephaly

8.1 Principles of care

Support, assessment and treatment should be tailored to the circumstances and needs of the child or young person and parents or carers.

8.2 Measurement

Occipitofrontal circumference (OFC) should be measured at all initial health visits between birth and three years of age, in any child neurodevelopmental concerns and in all follow-up visits in children less than 5 years of age.

The measuring tape should encircle the head and include an area 1 to 2 cms above the glabella anteriorly and the most prominent portion of the occiput posteriorly. A paper tape measure should be used and not a plastic one.

Measurement of OFC in the newborn may be unreliable until the third or fourth day of life since it may be affected by caput succedaneum, cephalhaematoma, or moulding.

In older infants, accuracy of the measurement may be affected by thick hair.

8.3 Monitoring

OFC measurements are most informative when plotted over time. Standards have been determined for head growth in healthy children between 0 to18 years of age.

8.4 Head Circumference Charts

The UK WHO growth charts should be used for children less than 1 year of age.

The Child Growth Foundation head circumference charts should be used for children over 1 year of age. We store growth charts at two children developmental centres and at the clinic where patients have appointments. However, we have a plan in place to transition to digital growth charts stored in an electronic database.

8.5 Overview of approach

Evaluation for Macrocephaly should be initiated when a single OFC measurement is more than 2 to 3 SD above the mean for their age or when serial measurements reveal a progressive increase in head size (i.e. crossing of several major centile lines.)

The evaluation of macrocephaly includes a thorough history and physical examination of the child and parents (in consideration of familial variation in head size).

Investigations, which are directed by clinical findings from the history and examination, they may include laboratory studies and imaging.

8.6 History

Important aspects of the history in a child with macrocephaly include:

- Birth weight, length, and OFC; to establish the onset of macrocephaly and to determine if it is proportionate to weight and length.
- Birth history; to look for predisposing factors for hydrocephalus e.g. meningitis, prematurity with IVH.
- History of seizures
- Family History; consanguinity, large OFC, neurocutaneous disorders, metabolic disorders, or malignancies.
- Full developmental history; rate of attainment and or loss of milestones indicative of metabolic disease.

8.7 Physical examination

Important aspects of the physical examination of the child with macrocephaly include:

- Urgent referral should be made if there are any signs of raised intracranial pressure.
- OFC should be plotted on relevant chart for age and sex and compared with previous readings.
- Height and weight trajectories should be plotted on standard curves, and these centiles compared with the OFC. Several macrocephalic syndromes are associated with tall and short stature.
- General appearance –Dysmorphic features may suggest a particular syndrome.
- Examination of the head; the shape of head should be noted. Persistent enlargement of the anterior fontanelle in macrocephaly is seen in children with hydrocephalus, achondroplasia, cleidocranial dysplasia, rickets, and osteogenesis imperfecta. Auscultation of the skull for a bruit may suggest arteriovenous malformation.
- Eye examination; the presence or absence of papilloedema, cataracts, retinal abnormalities (suggestive of metabolic disease or syndromic macrocephaly).
- Cardiovascular system- signs of congenital heart disease may be suggestive of a neuro-cardio-facial-cutaneous syndrome.
- Abdominal system –hepatosplenomegaly (suggestive of a metabolic storage disorder)
- Skin examination-looking for hypo- or hyper –pigmented areas, macules, angiomas, shagreen patches, papillomata.
- Musculoskeletal system- looking for evidence of skeletal dysplasia (e.g. short limbs absent or hypoplastic clavicles.)
- Neurological examination- hypotonia is a common feature of overgrowth syndromes; spasticity is a feature of leukodystophy (e.g. Canavan disease, Alexander disease)
- Developmental Assessment- children with macrocephaly are at risk of intellectual/developmental difficulties. Appendix 2

8.8 Parental OFC

Parental OFC should be obtained if possible, to assess familial variation in head size.

9 Investigations of macrocephaly

9.1 Diagnostic testing

Diagnostic testing may be warranted in children with macrocephaly and abnormal development or associated clinical findings.

Testing may include.

- Chromosome micro array analysis
- Blood tests including Full Blood Count Urea and Electrolytes BC U&E, Bone profile and vitamin, Lead level and iron studies,
- Urine for metabolic screen, amino and organic acids GAG.
- Lysosomal enzyme panel or other specific metabolic tests when indicated.
- Skeletal x-ray for trauma, bone age assessment and skeletal abnormalities

RED FLAG situations requiring urgent evaluation and neuro imaging include.

- **Rapidly increasing OFC crossing centiles.**
- **Signs and symptoms of raised ICP, hydrocephalus, CNS mass, trauma, or CNS infection.**

9.2 Neuroimaging

Neuroimaging studies may identify a structural cause of macrocephaly and is most helpful in children with macrocephaly and developmental delay without features of a specific syndrome.

- Cranial ultrasound is a reasonable initial study in infants with macrocephaly, normal neurodevelopmental examination, no evidence of raised ICP and an open anterior fontanelle.
- MRI or CT –Infants or children with neurological abnormalities, progressive enlargement of OFC or increased ICP require an MRI or CT. An MRI is generally preferable, however the choice between these depends upon suspected aetiology, acuity of symptoms, need for sedation and availability.

9.3 Genetic testing

Genetic studies including micro array are helpful. If macrocephaly is associated with developmental delay or other unusual features a clinical geneticist experienced in the diagnosis of dysmorphic syndromes may be helpful. Certain overgrowth syndromes are at an increased risk of malignancy. Clinical geneticists may be able to do a gene panel for overgrowth syndromes with macrocephaly.

9.4 Other tests

- Metabolic screening- e.g. plasma amino acids, urine organic acids glycosaminoglycans especially if the child has developmental delay, disordered development, loss of previously acquired milestones.
- Children with syndromic macrocephaly will need evaluation for associated abnormalities (e.g. Echocardiogram, ophthalmological examination, abdominal ultrasounds, and bone x-ray)
- Children with suspected primary skeletal dysplasia may need plain x-ray of long bones and specialist referral.
- Subdural haematoma-consider NAI and a skeletal survey.

10 Management of Macrocephaly

The management will depend upon the underlying diagnosis.
Children will require assessment of their learning and educational support as required.

11 Prognosis

The prognosis for children with microcephaly will depend upon the underlying cause.

The prognosis is worse where there is a genetic or metabolic cause defined.

12 Summary and recommendations

Head circumference (occipitofrontal circumference [OFC]) should be measured at health maintenance visits between birth and five years of age. OFC measurements are most informative when plotted over time.

A variety of genetic abnormalities and medical causes can affect brain development resulting in macrocephaly.

Evaluation for macrocephaly should be initiated when a single OFC measurement is more than 2 to 3 SD above the mean or when serial measurements reveal progressive increase in head size.

The initial evaluation includes a history and physical examination of the child and parents.

Factors that determine the urgency and extent of the investigations include age at onset; history of raised intracranial pressure; associated symptoms, neurodevelopmental abnormalities, or syndromic features; and family history.

Consultation with, or referral to, a clinical geneticist, paediatric neurologist or paediatric metabolic specialist can be helpful in determining the appropriate studies.

13 Consultation

This clinical guideline has been discussed with community paediatricians Dr D Short, Dr H Unsworth, Dr S Ogilvie, Dr S Buch, Dr S Postings, Dr G Minnaar, Mrs Kular and will be distributed widely for discussion amongst community paediatricians.

14 Dissemination and implementation

This clinical guideline will be distributed to relevant staff groups by managers and published on the Trust website.

These guidelines will be disseminated by the following methods:
• Managers Informed via DATIX system who then confirm they have disseminated to staff as appropriate
• Staff via Team Brief
• Published to the staff zone of the trust website

15 Monitoring compliance

Compliance will be monitored by review of any concerns raised about the service by staff or patients.

16 References

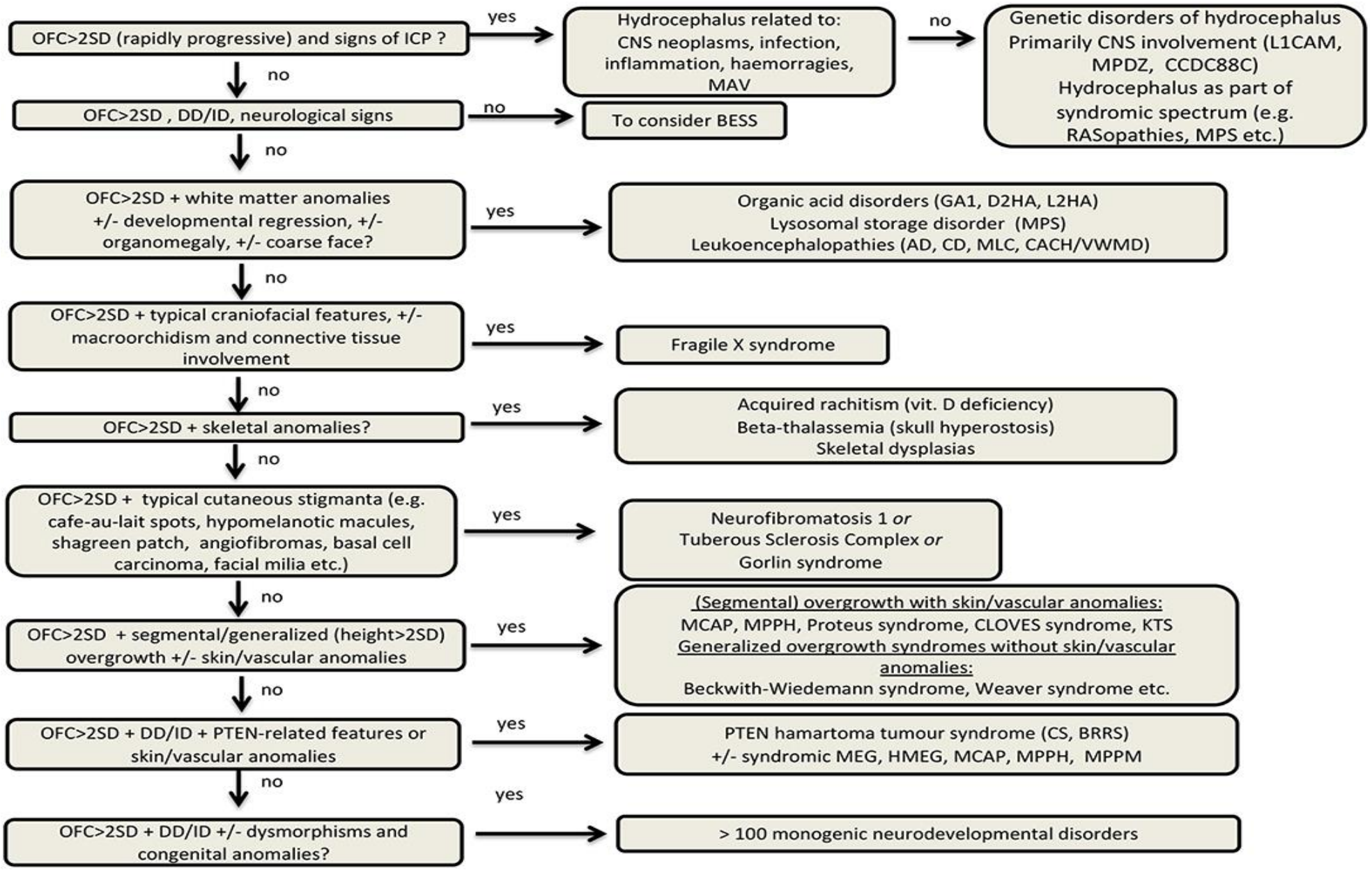
- NICE guideline (NG127)- Published May 2019- Suspected Neurological conditions: recognition and referral. Overview | Suspected neurological conditions: recognition and referral | Guidance | NICE
- Etiology and evaluation of macrocephaly in Infants and children. Julie A Boom. August 2017Macrocephaly in infants and children: Etiology and evaluation - Uptodate Free
- American Academy of Neurology Core Curriculum. Chapter13. Common problems in Paediatric neurology
- ACNRMJ Paediatric Neurology. Head Size: is it important? Vol 11 no2 June 2011
- BMJ 2014;348f7609 Baby with an abnormal head Baby with an abnormal head - PubMed (nih.gov)
- Diagnostic Approach to Macrocephaly in children- Frontiers in Pediatrics January 2022 Volume 9 Article 794069 Accogli et al. Frontiers | Diagnostic Approach to Macrocephaly in Children (frontiersin.org)

17 Appendices

Appendix 1: Flow chart for occipito frontal circumference and clinical syndromes

Appendix 2- Clinical features of selected syndromes associated with Macrocephaly

Appendix 1: FLOW CHART FOR OCCIPITO FRONTAL CIRCUMFERENCE AND CLINICAL SYNDROMES



Appendix 2- **Clinical features of selected syndromes associated with Macrocephaly.**

Predominantly cutaneous syndrome

Syndrome	Clinical Features (in addition to Macrocephaly)
Tuberous Sclerosis	Facial angiofibromas, shagreen patch, hypopigmented macules, periungual fibromas, gingival fibromas
NF Type 1	Café au lait spots, axillary freckling, dermal neurofibroma, short stature, Lisch nodules
Linear Epidermal Nevus Syndrome	Asymmetric overgrowth, coloboma (eye lids, iris, choroids), linear nevus sebaceous, associated with basal cell carcinoma
Klippel – Trenaunay Weber	Large cutaneous haemangioma with hypertrophy of related bones and soft tissues; syndactyl, polydactyl
Macrocephaly Cutis Marmorata Telangiectatica Congenita	Vascular mottling of the skin; congenital telangiectasias, syndactyl of second and third toes; polydactyly; asymmetry of the head, face, or body; nevus flameus of the lip and/or philtrum; overgrowth with prenatal onset
Nevoid Base Cell Carcinoma Syndrome (Gorlin Syndrome)	Frontoparietal bossing, broad nasal bridge, coarse facial features, highly arched eyebrows, pouting lower lip, odontogenic keratocysts of the mandible and maxilla; increased risk of basal cell carcinoma
Proteus	Asymmetric disproportionate overgrowth of body parts, epidermal nevi, hypertrophy of skin of soles, haemangioma (thorax, upper abdomen)

Predominantly overgrowth syndromes

Sotos	High prominent forehead, down slanting palpebral fissures. Long pointed chin, high arched palate, tall stature, advanced bone age. Normal adult height
Weaver	Accelerated growth with prenatal onset, advanced bone age, broad forehead, flat occiput, long philtrum, camptodactyly, broad thumbs, loose skin, deep set nails, deep palmer, and plantar creases
Simpson-Golabi	Accelerated growth with prenatal onset (weight more affected than height), coarse facial features, down slanting palpebral fissures, thickened lips, wide mouth, large tongue, high arched palate, prominent jaw, short neck, supernumerary nipples, hepatomegaly
Beckwith-Wiederman Syndrome	Omphalocele (or other umbilical abnormalities), hemihypertrophy, coarse facial features, macroglossia, neonatal macrosomia, neonatal hypoglycaemia, increases risk of certain tumours (e.g. Wilms, hepatoblastoma)

Neuro-cardio-facio-cutaneous Syndromes

Syndrome	Features in addition to Macrocephaly
Noonan	Short stature (postnatal onset), congenital heart defects (atrial septal defect, ventricular septal defect, pulmonary stenosis), webbed neck, abnormal chest, hypertelorism, down slanting palpebral fissures, epicanthal folds, deafness, deeply grooved philtrum
LEOPARD	Lentigines, ECG conduction abnormalities, occula hypertelorism, pulmonary stenosis, abnormal genetalia, retardation of growth, deafness (sensorineural)
Costello	Failure to thrive, short stature, developmental delay, coarse facial features, deep palmer and plantar creases, papillomata, cardiac abnormalities, risk for tumours
Cardiofaciocutaneous	Cardiac abnormalities (ASD, PS, hypertrophic cardiomyopathy), cutaneous abnormalities (ichthyosis, hyperkeratosis, haemangioma, post-natal short stature, prominent forehead, bitemporal narrowing, coarse facial features, prominent philtrum, down slanting palpebral fissures, short, upturned nose

Abbreviations used: Taken from Diagnostic algorithm of macrocephaly- From Diagnostic Approach to Macrocephaly in children- Frontiers in Pediatrics Volume 9 Article 794069 Accogli et al.	BESS, Benign enlargement of subarachnoid spaces. BRRS, Banaian-Riley-Rubalcaba syndrome. CS, Cowden syndrome; CNS, central nervous system. D2HA, D2-hydroxyglutaric aciduria. L2HA, L2-hydroxyglutaric aciduria. DD, developmental delay. KTS, Klippel-Trenaunay syndrome; ICP, increased intracranial pressure. GA1, glutaric aciduria type 1; MAV, arteriovenous malformations. MPS, mucopolysaccharidosis. AD, Alexander disease. CD, Canavan disease. MLC, megalencephalic leukoencephalopathy with subcortical cysts. MCAP, megalencephalic capillary malformation syndrome. MPPH, megalencephalic-polymicrogyria-polydactyly-hydrocephalus syndrome. MPPM, megalencephalic-polymicrogyria and pigmentary mosaicism. CACH/VWMD, childhood ataxia with central hypomyelination/vanishing white matter disease.