How to assess and support the child with microcephaly

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Abstract

With this review, our aim is to support community and secondary level acute paediatricians with a concise structured framework for the assessment and initial management of microcephalic children. Microcephaly can be classified in primary, when it is detected in pregnancy or secondary, when it develops after birth. We take into consideration: practical aspects of evaluating microcephaly; key parts of the consultation including focused history taking and examination; a structured approach to guide initial differential diagnosis with some examples; a description of available investigations; recommendations for referral to tertiary level neurologists and geneticists.

Keywords assessment; investigations; microcephaly; primary microcephaly; secondary microcephaly

Introduction

The measurement of head circumference is an important step in the assessment of general health, growth and development of infants and children. We stress the importance of measuring head circumference not only during infancy, but also during early and late childhood. A significant deviation from the normal value for age/sex may be the first hint of an underlying disease process and needs further investigations.

Microcephaly is defined as a significant reduction in the occipito-frontal diameter (OFC), compared to children of the same gender, age and ethnicity. It has an estimated prevalence of 1.53 per 10,000 births.

It is a clinical sign — an estimate of brain size — and not a diagnosis. There are a number of possible aetiologies, among which are genetic, neurometabolic disorders and brain injury. Microcephaly can be categorized in a number of ways: by aetiology, by relation to growth parameters (proportionate or disproportionate), or by time of onset, which is the classification that we use here.

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According to this classification, microcephaly can be primary, when brain growth is reduced during pregnancy, secondary or acquired, when head circumference is within normal limits at birth, but then fails to grow as expected. Studies suggest that primary microcephaly is a result of decreased neurogenesis, while acquired microcephaly results from decrease in dendritic complexity and impaired myelination.

In 41% of cases, the aetiology of microcephaly remains unknown, in many cases the cause is genetic, but the variation may not be found.

Practicalities

Head circumference should be measured with a non-stretchable tape across the occipitus and the supraorbital ridges, above the ears, midway between the eyebrows and the hairline. Take the measurement three times or until you get a consistent value.

Different OFC charts are available, but it is important to use the same chart for the same child over time; for example, the gender specific UK-WHO 1990 Head Circumference Chart for children living in the UK from 1 to 18 years of age. This is not the standard height weight head circumference 0—4 years chart, as these are based on an international cohort and tend to plot the value on a higher centile line, missing some cases of microcephaly. We propose a head circumference table indicating standard deviations (SD), which allows use for children and teenagers until 18 years of age (see Table 1A and B). Ethnicity based head circumference charts are not widely available. Microcephaly can be defined as either 2 or 3 SD below the mean, or below 0.4th centiles (the latter equal to −2.67 SD).

We recommend investigating microcephaly when the head circumference is less than the 0.4th centile or whenever a child with a head circumference below the 2nd centile (−2 SD) has significant risk factors from history or examination to suggest an underlying disease process that needs further clarification. This approach will increase investigation yield and likelihood of diagnosing pathology.

Serial measurements over time are more informative than single (spot) measurements as they provide a trend. For example, a decelerating OFC is typical of some metabolic disorders. It is also important to record the parental head circumferences, which can give the clinician hints on the possibility of benign familial microcephaly.

If no head circumference at birth is available, serial OFC measurements can provide a clue. Consecutive OFC measurements that create a curve parallel to a centile suggest primary microcephaly, while serial OFCs, which show a drop or a plateau, are more typical of secondary microcephaly.

Consultation

Families will often be unaware of the microcephaly and/or the implications, so it is important to set the scene for building a rapport with them. The consultation should be structured around the child, with the aim of involving them actively whenever possible. Allow time and a space for a comprehensive assessment and avoid bed spaces on a ward. Ideally, both parents should be present, and you may consider having a nurse or other members of the MDT who may be involved in the care of the child later on.

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Occipitofrontal head circumferences (OFC) from the mean to 6 standard deviations below the mean for boys up to the age of 18 years, from the UK90 data (reproduced with permission from Professor Tim Cole)

Occipitofrontal circumference for boys/cm

Age	Mean	−1 sds	−2 sds	−3 sds	−4 sds	−5 sds	−6 sds
Birth	35.2	33.9	32.7	31.4	30.1	28.8	27.6
1 month	37.6	36.4	35.1	33.9	32.6	31.4	30.1
3 months	41.3	40.1	38.9	37.6	36.4	35.2	34.0
6 months	44.5	43.3	42.1	40.9	39.8	38.6	37.4
9 months	46.4	45.3	44.1	42.9	41.7	40.5	39.3
1 year	47.7	46.5	45.3	44.1	42.9	41.7	40.5
1.5 years	49.2	48.0	46.7	45.5	44.2	42.9	41.7
2 years	50.2	48.9	47.6	46.3	45.0	43.6	42.3
2.5 years	50.9	49.6	48.2	46.8	45.5	44.1	42.7
3 years	51.5	50.1	48.7	47.3	45.8	44.4	43.0
3.5 years	51.9	50.4	49.0	47.6	46.1	44.7	43.2
4 years	52.2	50.7	49.3	47.8	46.3	44.9	43.4
4.5 years	52.5	51.0	49.5	48.0	46.5	45.1	43.6
5 years	52.7	51.2	49.7	48.2	46.7	45.2	43.7
5.5 years	53.0	51.4	49.9	48.4	46.9	45.4	43.8
6 years	53.2	51.6	50.1	48.6	47.0	45.5	44.0
7 years	53.5	52.0	50.4	48.9	47.3	45.8	44.2
8 years	53.9	52.3	50.7	49.2	47.6	46.0	44.4
9 years	54.2	52.6	51.0	49.4	47.8	46.2	44.7
10 years	54.	52.9	51.3	49.7	48.1	46.5	44.9
11 years	54.8	53.2	51.6	49.9	48.3	46.7	45.1
12 years	55.1	53.5	51.9	50.2	48.6	47.0	45.3
13 years	55.5	53.8	52.2	50.6	48.9	47.3	45.6
14 years	55.9	54.3	52.5	50.9	49.2	47.6	45.9
15 years	56.2	54.6	52.9	51.2	49.5	47.9	46.2
16 years	56.6	54.9	53.2	51.5	49.8	48.2	46.5
17 years	56.9	55.2	53.5	51.8	50.1	48.4	46.7
18 years	57.3	55.5	53.8	52.1	50.4	48.7	47.0

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Table 1A

History

A comprehensive history should include the following points:

Antenatal history: suspected or proven maternal infections during pregnancy, e.g. TORCH (TOxoplasma, Rubella, Cytomegalovirus, Herpes), other rashes or pyrexia of unknown source; foetal exposure to alcohol, medications (e.g. maternal antiepileptic medications), or drugs (e.g. heroin or cocaine); maternal medical problems (e.g. HIV, phenylketonuria, autoimmune conditions, thyroid disease, malnourishment); placental insufficiency; antenatal scans abnormalities and in utero growth (disproportionate foetal growth, IUGR); travel history during pregnancy (e.g. Zika areas) and maternal abdominal injury.

Birth history: need for resuscitation, hints to suggest perinatal asphyxia or stroke e.g. seizures.

Medical history: including seizures, hypoglycaemia and relevant systems review.

Developmental history: development milestones in gross/fine motor, social and language domains; school attendance and academic progress. Ask specifically about concerns around hearing and vision.

Family history: including history of neurological or metabolic conditions and premature deaths. Ask about parental consanguinity.

Examination

Anthropometric measurements of height/length, weight and nutritional status are essential parts of the assessment, as microcephaly can be isolated or associated with growth failure or short stature in syndromes like Seckel and Rubinstein-Taybi. Similarly, chromosomal breakage disorders like Bloom syndrome or Fanconi anaemia present with growth retardation unresponsive to nutritional supplementation.

Attentive observation will provide you with important information for both developmental and general or neurological examination.

In particular, it's important to inspect:

Facial features: ears (e.g. low set), nose shape, philtrum (a smooth philtrum, thin upper lip and narrow eyes are features of foetal alcohol syndrome), chin, hypo or hypertelorism (Wolf-Hirschhorn syndrome), eyebrows (arched eyebrows which meet in the middle suggest synophrys in Cornelia De Lange syndrome), teeth (single maxillary incisor is associated with holoprosencephaly);

Check head shape, sutures and fontanelles: the anterior fontanelle normally closes between 10 and 24 months of age. Premature closure is associated with craniosynostosis and hyperthyroidism; a late closure is associated with syndromes like Rubinstein-Taybi, or chromosomal abnormalities like trisomy 21, or cri du chat (5 p deletion).

Check skeletal system: spine for scoliosis and limbs for dysplasia.

The skin and integuments: nails and hair (hypertrichosis in Cornelia De Lange); skin: chromosomal breakage disorders like ataxia telangiectasia and xeroderma pigmentosum can be associated with microcephaly; severe photosensitivity in Cockayne syndrome.

The general physical examination should also include abdominal palpation (hepato/splenomegaly can be suggestive of metabolic disorders or congenital infection) and cardiovascular assessment. A full neurological examination is essential, as microcephaly can be associated with motor dysfunctions, therefore assessment of tone, power, and reflexes should be performed, as well as observation for movement disorders such as dystonia or dyskinesia.

An ophthalmology assessment is crucial to identify clues, e.g. chorioretinitis (TORCH intrauterine infection) or cataract (metabolic disorder); similarly, a hearing assessment is

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