Achondroplasia : medical, orthopaedic features and management

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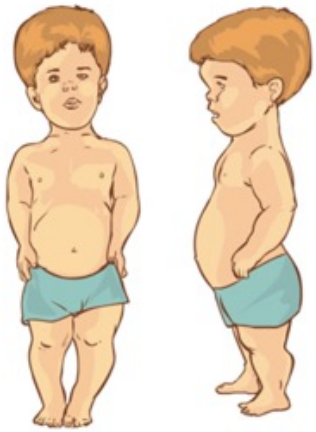
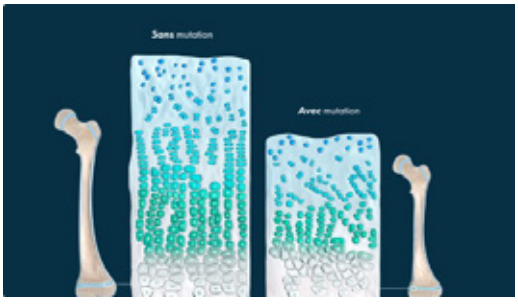
1/ DIAGNOSIS

Achondroplasia is a condition known throughout the ages and described medically for a century ;
(from greek achondro meaning without cartilage and plasia tissue formation) It is an autosomal dominant genetic disease, with equal involvement between men and women, with no ethnic predisposition. 8000 people are affected today in France (1, 2).

This term was first used in 1851 by Jules Parrot, a French pediatricist, to distinguish this growth disorder from rickets. This disease is therefore classified in physaire damage.
Achondroplasia is the most common form of chondrodysplasia. The clinical features were described in detail in 1900 by Pierre Mary and natural history including final height are today well known as follows : a rhizomelia, hyperlordosis, brachydactyly and macrocephaly with prominent forehead and hypoplasia of the middle part of the face (3). Fig 1.

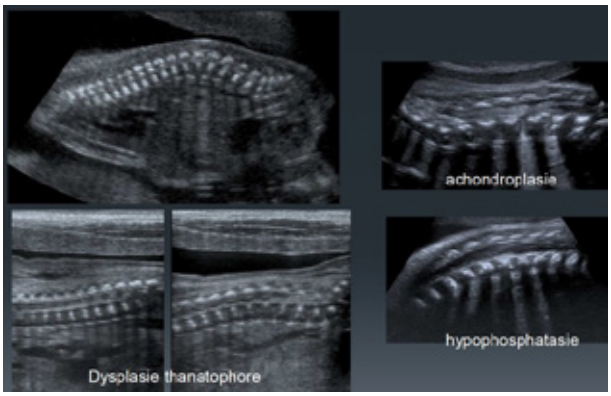


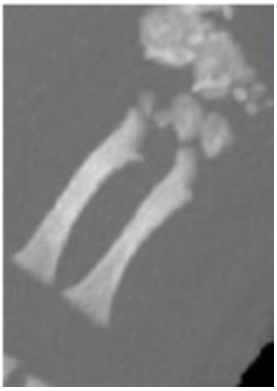
There is a clinical and genetic continuum between Thanatophore dysplasia-Achondroplasia-Hypochondroplasia (4). The main defect is a false sense mutation of the FGFR3 gene discovered in 1994 (5). This mutation may occur de novo (increased risk with the increase of the age of the father) or be family. It disorganizes the growth plate by premature differentiation of chondrocytes and thus reaches endochondral growth. Fig 2.



The FGFR3 gene codes for receptor 3 of fibroblast growth factor on chromosome 4. This receptor usually decreases cartilage production and development. In the mutation, glycine becomes arginine and leads to overexpression of this receptor

The prenatal diagnosis can be done on ultrasound from 28 weeks of amenorrhea: short long bones with growth curve break, macrocrania, hydramnios, characteristic effilate and clenched proximal femur ; small vertebral bodies, intervertebral gap ; horizontal cotyls, small and round iliac wings (6). Fig 3a. 3b.





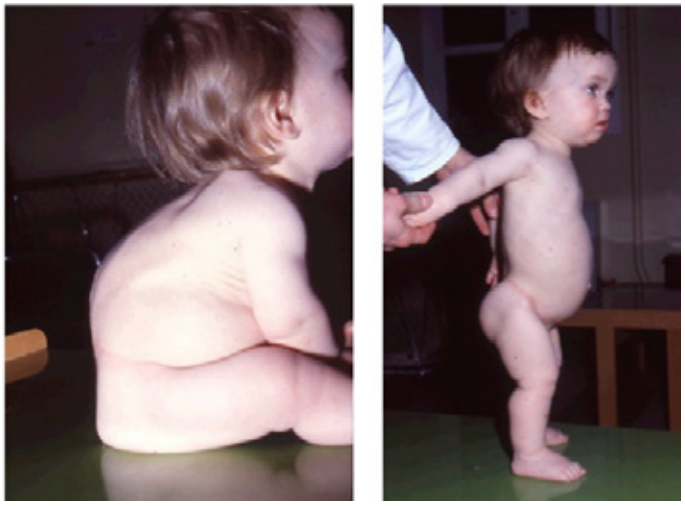
After suspicion suspicion, the family is addressed in CPDPN. We can then propose the realization of a low dose scanner that will confirm the diagnosis. If this is unavailable, a molecular study after amniocentesis can be carried out (search for the pathogen variant, which is in 99% of cases FGFR3.
In some centers, prenatal diagnosis can also be done by fetal DNA testing on maternal blood (impossible if the mother herself is affected because there is a risk of confusion). This technique will probably become widespread in the coming years.
Some couples prefer to wait for birth to do the diagnostic (about 10 to 20% of cases).
Families will then have to be referred to the OSCAR network (about 20 centres in France).
Medical interruption of pregnancy is not usually

discussed in this pathology.

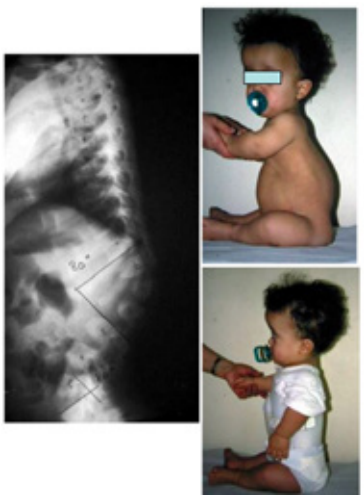
2/NEWBORN-FIRST YEAR

It is imperative to know the possible complications in newborns in order to be proactive in their management. Disease in soft progress can lead to severe complications. This will require specialized care and therefore a network of care. The multidisciplinary team usually includes at least one clinical geneticist, an orthopedic surgeon, a neurosurgeon and an ENT (7).
The first examination will be an MRI of the cervical cervical between 4 and 6 months looking for a spinal compression type Chiari for example. Other neuro defects are sought : craniosynostosis, stenosis of foramen magnum, hydrocepalus, central sleep apnea. It's been demonstrated that sudden death risk was 7,5% the first year of life, and 2,5% between 1 and 4 years old (8).
It will also be necessary to organize a polysomnography for sleep apnea.

For orthopaedists it will be important to see the child as soon as he starts sitting. It is essential to clinically and radiologically detect thoracic lumbar kyphosis following axial hypotonia that exists in different degrees in almost all these children (Fig 4).

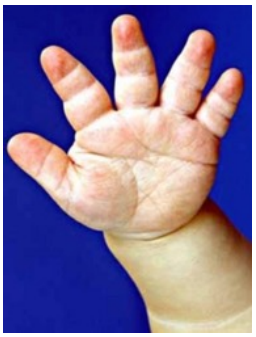


When cyphosis is confirmed, it is necessary to set up for a few months a support brace at waking hours, to avoid aggravation. Most often around 3 years, the axial tone allows to wean the child (Fig 5).



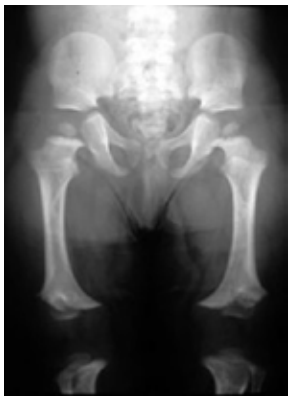
3/CHILDHOOD

During childhood, orthopedic follow-up is regular, annual. The value of preventing overweight must be reexplained at each consultation. The child must be muscular and flexible. In particular, play, read on your stomach to combat hip flessum which is one of the factors of hyperlordosis. It will be necessary to detect laxity of the ankles which can be a brake on sports practice.
Congenital dislocations of radial head are found with little functional consequences and that should not be treated. Hands comprise short trident fingers (Fig 6).



Hypoplasia of the middle face with a nasal bridge collapsed are common to all patients.

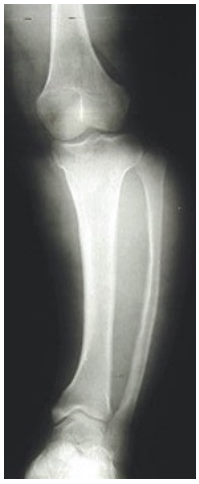
In X-rays, flat and rounded iliac bones, horizontal acetabulum and sciatic sacral notches are described (Fig 7).



The school should seek out occupational therapists and implement simple measures such as a walk to rest your feet when sitting at a desk, for example.
In order to contribute in patients and families education, didactic tutorials exist in free access following Youtube channel : OSCAR Achondroplasie
https://www.youtube.com/watch?v=9VcyU2W24sg

Growth modulations have been described (9) but remain controversed as they can affect final height. Thus, evaluation of skeletal age in these patients requires specific methods as a delay in maturation has been shown (10).
In order to manage the genu varum (60 to 80% of patients) which gets worse around 4 years, some teams propose proximal epiphysiodesis of the fibula with a small anterior approach, good results in 50% of

cases (11). Fibula was always found longer than the tibia (12) (Fig 8).



However, this practice is being challenged by the advent of new therapies.
In our experience, after starting medical treatment, a patient sufferd from overcorrection. For now, this technique should be hung up.

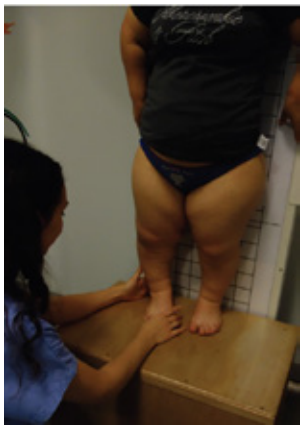
4/MEDICAL TREATMENT

Vosoritide (VOXZOGO®) is a modified recombinant human C-type natriuretic peptide (CNP) analogue, being developed by BioMarin Pharmaceutical for the treatment of achondroplasia.
Vosoritide was approved in August 2021 in the EU for the treatment of achondroplasia in patients aged ≥ 2 years whose epiphyses are not closed (13).
On average, treated patients grew 1.57 cm more per year than untreated patients (14).
It still represents a major hope for patients today.

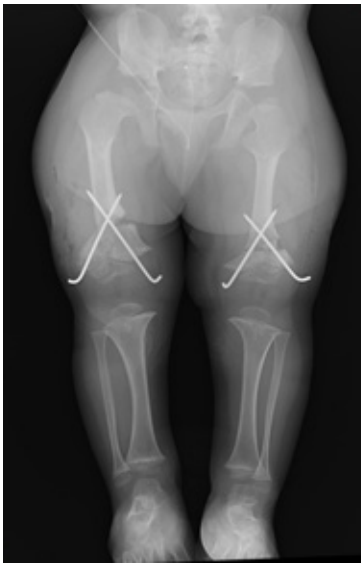
Vosoritide, growth hormone (GH) and limb lengthening all conferred benefits for height or growth velocity; however, the long-term effects of GH therapy were unclear, data for vosoritide were from a limited number of studies, and limb lengthening was associated with complications (15).

5/ ADOLESCENCE/PUBERTY

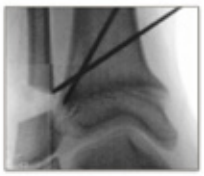
As the growth cartilage matures, skeletal deformities stabilize and the risk of recurrence after correction decreases. It is at this age that corrective osteotomies are proposed.
First, in order to properly assess the axes at the radiography, the position must take into account torsional disorders (Fig 9).

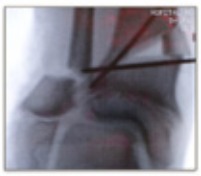


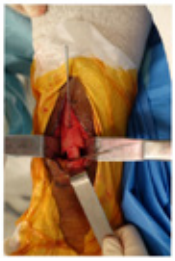
The osteotomies will be at best metaphyseal and close to CORA.
It may be useful to use arthrorise pins to stabilize the hyperflexed knee during surgery.
The synthesis should not seek maximum stability because bone quality is poor. Pins and cast immobilization may be considered (Fig 10).



The most common deformities are lower femoral and tibial.
Especially the distal tibial varus can be corrected by an addition osteotomy using a fibular graft (11).
The angle to be corrected is measured on a pre-operative face x-ray. Pins are placed as a guide and will allow the measurement of this correction. An external derotation will be most often associated (Fig 11).







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At this time of life, the psychological aspect should not be neglected. Support and evaluation can be offered to each patient.

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