GROWTH ABNORMALITIES

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Growth abnormalities

Introduction

- Growth failure in TM was recognized for many years, and persisted despite therapeutic advances
- In the past, prevalence of growth failure and short stature reported from 30 to 60%
- In the current era, the adherence to modern transfusion and iron chelation protocols and avoidance of iron chelator overdosage has reduced the risk of short stature

Growth abnormalities

Introduction

- The child with TM has a particular growth pattern, which is normal until age 9-10
- Then a slowing of growth velocity and reduced pubertal growth spurt are observed
- Short stature encountered in thalassaemia is often disproportionate with a low upper segment to lower segment ratio.

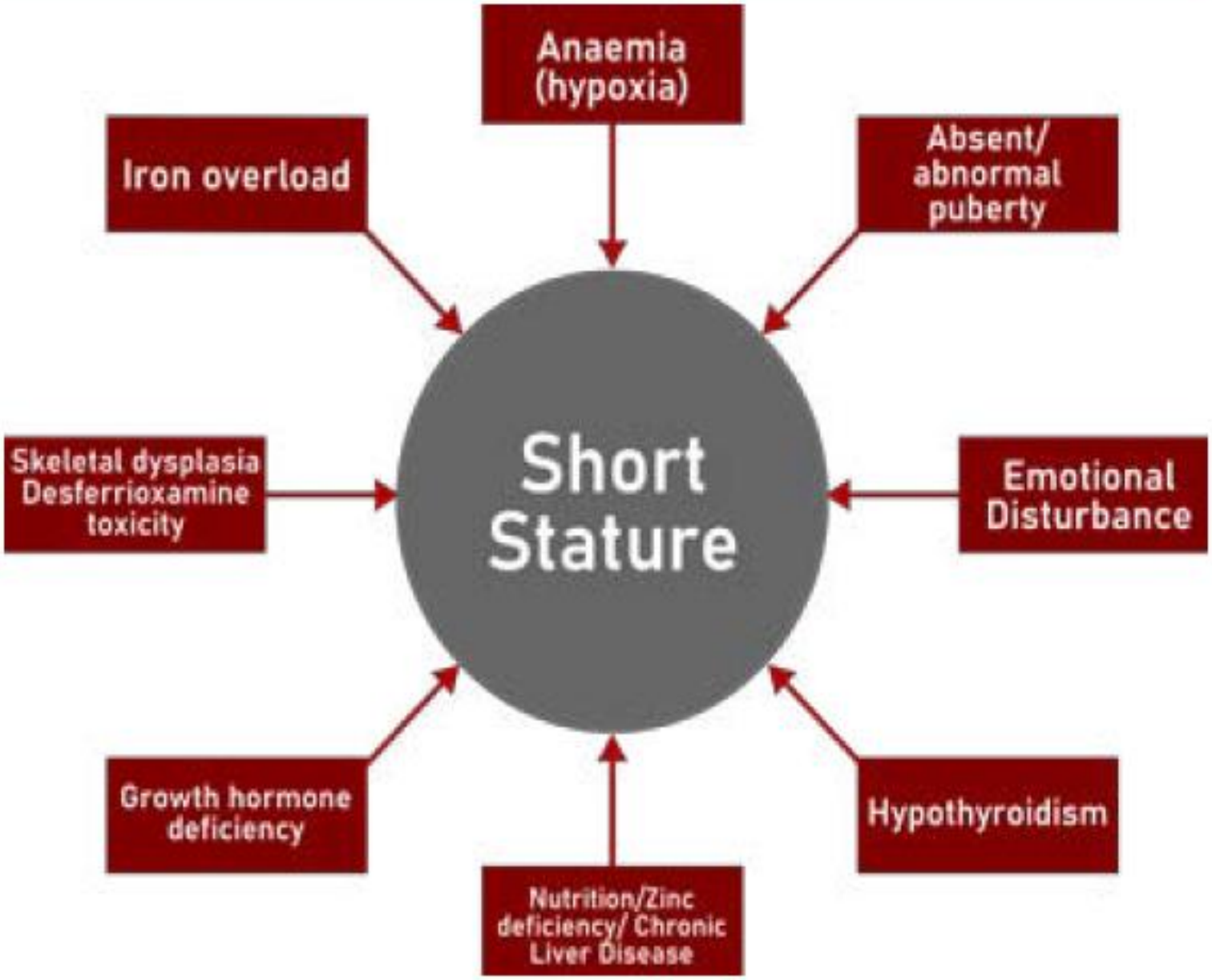
Growth abnormalities

- The exact reason is not clear and an interplay of multiple factors but:
- The fundamental problem is the free iron induced damage of the endocrine glands *but*:
  - Iron overload (impaired cartilage growth),
  - Early use of DFO
  - Chronic anemia and hypoxia,
  - Chronic liver disease,

Growth abnormalities

Introduction

- Endocrinopathies (hypogonadism, delayed puberty, hypothyroidism, hypocalcemia and bone disease) and dysregulation of the axis (GH-IGF-1)
- Zinc, folic acid and…… deficiencies,
- Intensive use of chelating agents,
- Emotional factors,


Anaemia (hypoxia)
Iron overload
Absent/ abnormal puberty
Short Stature
Skeletal dysplasia Desferrioxamine toxicity
Emotional Disturbance
Growth hormone deficiency
Nutrition/Zinc deficiency/ Chronic Liver Disease
Hypothyroidism

Growth abnormalities

Introduction

- Three phases of growth disturbances according to age of presentation recognized :
- First phase growth disturbance is mainly due to hypoxia, anemia, ineffective erythropoiesis and nutritional factors
- During late childhood (second phase), is due to iron overload affecting the GH-IGF-1 axis and other endocrine complications
- After the age of 10-11 years (third phase), delayed puberty decreases normal growth spurt

Growth abnormalities

Assessment of thalassemic child with short stature

- Onset of disease and need for transfusions
- TM Patients have higher prevalence of growth retardation compared to TI
  - Pre-transfusion hemoglobin level
  - Annual blood requirement
  - Chelation therapy (type, dose, compliance)
  - Serum ferritin levels
- Comorbidities (endocrine complications, chronic liver disease, chronic cardiac failure, HIV infection)

Growth abnormalities

Diagnosis of Growth abnormalities

- Short stature: height< 3rd percentile, and/or
- Slow growth rates(cm/year), <10th percentile

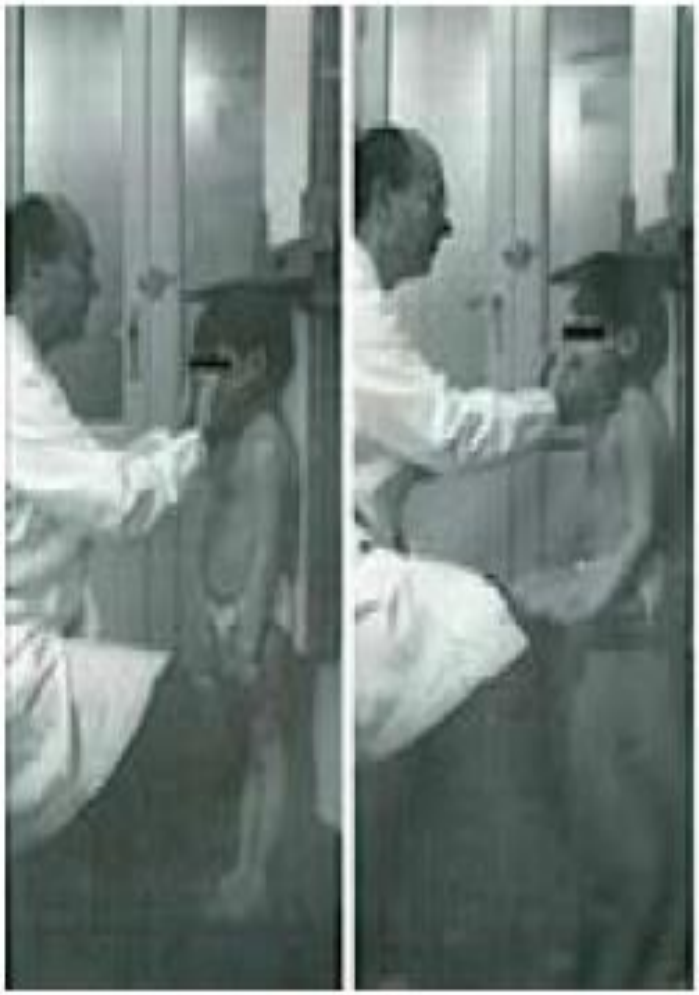
Other investigations

- Other pituitary hormone deficiencies:GH, gonadotrophins, central hypothyroidism)
- Other causes: nutritional deficiencies, chronic hepatic disease, chronic heart failure

Growth abnormalities

Diagnosis and investigations

- The 1st step in the management is the regular (q 6 month) measurement of standing and sitting height and pubertal staging
- **Annual growth screening** should be started from the age of 9 years, or earlier if clinically indicated



Growth abnormalities

Diagnosis and investigations

1. TSH and FT4
2. Ca, P, Mg and ALP
3. Serum IGF-1 and IGF BP-3
4. Serum zinc (in selected cases)
5. Screening for celiac disease
6. X- ray of wrist and hand, tibia and spine should in patients who have body disproportion
7. Assessment of GH secretion
8. MRI of the hypothalamic–pituitary region
9. LH, FSH and sex steroids, starting from the pubertal age

Growth abnormalities

- There are no guidelines for assessment of GH in adult patients
- This contrasts with childhood GHD where growth failure acts as a useful biomarker
- GHD in adults is associated with:

- Lack of positive well-being,
- Depressed mood,
- Feelings of social isolation,
- Decreased energy,
- Reduced bone and muscle mass,
- Diminished exercise performance
- Increase in adiposity

Growth abnormalities

Criteria for the assessment of GH adult TM patients

- Short stature
- Severe /prolonged iron overload,
- Dilated cardiomyopathy,
- Low IGF 1 levels
- Severe osteoporosis and
- In adult TM patients with normal liver function and low IGF-1 level

Growth abnormalities

Treatment

- PC transfusion to maintain Hb >9 g/dl
- Adequate chelation to keep ferritin < 1,000
- Use of chelators with lower toxicity on the skeleton
- Correction of nutritional deficiencies (protein-calorie, folate, vitamin D/A, zinc, carnitine)
- Zinc supplementation if indicated
- Correction of hypersplenism.
- Management of pubertal delay
- Diagnosis and management of hypothyroidism diabetes mellitus

Growth abnormalities

Treatment

- The management of GHD has not clear
- The growth velocity after GH administration in TM is lower than children with primary GHD,
- There are no guidelines for use of GH in adult patients with TM and GHD but:
- May be useful in patients with cardiac failure
- During GH treatment, patients should be checked every 3-4 monthly

Summary

The pathogenesis of growth failure is multifactorial but:

- Chronic anemia,
- Iron overload and
- Chelation toxicity are Key contributing factors

Other contributing factors include

- Hypothyroidism, hypogonadism
- GH deficiency
- Zinc deficiency,
- Chronic liver disease,
- Under-nutrition and
- Psychosocial stress

Summary

- Standing and sitting height and weight should be assessed every 6 months
- Management consists of:

- Optimising blood transfusion;
- Improving nutrition by high caloric balanced diet
- Optimising iron chelation
- Early diagnosis and treatment of endocrinopathies
- GH treatment is not always as effective as in non-thalassaemic children with GHD

Short statement

- Modern transfusion and iron chelation protocols and avoidance of chelator overdosage reduced the risk of short stature
- It is believed to be multifactorial
  - Besides hypothyroidism and hypogonadism , GHD also plays a role
- Iron overload in the pituitary and liver is the major etiology for GHD

Short statement

- Efficacy of rhGH treatment in TM patients with growth failure secondary to GHD is not clear
- The growth velocity attained after GH administration in children with TM is lower than children with primary GHD
- GH treatment may be useful in some patients with cardiac failure

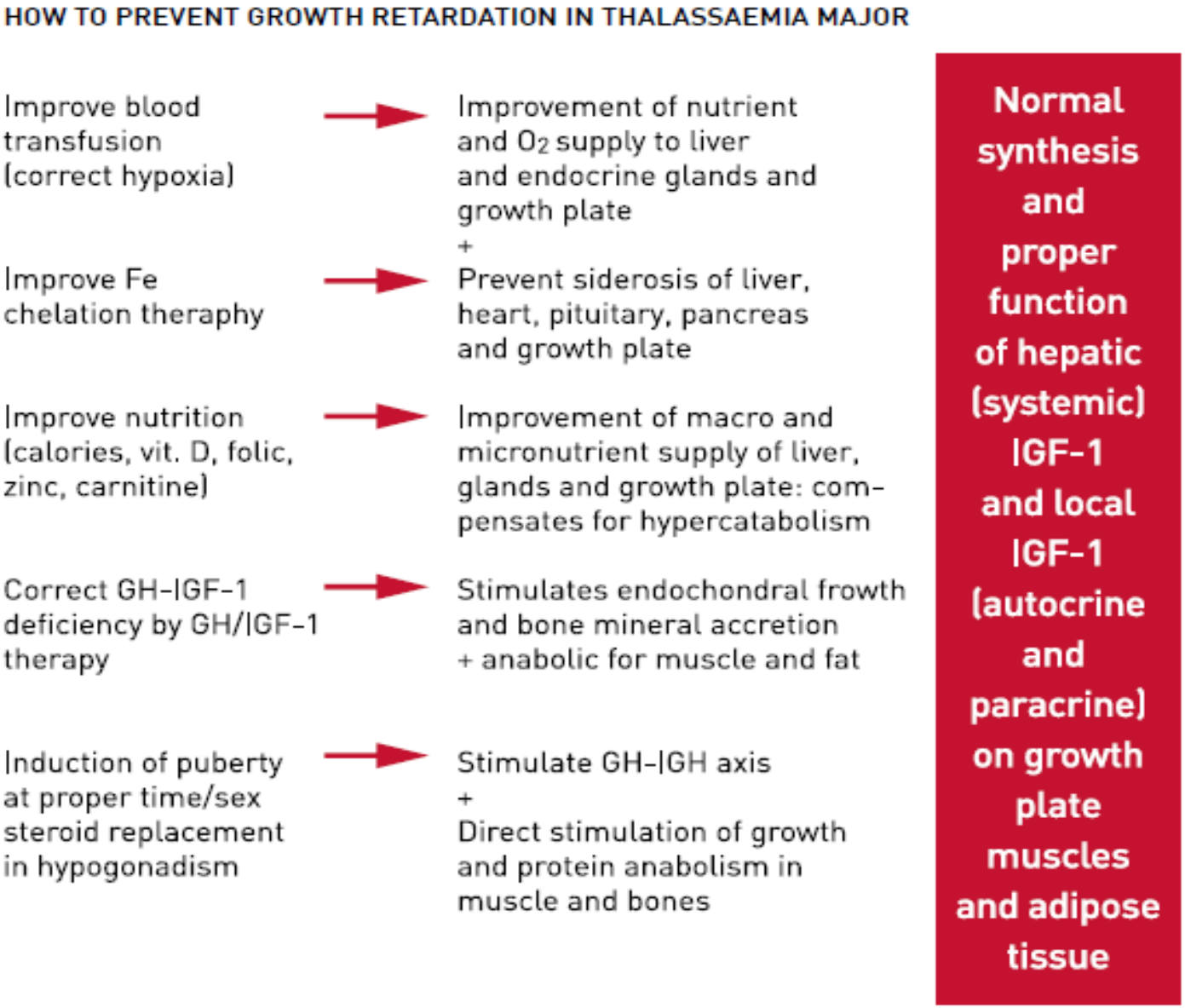


Figure 2. Practical approach to the treatment of growth retardation in thalassaemia. Reproduced with permission from (Soliman 2013).

THANK YOU