Singapore Med J 1997; Vol 38(9):402-404

Clinics in Diagnostic Imaging (29)

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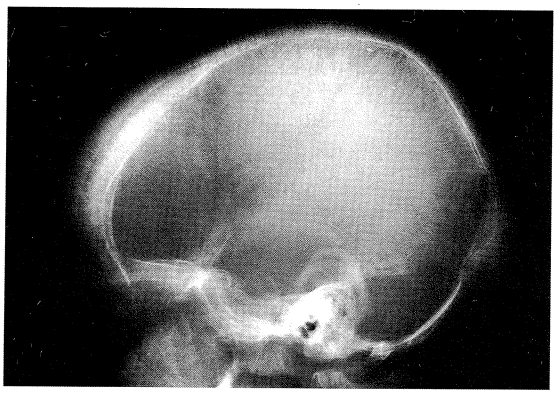

Fig 1 - Lateral radiograph of the skull

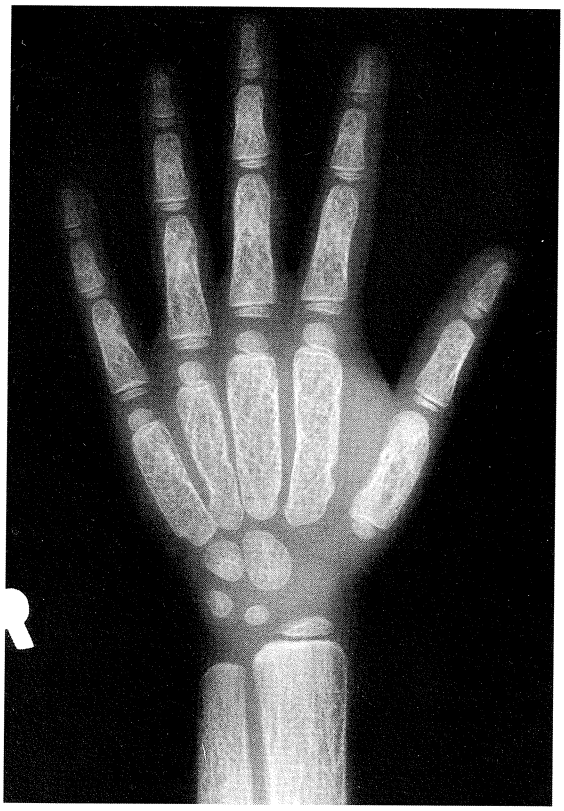

Fig 2 - Antero-posterior radiograph of the right hand

CASE REPORT

A 5-year-old Chinese girl was noted to have increasing facial deformity and was brought to the Accident and Emergency Department by her parents. She had suffered from lethargy and diminished exercise tolerance for over a year. Her parents had also noticed pallor, forehead prominence and poor dentition. They had tried to provide more nutritious food and had sought the advice of a Chinese herbalist.

What abnormalities do the radiographs of the skull (Fig 1) and the hand (Fig 2) show?

What is the diagnosis?

What complication of this disease is seen on the magnetic resonance (MR) examination of the abdomen (Fig 3) ?

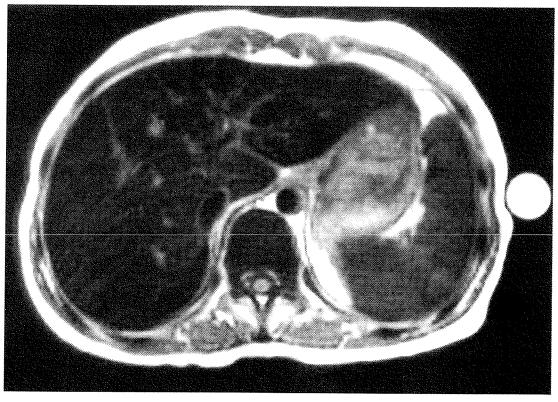

Fig 3 - Axial T2-weighted MR image of the upper abdomen

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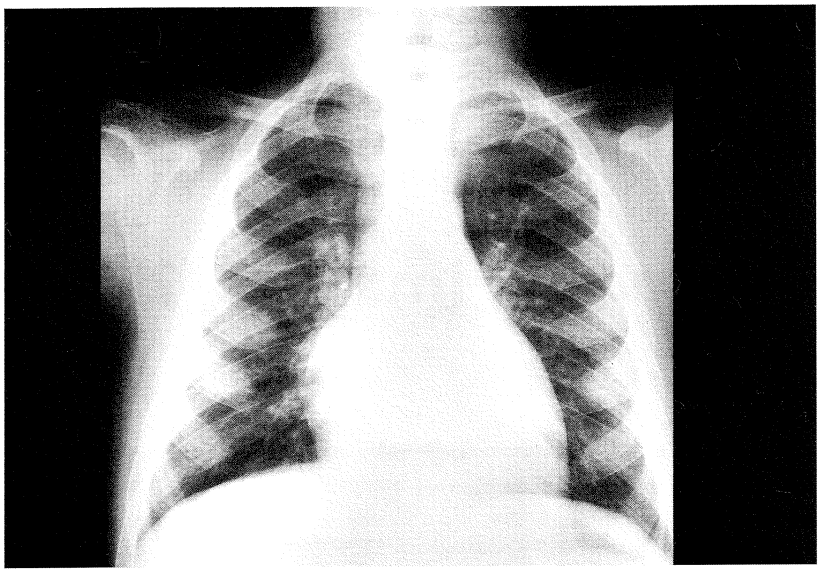

Fig 4 - Postero-anterior chest radiograph showing diffuse medullary expansion of the ribs.

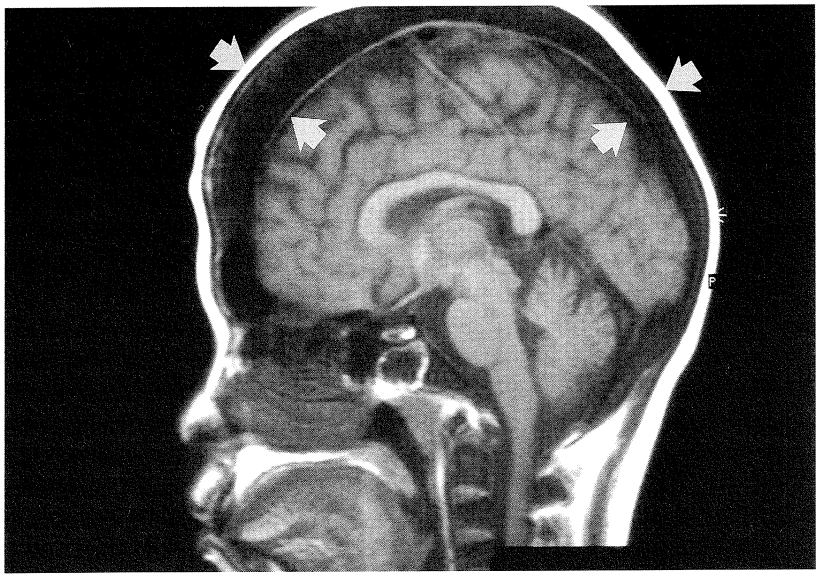

Fig 5 - Sagittal T1-weighted image of the skull. There is severe medullary expansion (between arrows) particularly in the frontal region. Note how the inferior portion of the occipital bone is spared as red marrow is sparse in this area. There is also loss of marrow signal within the upper cervical vertebral bodies due to iron deposition.

IMAGE INTERPRETATION

The skull radiograph (Fig 1) shows marked widening of the diploic spaces with radially-orientated thickened trabeculae joining the inner and outer tables producing the "hair-on-end" appearance. The inferior portion of the occiput is spared. The hand radiograph (Fig 2) also shows diffuse medullary expansion of the shafts of the tubular bones with thinning of the cortices. There is coarsening and thickening of the trabeculae.

The MR image of the abdomen (Fig 3) shows diffuse low signal intensity in the liver and, to a lesser extent, the spleen, relative to the paravertebral musculature (normally the liver and spleen are higher in signal intensity than muscle). This lowered signal intensity is due to iron overload. The vertebral body marrow signal intensity is also lower than normal due to iron deposition.

DIAGNOSIS

Thalassaemia major with iron overload.

CLINICAL COURSE

Both parents were found to have beta-thalassaemia minor. The patient's haemoglobin level was 6.7 g/dL on admission, with a low mean cell volume (62 fL (range 81-97 fL)) and low mean cell haemoglobin (20 pg (range 27-33 pg)). Peripheral blood smear analysis revealed marked red cell anisopoikilocytosis with target and pencil cells. Haemoglobin electrophoresis showed that haemoglobin F concentration was 81%. She was commenced on regular blood transfusions.

DISCUSSION

Thalassaemia which, in Greek, literally means "anaemia of the sea" extends in a broad geographical band from the Mediterranean ("Mediterranean anaemia") through Asia. The fundamental defect is an inherited defect in the rate of synthesis of one of the globin chains. There are two main groups, alpha- and beta-thalassaemia, characterised by deficiencies in alpha- and beta-globin chain synthesis, respectively. Homozygous and heterozygous forms exist. Although homozygotes (thalassaemia major) are more severely affected than heterozygotes (thalassaemia minor), there is considerable variation amongst both groups, with respect to severity of involvement.

The anaemia resulting from excessive destruction of immature and mature red blood cells leads to compensatory hyperplasia of the erythroid marrow[1]. Thalassaemia major has the highest level of erythroid proliferation of any disorder seen in man with ferrokinetic studies demonstrating red cell production rates of 10-20 times the basal level in severely anaemic patients[2]. Marrow hyperplasia results in medullary expansion and the distinctive skeletal abnormalities. These skeletal abnormalities are most noticeable where both the red marrow is abundant and the overlying bone cortex is thin. They are seen particularly in the short bones of the hands (Fig 2) and feet, the ribs (Fig 4), the spine and the skull[1]. The skull changes occur late and consist of expansion of the diploic space with thickening of the traversing trabeculae leading to a "hair-on-end" appearance. This process starts in the frontal region ("frontal bossing") and spares the inferior portion of the occiput (where red marrow is relatively sparse)[1]. This is clearly demonstrated on cranial MR imaging (Fig 5). Marrow hyperplasia in the facial bones leads to reduced pneumatisation of the sinuses, anterior displacement of the incisors, dental malocclusion and a "rodent" facies. All these changes may occur in other chronic anaemias though not with the same severity as in thalassaemia major. Hypertransfusion regimes, if employed early in life, can prevent the development of skeletal abnormalities[1].

In spite of the extreme marrow compensation, if thalassaemia is undertreated, extramedullary haemopoiesis may still occasionally occur (commonly in the liver, spleen and lymph nodes, uncommonly in the mediastinum, thymus, breast, retroperitoneum,

Table I - Mechanisms of iron overload and sites of iron deposition in thalassaemia

Source	Mechanism	Tissue of accumulation	Organ of accumulation
Increased gut absorption	Stimulated by excessive haemopoiesis	Parenchymal	Liver Pancreas Heart
Extravascular haemolysis	Breakdown of RBC's	Reticuloendothelial tissue	Spleen Bone marrow
Intravascular haemolysis	Breakdown of RBC's	Parenchymal	Liver Kidneys
Transfusional haemosiderosis	Breakdown of senescent or damaged transfused cells	Reticuloendothelial tissue	Spleen Bone marrow

prostate, epididymis)[3]. Rarely, spinal cord compression can occur as a result of haemopoietic transformation of embryonic epidural cell rests or direct extrusion of hyperplastic marrow from adjacent vertebrae[3].

Thalassaemic patients are also susceptible to iron overload (Table 1), avascular necrosis, premature epiphyseal fusion (which may be deferoxamine (desferrioxamine)-related[4]) and infections[3]. Unlike most other chronic anaemias which develop iron overload secondary to transfusions and haemolysis, the extreme demands of the thalassaemic marrow also stimulates extra iron absorption from the gut[2]. (Iron overload in thalassaemia is thus occasionally referred to as "erythropoietic haemochomatosis"). This is important as excessive iron absorbed from the gut accumulates predominantly in parenchymal tissues (notably the liver, heart and endocrine glands) whereas siderosis resulting from transfusions and extravascular haemolysis accumulates predominantly in the reticuloendothelial system (notably the spleen and bone marrow)[5]. Iron deposited in the tissue parenchyma is more detrimental to tissues than iron within the reticuloendothelial system[5]. However, with heavy iron overload, the distinction is less clear as reticuloendothelial iron "overspills" into the parenchyma tissues[5].

MR imaging is very sensitive to the presence of iron and its potential deposition in thalassaemia and other iron overload states has been investigated[5-10]. Iron shortens the transverse relaxation time of surrounding water protons. The presence of iron in tissues thus makes these tissues appear darker, particularly on T2-weighted and gradient-echo sequences. Using skeletal muscle (which does not accumulate iron) as the benchmark, the relative lowering of signal from the liver, pancreas and those organs where iron is being preferentially deposited. This allows prediction of the dominant source of extra iron (ie whether iron overload is predominantly transfusion-related or secondary to gut absorption) (Table 1)[5]. Conventional MR is not good at accurately quantifying either mild (ie < 80 μmol Fe/g dry weight) or severe (ie > 300 μmol Fe/g dry weight) liver iron stores[6,7]. However, recent studies using short echo times, signal intensity ratios (between the liver and skeletal muscle)[8] or spectroscopy[9], have shown a good correlation with liver biopsy up to values of 400 μmol[8] and 500 μmol Fe/g dry liver weight[9]. Above this level, the liver signal intensity is so low it is not measurable. Although not widely available, fairly accurate estimation of iron stores can also be achieved using a non-imaging superconducting susceptometer (SQUID) which analyses magnetic susceptibility[10]. Potentially, these non-invasive methods may provide clinicians wishing to monitor the response to chelation therapy with an alternative to liver biopsy in the future[9].

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ABSTRACT

A 5-year-old girl presented with lethargy, anaemia and facial distortion. Both parents had beta-thalassaemia minor. Radiographs confirmed the characteristic features of thalassaemia major. A treatment regime comprising regular blood transfusions was commenced. The basis of the radiographic changes and the current role of magnetic resonance imaging, particularly with respect to assessing iron overload, are emphasised.

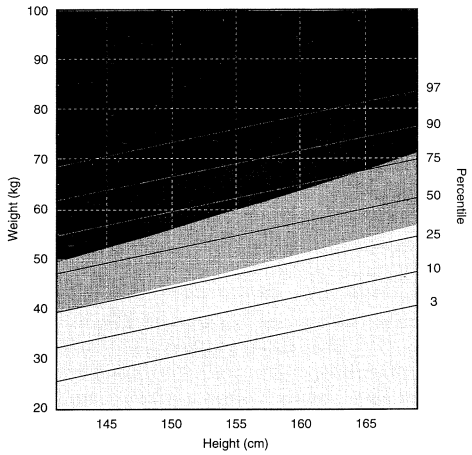
Keywords: thalassaemia, erythropoiesis, iron overload, radiography, magnetic resonance imaging

CORRIGENDUM

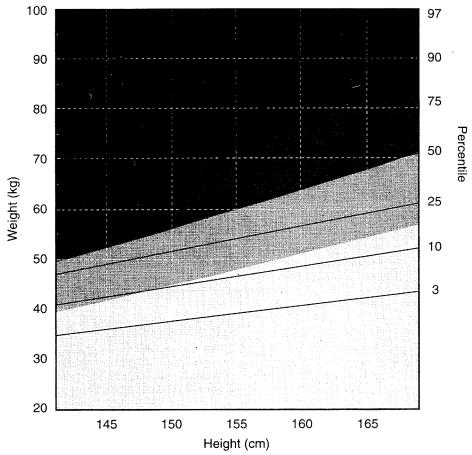
The editor wishes to apologise for the inadvertent error of missing out on the following charts in the previous issue of Singapore Med J 1997; 38(8):352.

Weight for Height Reference Charts by Ethnic Group and Gender

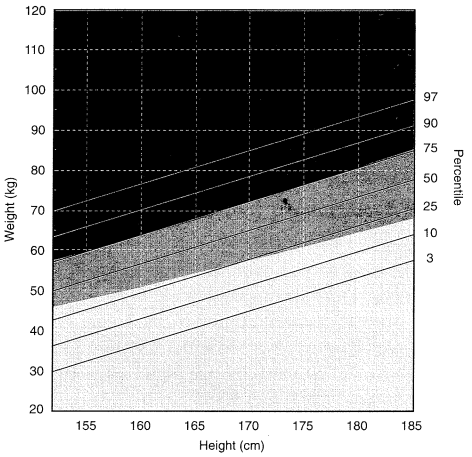
Malay Females (18 - 29 years)



Malay Females (30 - 69 years)



Indian Males (18 - 29 years)



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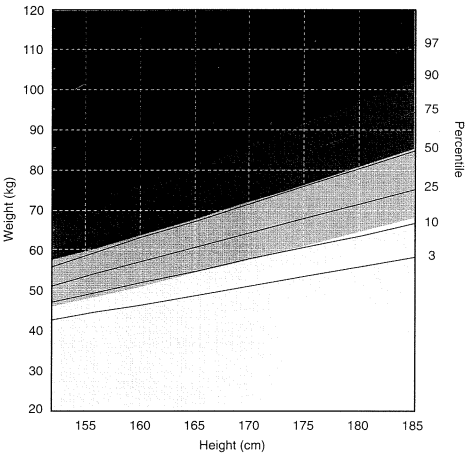

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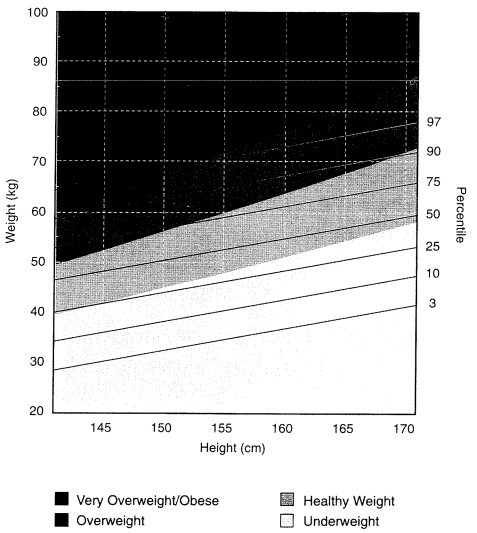

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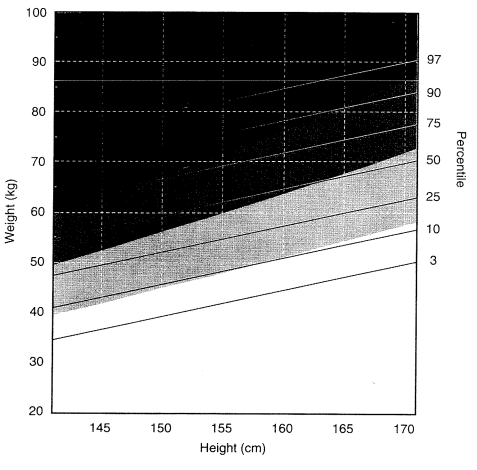

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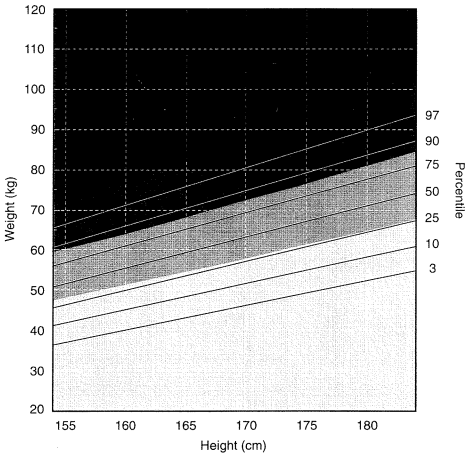

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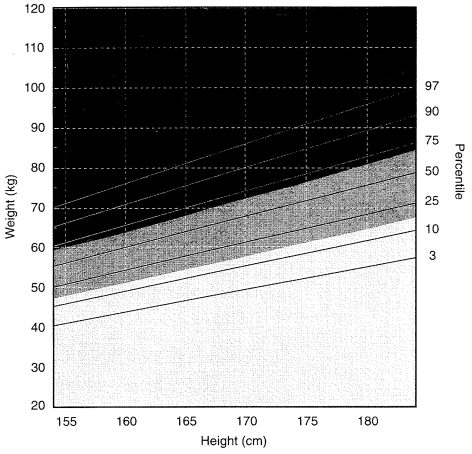

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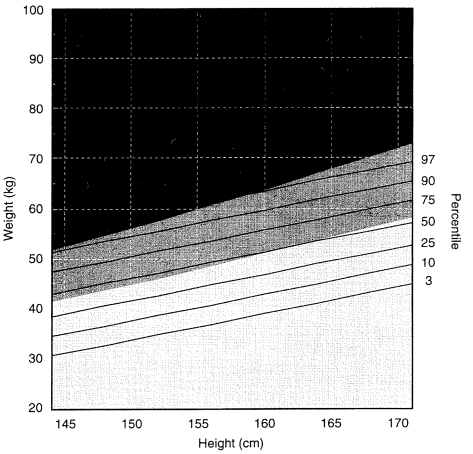

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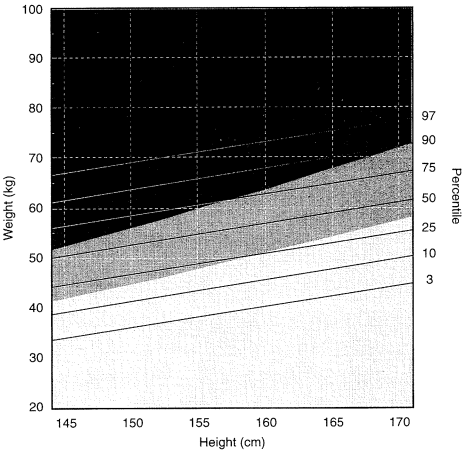

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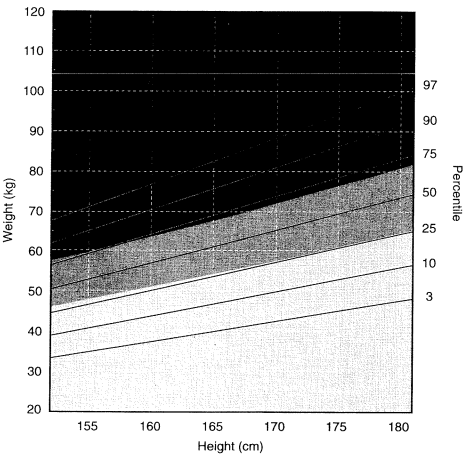

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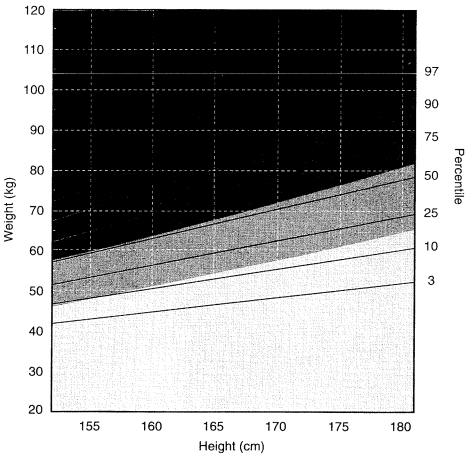

■ Very Overweight/Obese
■ Overweight
▒ Healthy Weight
□ Underweight