# SKULL CHANGES IN NEUROFIBROMATOSIS

By Tan Kwang Hoh, M.B.B.S.(H.K.) M.R.C.P.E., D.C.H.
(Paediatric Unit, General Hospital, Singapore)

In 1881 F. Von Recklinghausen first described a clinical syndrome which was later to be known as neurofibromatosis. Since then numerous articles had been written about this syndrome with different manifestation in various organs. The condition is best considered as a clinical syndrome with manifestation in different organs simultaneously or singly, viz.

i) The skin, resulting in cutaneous pigmentation, cutaneous fibromas or mollusca fibrosa and sometimes over growth of skin and subcutaneous tissues.

ii) The nervous system involving the brain sometimes known as the central type or the peripheral nerves also known as the peripheral type.

iii) The viscera with or without tumour formation, and with gigantism of the intestinal organs.

iv) The bones, including pseudoarthrosis, kyphoscoliosis, disorder of growth either over or under development, erosive defects and intra osseous cystic lesions.

v) The endocrine system including acromegaly, adiposo-genital dystrophy and Addison's Disease.

Ever since Adrian (1901) reviewed the literature and found skeletal changes and Gould (1918) commented on the frequency of osteomalacia in Von Recklinghausen's disease, many articles had been written on the osseous involvement (Brooks & Lehman 1924: Lehman 1926; Uhlmann & Grossman 1940-41). According to Reuben (1939) about 7% of patients with neurofibromatosis showed bony changes. Miller (1936) mentioned that of all the cases showing skeletal changes, 43% of them had involvement of the vertebral column. Holt & Wright (1948) in a review of 127 cases of neurofibromatosis seen over a period of 13 years found that 29% of the patients showed some form of skeletal defect.

The above papers dealt mostly with the skeletal involvement and little was written about atrophic changes in the skull. Rosendal (1938) mentioned about the scarcity of report of cranial changes.

This article is mainly concerned with bony defects in the skull associated with overlying plexiform neuroma as seen in 2 patients aged 2½ years and 14 years.

## CASE REPORTS

### Case 1.

L.P.M. a 14-year-old Chinese boy was first seen at the age of 8 years with a history of a gradual enlarging mass over the right side of neck for about 5 years and cutaneous pigmentation since birth (Figs. 1 & 2). At the age of 6 years he also noticed that the right side of his tongue was becoming bigger than the left. The family history revealed that his late paternal grandfather had similar type of swelling over the right side of the face. His parents and other siblings had no cutaneous pigmentation or tumours. On examination, the boy showed patches of cutaneous pigmentation over the body, neck and limbs. The right side of his face appeared larger than the left. There were 2 soft tissue masses, one over the supra scapula area and the other over the right sternomastoid muscle and the right mastoid area. These two masses consisted of soft tissue with several small nodules embedded in them. Some of these nodules felt like strings of beads. The skin overlying these two swellings were more deeply pigmented than the surrounding area. There was a depression on the right side of the skull about two inches above the right mastoid process. A pulsation could be felt over the depression. The tongue was asymetrical in shape with a cauliflower like growth over the right side. X-ray of the skull (Fig. 3) showed a large well defined oval defect in the occipito-parietal region with a few smaller defects anterior to it. The right clavicle was thinner than the left. Biopsy of the soft tissue mass over the right shoulder revealed histological evidence of neurofibromatosis. No evidence of malignant changes had occurred since the biopsy 5 years ago. The boy is at present

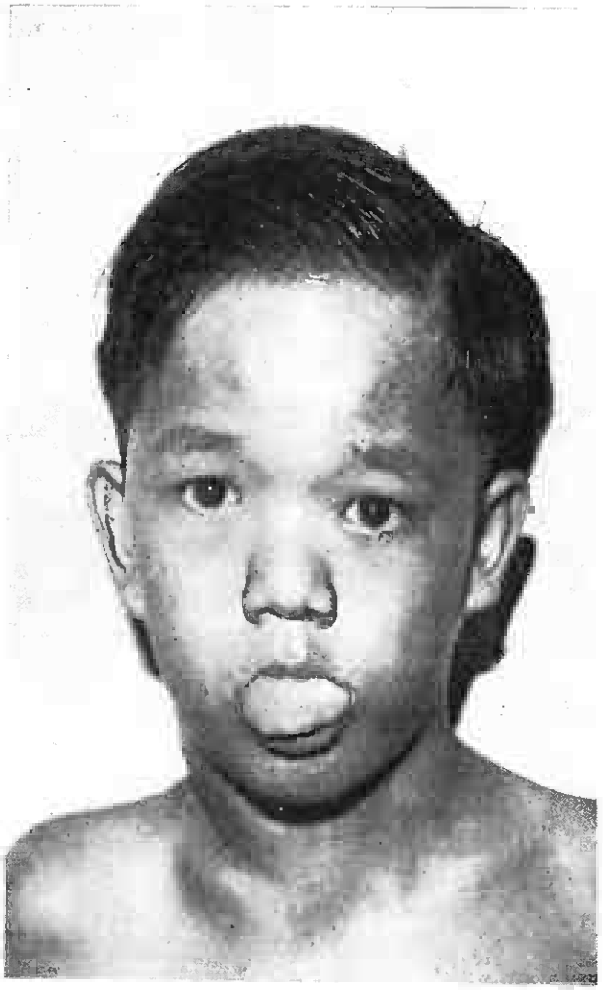

Fig. 1 Case 1, showing hemihypertrophy of right side of face and tongue.

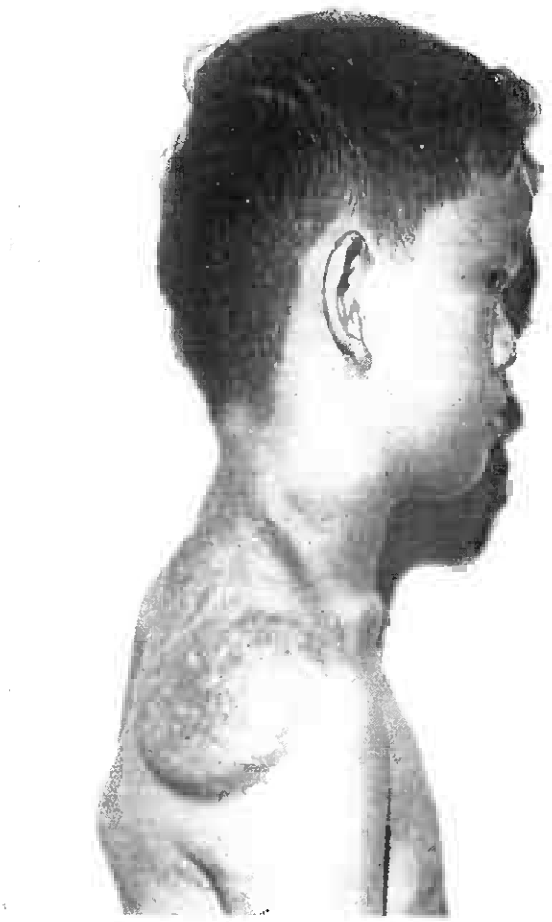

Fig. 2. Case 1, note plexiform neuroma over right shoulder and right sternomastoid area.

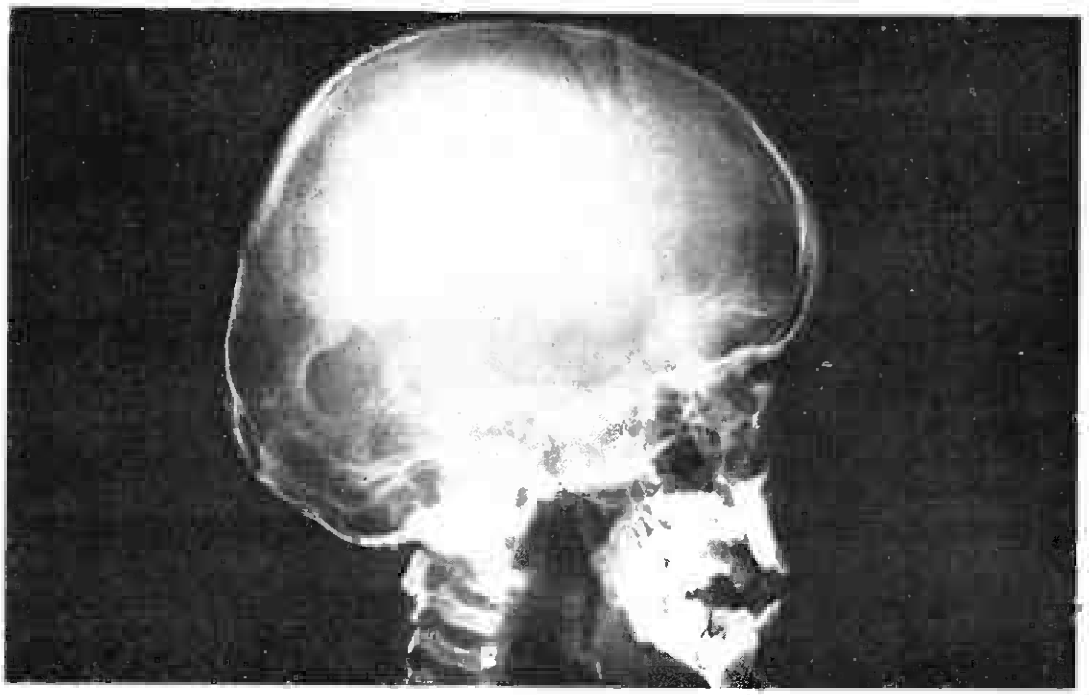

Fig. 3. Case 1, X-ray of skull revealed well defined oval defect in occipital parietal region.

attending a vocational school having failed to pass the entrance examination to the secondary school.

## Case 2.

F.B.H. a 2½-year-old Malay girl was admitted to the Paediatric Unit in August 1963 with the history of a swelling over the right parotid area since the age of 2 months. The mother also noticed another swelling over the right occipital area at the age of one year. The two swellings were noticed to have increased in size progressively (Fig. 4).

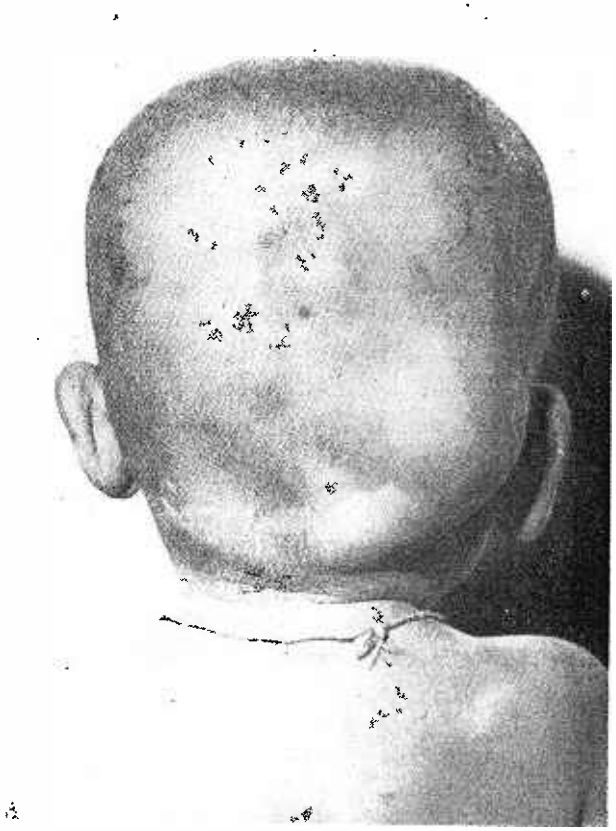

Fig. 4. Case 2, note swelling over right occipital and right parotid region.

The swelling over the right occipital region was 2 inches x 2½ inches, pulsating and was soft in consistency with occasional firm nodules embedded in it. Deep palpation revealed an irregular bony defect underneath the soft tissue swelling. A second bony defect could be felt over the right frontal region. Over this region one could feel two nodular chains in the soft tissue, overlying the skull, one chain extending towards the right occipital mass. Palpation over the lambda region revealed another large bony defect with irregular margin. The soft tissue overlying the lambda did not show any swelling or nodules. The swelling over the right parotid region was also soft, slightly rubbery with several nodules embedded in it. The underlying bone felt intact. The skin over the above two swellings was more deeply pigmented than the surrounding skin. There

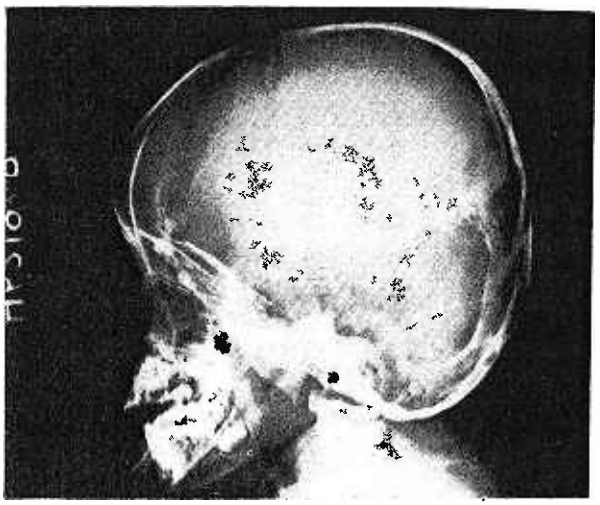

Fig. 5. Case 2, X-ray skull showed large defect in right occipital and several smaller defects in frontal region.

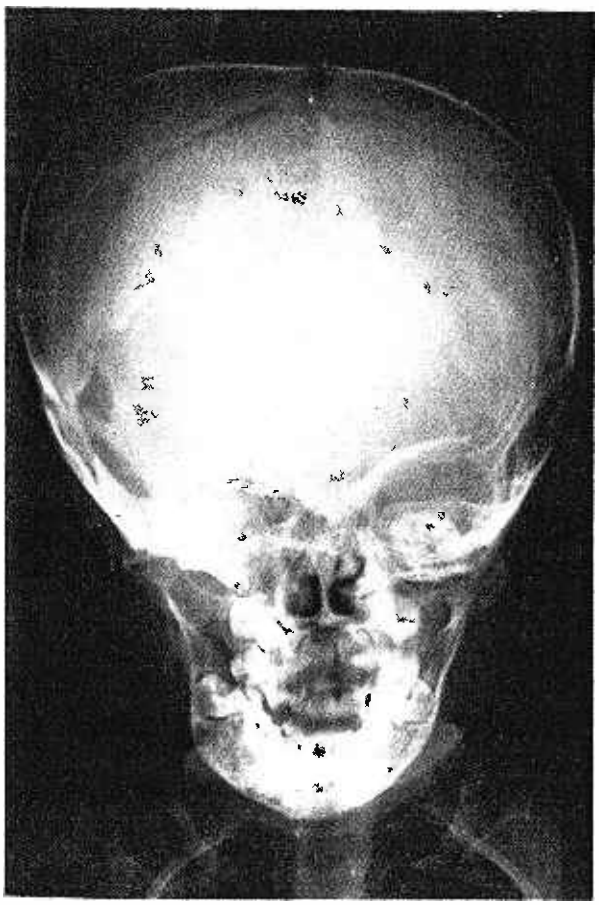

Fig. 6. Case 2, X-ray skull showed strophic areas over lambda and right occipital region.

were also scattered patches of cafe au lait spots over the upper and lower limbs. X-ray of skull (Figs. 5 & 6) showed multiple bony defects over the lambda, right occipital, and frontal area. The long bones and vertebral column were radiologically normal. Biopsy of a nodule over the right frontal region revealed histological evidence of neurofibromatosis.

Patient is the 6th child in a family of 7 children. The other children were all examined and only the 3rd child, a girl aged 7 years, and the 5th child, a boy aged 4 years, showed clinical evidence of cafe au lait spots on the body. The mother of this patient did not have any cutaneous pigmentation suggestive of neurofibromatosis.

## DISCUSSION

As early as 1918 Gould emphasised that Von Recklinghausen's neurofibromatosis is a condition effecting bones as well as skin and nerves. Of the 5 cases described by him, it was noted that only in one case (Case IV female aged 46) was there mentioned of cranial involvement viz. that section of the ribs vertebrae and skull at autopsy showed definite softening of the bone. There was no X-ray report of the skull. Lehman (1926) described 9 cases of neurofibromatosis with bone involvement. Cystic areas in the skull were found in Case 9, a white woman of 38 years, who had no external manifestation of cranial findings and had almost no pigmentation. Uhlmann (1940) examined 60 members of 3 families and found that 13 had clinical evidence of neurofibromatosis. 5 of the 13 had osseous lesions mainly in the form of scoliosis and cystic changes in the skull. Rosendal (1938) described 8 cases of Recklinghausen's neurofibromatosis with cranial involvement, of which 5 had extensive atrophic changes of the skull. The youngest of these 5 cases was 14 years and the oldest 38. In his review of literature he cited a monstrous case recorded by Heine (1927) where there was unilateral facial elephantiasis with atrophic cranial changes verified radiologically and at autopsy.

The atrophic changes in the skull as seen in the 2 cases mentioned in this paper could be due to erosion of the bone by adjacent neurofibromata or they could be intra osseous cyctic lesions. These erosive defects are more commonly seen in the bones of extremities and vertebral column rather than the skull. The other possible explanation for the skull lesion in the 2 cases where over some of the bony defects there were no overlying neurofibromata and where the bony defects were not palpable, but could only be detected radiogically, could be the presence of subperiosteal cysts. Brooks and Lehman (1924) postulated the mechanism of these cysts as due to a neurofibroma arising in periosteal nerve eroding the adjacent bone and comes to lie partially or entirely within it. In Case 1 it was also noticed that the right clavicle was smaller than the left. This was due to disorder of growth associated with neurofibromatosis where there was underdevelopment of the affected bone as opposed to overgrowth as seen in other cases. This underdevelopment of bones may resemble the thin, unusually gracile bones of osteogenesis imperfecta.

The diagnoses of these 2 cases were not difficult because the atrophic changes in the skull were associated with characteristic cutaneous pigmentation and the presence of plexiform neuroma overlying some of the bony defects. In cases where one could only see bony defects in the skull of children radiologically without the associated characteristic clinical features of neurofibromatosis. various differential diagnosis have to be considered. Hands Schuller Christian Disease could present with erosive defects of the skull not unlike those seen in Case 1 & 2. Other possible diagnosis would be bone cysts, metastasis from neuroblastoma and hyperparathyroidism.

Lehman (1926) emphasised that the recognition of bone changes was important in diagnosis especially when the complete picture of neurofibromatosis is not developed. Khoo (1945) suggests "that the finding of one or several isolated bone cysts is as suggestive of the existence of Recklinghausen's neurofibromatosis as the presence of an isolated neurofibroma of the skin or of one or more cafe au lait spots".

## SUMMARY

This paper described 2 children aged $2\frac{1}{2}$ years and 14 years who had multiple bony defects in the skull which could be felt clinically and seen radiologically. Some of these bony

defects had overlying plexiform neuroma. The 14-year-old boy also had underdevelopment of his right clavicle and hypertrophy of the right side of his tongue.

The literature regarding skeletal and skull changes in association with neurofibromatosis was briefly reviewed.

## REFERENCES


Adrian, C. (1901): Beitr. z. Klin. Chir. 31. 1. 98. cited by Holt (1948).

Brooks, B. & Lehman, E. P. (1924): The Bone Changes in Recklinghausen's Neurofibromatosis. Surg. Gyn. & Obst. 38. 587.

Gould, E. P. (1918): The Bone Changes occurring in Von Recklinghausen's Disease. Quart. J. Med. XI. 221.

Heine, J. (1927): Beitr. z. Pathol. Anatomie, 78. 122 cited by Rosendal (1938).

Holt, John F. & Wright, Edwin M. (1948): The Radiological Features of Neurofibromatosis. Radiology. 51. 647.

Khoo, F. Y. (1945): Bone Dystrophies. Canadian Mission Press. cited by Holt & Wright (1948)..

Lehman, Edwin P. (1926): Recklinghausen's Neurofibromatosis and the Skeleton. Arch. Dermat. & Syphil. 14. 177.

Miller, A. (1936): Neurofibromatosis with reference to Skeletal Changes. Arch. Surg. XXXII. 109.

Reuben, M. S. (1939): Von Recklinghausen's Disease. Arch. Pediat. Ii, 522.

Rosendal Thomas (1938): Some Cranial Changes in Recklinghausen's Neurofibromatosis. Acta Radiologica, 19, 373.

Thannhauser, S. J. (1944): Neurofibromatosis (Von Recklinghausen) and Osteitis Fibrosa Cystica Localisata et Disseminata (Von Recklinghausen). Medicine 23. 105.

Uhlmann, E. & Grossman, A. (1940-41): Von Recklinghausen's Neurofibromatosis with Bone Manifestation. Ann. of Int. Med. 14. 225.