DYSCHONDROPLASIA WITH HAEMANGIOMATA
(MAFFUCCI'S SYNDROME)

Report of a Case Complicated by Intracranial Chondrosarcoma

CHRISTOPHER STRANG and IAN RANNIE, NEWCASTLE-UPON-TYNE, ENGLAND

From the Departments of Medicine and Pathology, the Royal Victoria Infirmary

The association of dyschondroplasia with haemangiomata is a rare condition first described by Maffucci in 1881. Of the two components of the syndrome, the dyschondroplasia is identical with Ollier's disease and the vascular abnormalities in the form of cavernous haemangiomata and phlebectasia appear to be coincidental. Carleton, Elkington, Greenfield and Robb-Smith (1942) reviewed eighteen cases from the literature and added two of their own, suggesting that the syndrome be named after Maffucci. They and Krause (1944), who described a further case, remarked that mild degrees of the syndrome were probably more common than the small number of reported cases would indicate. Umansky (1946) has since described a mild case in a coloured girl, but notes that at the Hospital for Joint Diseases, New York, no other example of the combination was found in seventy-one cases of haemangiomata, sixty-five cases of dyschondroplasia and sixty cases of osteochondromata collected over a period of fifteen years. The case now reported, which appears to be the fifth of which an autopsy record is available, is unusual in that the base of the skull was involved.

Dyschondroplasia, or Ollier's disease, is characterised by a disturbance of bone formation in cartilage, particularly at the growing ends of the bone. There is no evidence that the condition is familial; the patients usually appear normal at birth, the disease being first noted at any time up to puberty. The lesions are often predominantly unilateral. The cartilage persists as islands in the diaphysis and may grow to form enchondromata; in some situations such as the phalanges, there may be great expansion and deformity of the bone. Enchondromata are also formed, especially near the epiphyseal lines. As a result of the imperfect ossification and irregular growth, bowing of the affected bones may lead to marked skeletal asymmetry, and the stresses of weight-bearing often cause secondary deformities. Owing to the delay in skeletal growth the patients are usually of small stature, and may show pronounced muscular atrophy. The lesions affect any part of the skeleton: involvement of the long bones and phalanges is common, of the skull, carpus and tarsus, uncommon. Fractures occur readily and may be slow to unite. Malignant change may develop in the enchondromata.

The vascular abnormalities of Maffucci's syndrome consist of multiple cavernous haemangiomata and phlebectasia. The haemangiomata may occur in the subcutaneous tissue anywhere, but have also been noted in the lips, palate and mesocolon. They form blue or reddish-blue tumours which are soft, compressible, and sometimes tender on pressure. Thrombi may form and sometimes become calcified; as phleboliths they produce a striking radiographic picture in the soft tissues. Phlebectasia is common and may affect large groups of veins or be confined to a few local areas in a vein, causing bead-like swellings.

CASE REPORT

The patient, a small, grossly deformed woman aged forty-seven years, had been found unconscious in bed and admitted to hospital with a diagnosis of subarachnoid haemorrhage. When examined, she co-operated in response to instructions but was partly aphasic, being able to answer little more than "yes" or "no."
**Previous history**—This was obtained from her brother. Her mother and father were unrelated and there were no known physical abnormalities in any near relatives. No deformities were noticed during early childhood, but at the age of seven a broken leg caused by a fall united with deformity: after this she wore irons on both legs and a raised boot on one side. When she was eleven years old, lumps were noticed on her hands and feet; they were excised but soon recurred. Another attempt at removal was made but the swellings again recurred and gradually increased in size. Many of the lumps were blue in colour but none of them ever bled. Fluid exuded from the swellings on her feet and affected the leather of her boots. She married at twenty-seven but there were no children and her husband died a few years later. She then took up hairdressing and was able to support herself until the lumps on her fingers made it impossible for her to hold the instruments. She had originally trained as a milliner, and up to the time of her final illness she was able to sew beautifully and to play the piano well. For five days before her admission she had complained of a spasmodic pain over the left eye; it had been noticed that her left eye moved upwards when she looked to the left.

*Figs. 1 and 2*

Figure 1 *(left)*—A photograph of the foot, showing the haemangioma on the toes. The bead-like subcutaneous swellings are localised varices. Figure 2 *(above)*—The right hand, showing swellings near the interphalangeal joints.

**Examination**—The patient was grossly deformed. The right leg was short, with forward bowing of the femur and a hard swelling at its lower end. The tibia was S-shaped, concave forwards above and convex forwards in the lower third. The ankle was fixed in plantar flexion and the knee and hip joints showed only slight movement; there was no crepitus in any of the joints. On the foot there were multiple soft tender tumours, bluish in colour and covered by horny skin; the largest were on the inner side of the heel and great toe, with smaller ones on the dorsum and sole of the foot (Fig. 1). Localised simple varices were also found, mainly round the ankle. The left leg was even more deformed, with outward and forward bowing of the femur. There was enlargement of the lower end of the femur, and also of the upper end of the tibia—which was nevertheless relatively straight. The foot was inverted and fixed in plantar flexion. There were soft swellings on the foot; one especially large growth on the medial aspect measured 7·5 by 5·0 centimetres. Bead-like swellings of the veins were
palpable in the subcutaneous tissue. The anterior surfaces of both legs showed a reticular pattern of deep brown pigmentation.

The right hand (Fig. 2) showed hard swellings covered by shiny skin of normal colour over the interphalangeal joints of the first, second and third fingers, and the proximal phalanx of the second finger appeared irregularly expanded. Otherwise the upper limbs showed no abnormality. On the abdominal wall above the left iliac fossa were several soft bluish growths, and three small tumours—"like raisin skins without pips"—were present on the skin of the thorax.

Central nervous system—There was complete ptosis of the left eyelid with some proptosis. The right pupil was central, circular and moderately dilated, with a brisk direct and consensual light reflex and normal reaction on convergence; the left pupil was dilated and fixed. The left eye moved only slightly in a lateral direction but was completely immobile when upward or downward movements were attempted; movements of the right eye were normal. There was no papilloedema; the retinal vessels appeared healthy and there were no haemorrhages or exudate.

The sense of smell was absent in the left nostril but present in the right. There was diminished sensibility in the area supplied by the fifth nerve on the left side, and the left corneal reflex was absent. The right lower facial muscles showed a definite weakness of upper motor neurone type. The hearing was normal and the movements of the tongue and palate showed no abnormality. Neck stiffness was marked, with pain on movement.

The right arm was powerless and spastic and showed brisker reflexes than the normal left arm. There was no sensory loss. The superficial abdominal reflexes were absent on the right, present on the left. The right leg was weak with a slight increase in tone. The knee and ankle jerks were present and equal on both sides. The right plantar response was extensor and the left flexor. Kernig's sign was not present. The heart, lungs and abdomen appeared normal; the blood pressure was 165/85.

The diagnosis of subarachnoid haemorrhage was confirmed by lumbar puncture, when blood-stained fluid under increased pressure was obtained. The patient lapsed into coma; three days after admission there was bilateral papilloedema and incontinence of urine and faeces. The neck stiffness persisted and the hemiplegia on the right side became complete. There was no elevation of temperature at any time. The patient died eleven days after admission.

The following investigations were carried out in hospital: Radiographs (portable machine)—All the bones with the exception of the skull, clavicles and spine showed the characteristic changes of dyschondroplasia (Figs. 3 to 5). In addition, there were multiple soft tissue tumours corresponding to the vascular dilations and haemangiomata, and small circumscribed calcifications due to phleboliths.

Blood examination—There was a moderate polymorphonuclear leucocytosis of 13,900 per cubic millimetre; serum calcium—10·4 milligrammes per 100 cubic centimetres; plasma phosphorus—3·0 milligrammes per 100 cubic centimetres; alkaline phosphatase—6·9 units (Jenner and Kay); blood urea—96 milligrammes per 100 cubic centimetres; serum protein—total protein 8·10 grammes per 100 cubic centimetres, serum albumin 5·60 grammes per 100 cubic centimetres; erythrocyte sedimentation rate 26 millimetres in one hour (Westergren). The urine contained no albumin or sugar.

Autopsy—An autopsy was carried out twenty-four hours after death. The deformities present have already been noted.

The bones—The right femur measured 30 centimetres in length. Its head was of normal size but showed erosion of articular cartilage. The shaft showed angulation of approximately 30 degrees at 8-0 centimetres below the greater trochanter, and between this and the lesser trochanter the shaft was expanded. The lower end was rotated medially on the shaft through
FIG. 3
The shaft of the right femur is twisted and its lower end greatly expanded.

FIG. 4
The right tibia and fibula. There are many phleboliths in the soft tissues of the foot.

FIG. 5
A radiograph of the right hand showing enchondromata.

an angle of about 45 degrees and the distal 80 centimetres were expanded to a maximum diameter of 70 centimetres. The lower articular surface was eroded. Section of the bone showed that the expansions were associated with chondromata in the diaphysis ranging from 0.2 to 2.5 centimetres in diameter. Where they occurred the overlying cortex was thinned and in places the neoplasms projected through the cortical bone. The epiphyseal lines were not evident. Red bone marrow was scanty but subcortical streaks were present and reddish marrow was present at the periphery of the cartilaginous masses.

The right tibia measured 28.5 centimetres in length and was roughly S-shaped with expansion of the upper and lower ends caused by multiple chondromata up to 240 centimetres in diameter (Fig. 6). The right fibula measured 27.5 centimetres in length and showed on section a chondroma 240 centimetres from the head which had expanded the shaft and burst through the cortex to form a mass 40.30.50 centimetres in the soft tissues. At 5.0 centimetres from the lower end a collection of chondromata occupying an area 340 centimetres in diameter was present. The first right metatarsal showed a chondroma 0.7 centimetres in diameter in the centre of the shaft.

Chondromata were visible on the pleural surfaces of five ribs on the right side and four on the left side. The sternum showed multiple chondromata. No chondromata were found in the spine.

Skull—The vault showed no abnormality. Rising from the basi-sphenoid in the region of the sella turcica was a rounded nodular neoplasm 80 centimetres in width which projected upwards to a height of 50 centimetres (Fig. 7). The posterior part of the neoplasm was soft and infiltrated with blood. Anteriorly the capsular surface was smooth, glistening and yellowish-white in colour, with the pituitary stalk stretched over it and elongated to 30 centimetres. The tumour lay just to the left of the midline and distorted the structures at the base of the brain. The optic chiasma was stretched over the surface of the tumour, and
A section through the upper end of the right tibia showing multiple chondromata and penetration of the cortex.

A sagittal section of the base of the skull through the pituitary fossa, showing a haemorrhagic chondrosarcoma growing from the basisphenoid. The pituitary is largely necrotic.
the left side of the circle of Willis was markedly elongated. The pituitary appeared almost entirely necrotic. The basi-sphenoid contained several minute chondromata. There was thrombosis of the left cavernous sinus and blood had infiltrated along the sheath of the left optic nerve. The brain (1.235 grams) showed softening of the left basal nuclei; there were deep indentations from the neoplasm at the base and on the under surface of the left frontal lobe.

Distribution of the cavernous angiomata—These were found only in the subcutaneous tissues and in the synovial membrane of the joints of the lower limbs (the joints of the upper limbs were not opened). Many contained phleboliths. Of the subcutaneous angiomata, those on the feet projected considerably from the surface and were covered by hyperkeratinised epithelium. Those on the legs and abdominal wall did not project and many were not visible from the surface. In the joints the angiomata were eroding the adjacent bone; this was most marked in the patellae. In addition to the tumours, many of the leg veins showed a general phlebitasia.

Other findings—The uterus contained a solitary leiomyoma. The left ovary was replaced by a yellowish neoplasm measuring 3·0 x 2·0 x 1·0 centimetres. Both adrenals contained cortical adenomata measuring 2·5 centimetres in diameter. The other viscera showed no significant abnormality.

Histological examination. Bones—Apart from the intracranial neoplasm these showed the recognised picture of dyschondroplasia with large areas of hyaline cartilage covered by normal lamellar bone or by perichondrium (Fig. 8). The presence of haemopoietic marrow in the neighbourhood of the chondromata was confirmed.

The tumour arising from the base of the skull showed a much more cellular structure with occasional mitoses and tumour giant cells, and was regarded as a well-differentiated chondrosarcoma of low malignancy (Fig. 9). A great part of the neoplasm was the seat of recent haemorrhage.

Haemangiomata—Typical cavernous haemangiomata showed much organised thrombus with calcification (Fig. 10). The ovarian tumour was composed of cellular tissue having the characteristics of a theca-cell tumour (Fig. 11). The adrenal tumours were simple cortical adenomata. The uterine tumour was a simple leiomyoma. The endometrium was atrophic. The pituitary showed recent necrosis of almost the entire gland. None of the other organs was remarkable; particularly, the other endocrine organs including the parathyroids appeared normal.

DISCUSSION

Maffucci’s syndrome appears to originate from a mesodermal dysplasia. There is no evidence of familial incidence and there is nothing to suggest that either of the component abnormalities induces the other. The subjects usually appear normal at birth, the lesions becoming noticeable in childhood because of deformity, fractures, or the appearance of chondromata or haemangiomata. The disease progresses and gives increasing disability, but may become static after the growth period has ended. Malignant change in the chondromata is not uncommon; it occurred manifestly in four of the twenty-three recorded cases, and was probable in another two.

The present case is unusual in that the skull was involved. Only three of the other recorded cases showed such involvement; one of these showed a chondrosarcoma of the body of the sphenoid. The present case presented an interesting clinical picture caused by the intracranial neoplasm. The subarachnoid haemorrhage was due to haemorrhage into the tumour, leading to further interference with the already distorted arteries of the base of the brain and causing cerebral softening and hemiplegia. There was also cavernous sinus thrombosis; this probably should be attributed the recent necrosis of the pituitary, although direct pressure on the gland with distortion of the stalk may have played some part. Walsh
FIG. 8
H. & E., × 230. A section of a tibial chondroma showing the degree of cellularity (cf. Fig. 9).

FIG. 9
H. & E., × 230. A section of the intracranial chondrosarcoma showing de-differentiation and greatly increased cellularity (cf. Fig. 8).

FIG. 10
H. & E., × 21. A section of a verrucous haemangiomata showing marked hyperkeratosis and calcified phleboliths.

FIG. 11
H. & E., × 180. A section of the ovarian tumour, probably a thecoma, showing the very cellular fibromatous neoplasm.

THE JOURNAL OF BONE AND JOINT SURGERY
(1937) described necrosis of the pituitary gland in five out of six cases of cavernous sinus thrombosis. It is difficult to assess the part played by the pituitary necrosis in the progress of the disease described here because the patient was so gravely ill.

The finding of other simple neoplasms in the adrenals, left ovary and uterus was of interest. The ovarian neoplasm was regarded as a thecoma, and it is unfortunate that there was no information regarding menstruation.

**SUMMARY**

1. Maffucci's syndrome consists of dyschondroplasia (Ollier's disease) in association with cavernous haemangiomata and phlebectasia. Twenty-two cases have hitherto been described.

2. A further case is recorded with autopsy findings showing the characteristic features of the syndrome. Death was caused by a chondrosarcoma of the sphenoid, which led to subarachnoid haemorrhage, cranial nerve palsies, crossed hemiplegia and cavernous sinus thrombosis with almost total pituitary necrosis.

Our thanks are due to Dr A. G. Ogilvie for permission to publish this case, and to Dr Brian Houston for the radiological report.

**REFERENCES**


Maffucci, A. (1881): Movimento medico-chirurgico (quoted by Carleton et al.).
