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September 1954

EOSINOPHIL GRANULOMA

(EOSINOPHIL GRANULOMA, LETTERER-SIWE DISEASE AND HAND–SCHÜLLER–CHRISTIAN DISEASE)

By J. D. K. DAWES (Newcastle-upon-Tyne)

EOSINOPHIL granuloma in the temporal bone has occurred often enough to attract the attention of otologists. Several cases were reported in 1948 by Schuknecht and Perlman, and one case by Dingley in 1952. Because of a recent case of bilateral temporal bone involvement presenting at the Royal Victoria Infirmary, Newcastle, interest was aroused and hospital records were searched for further material of otological interest. This paper is based upon some of these case histories and a survey of the medical literature.

Eosinophil granuloma is a diffuse non-lipoid storage disorder of the reticulo-endothelial system; the histiocytes are the essential cell type, and they have a follicular or diffuse distribution within an organ. The histiocytic nodules may be infiltrated by lymphocytes, plasma cells and eosinophils. It is this eosinophilic infiltration which gives the name of eosinophilic granuloma to the morbid anatomical entity.

Mallory (1942) classified these similar pathological lesions into the following clinico-anatomical concepts :—

(*a*) A disorder of infancy or early childhood often rapidly fatal in which the histiocytic lesions are widely distributed both through the soft tissues (especially the lymphoid tissues) and the skeleton. The syndrome has been given the name of Letterer-Siwe disease.

(*b*) A more chronic form which occurs in children and adults, wherein the histiocytic lesions are also usually limited to the skeleton and tend to undergo collagenization and lipidization. Because of the likelihood of

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damage to the lungs, heart, brain and pituitary in the later stages of the disease the prognosis is grave. The name of Hand-Schüller-Christian disease or lipogranulomatosis is usually given to this clinical entity.

(*c*) A disease of children or young adults which is comparatively benign and often localized to the skeleton or perhaps one bone, and which may heal spontaneously without active treatment. This disease has been named eosinophil granuloma.

Letterer (1926) is usually credited with the first pathological description and he regarded the lesion as an aleukæmic reticulosis. His patient was a 6-month-old infant with otitis media, anæmia, splenomegaly, hepatomegaly and a rash. Siwe (1933) described a similar patient and found others in the literature. Abt and Denenholz (1936) suggested the name of Letterer-Siwe disease, and reported a further case in which they stressed the findings of hepatomegaly, splenomegaly, a hæmorrhagic tendency often manifested as a purpuric eruption, lymphadenopathy and localized skeletal lesions with anæmia. However, the diagnosis must finally rest upon the histopathology.

Schüller (1915) had previously described the peculiar defects of membranous bones, and Christian (1920) had associated these calvarial lesions with exophthalmos and diabetes insipidus. Hand in 1893 had published a similar case but he had regarded the calvarial lesion as of tuberculous origin. The picture of Hand-Schüller-Christian disease was well described by Frazer (1935).

Farber (1941), Farber and Green (1942), Jaffe and Lichtenstein (1944), Ponseti (1948), and others have held the belief that these three lesions are essentially the same, and that the clinical pictures are only different manifestations of the same lesion.

Case Histories

Case I. A.C., æt. 4, Male. Rec. No. 207642.

This boy was first seen when he was almost 2 years of age at the North Riding Infirmary, Middlesbrough, by Mr. J. H. Appleton. At that time he had a history of 3 months' discharge from the right ear. Systemic penicillin and local aural toilet failed to produce any improvement. Granulation tissue was then found in the external auditory canal and on October 19th, 1951, the granulations were partially removed by curettage. However, by November 7th, 1951, the granulation tissue had not only recurred to involve the meatus but was also invading the postaural skin. Mr. Appleton exposed the mastoid cortex through a postaural incision and found the mastoid cortex was eroded and the cavity filled by hæmorrhagic granulation tissue. Interference was limited to simple removal of granulation tissue.

In January 1952 granulation tissue was noticed in the left external auditory meatus and this was also removed. Because of the marked increase in the amount of granulation tissue in this left ear, a postaural incision was made and again the whole mastoid was found to be infiltrated by granulations.

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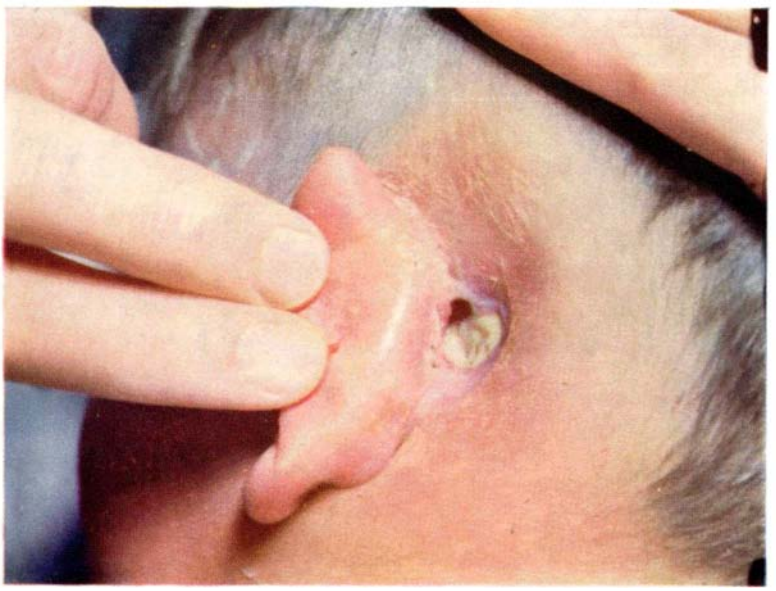


FIG. 1.
Case I. Photograph of the left postaural wound.



FIG. 2.
Case I. Similar photograph of the right ear.

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The report on the biopsy of the granulation tissue stated: "These fragments show a very acute polymorphous sepsis invading the whole of the tissue but there is no evidence of tuberculosis. An interesting feature is that among the polymorphs there are an enormous number of eosinophils."

Radiologically there was a suggestion of an early tuberculous focus in the lungs but no further confirmation of a diagnosis of tuberculosis was obtained.

From July 1952 to August 1953 neither ear was ever free from granulation tissue although several attempts were made to remove them.

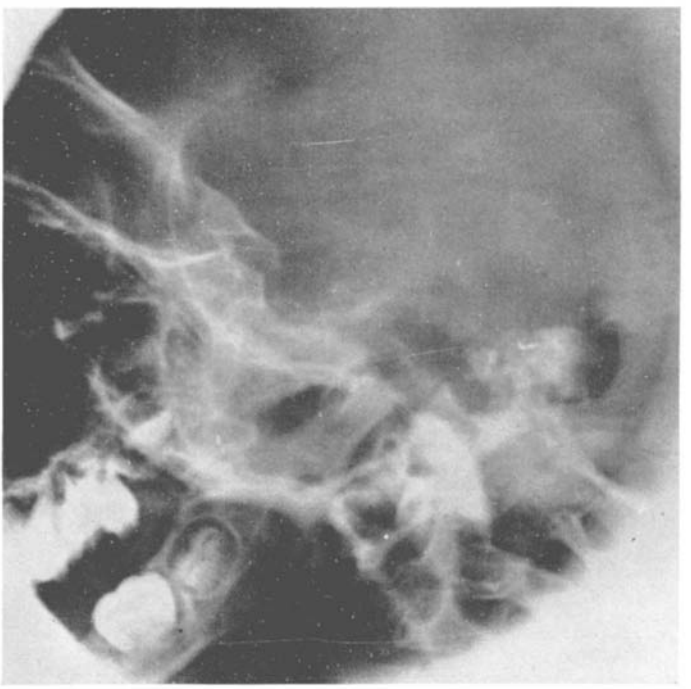


FIG. 3.

Case I. Lateral view of the left mastoid temporal bone to show the degree of destruction.

In September, 1953 the child was seen by Mr. F. McGuckin at the request of Mr. Appleton. There was a history of painless discharge from the left ear for 3 years and the right ear had presented with a postaural swelling. Speech had shown no improvement since the age of 2. The mother believed the child could hear a loud noise in the right ear but nothing in the left.

The patient had bilateral postaural wounds with bluish edges and the mastoid cavities were filled by dirty granulation tissue (see Figs. 1 and 2). The child was very deaf. A provisional diagnosis was made of tuberculous mastoiditis.

The boy was admitted to the Royal Victoria Infirmary on November 10th, 1953. Throughout the whole illness the boy's general health had been good. There was no history of a high fluid intake or output and his weight had been

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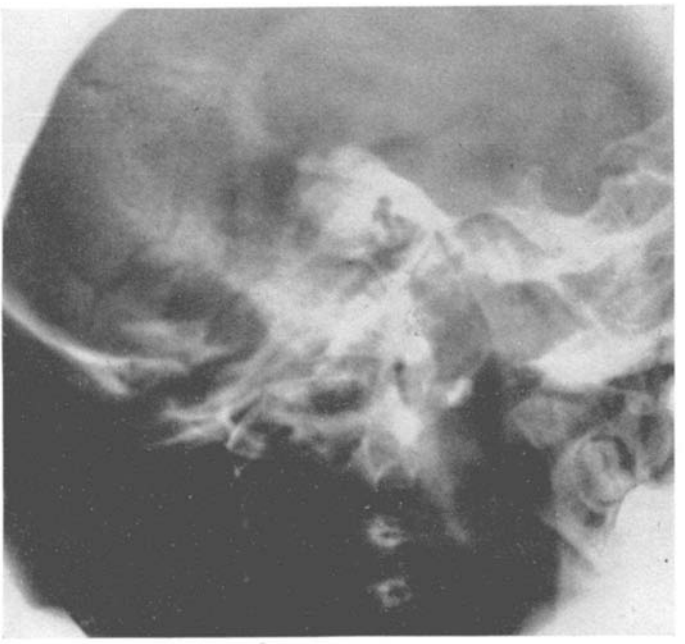


FIG. 4.

Case I. Similar radiograph of the right mastoid temporal bone.

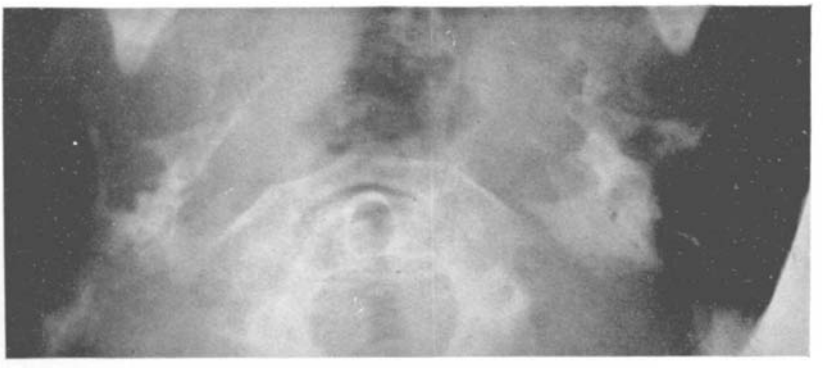


FIG. 5.

Case I. Submento-vertical view of the base of skull. Notice the amount of petrous temporal bone involved.

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fairly steady. The only additional clinical sign was the presence of a left lower motor neurone facial weakness.

On November 11th, 1953, a biopsy of the right mastoid was taken. The soft masses of granulation tissue were found to run right down into the neck. A radiological examination of the skeleton demonstrated an extensive destruction of both mastoid regions and involvement of the basi-occiput (see Figs. 3, 4 and 5) honeycombing of the right scapula (Fig. 6), expansion of 2nd and 4th left ribs (Fig. 7), and cyst-like changes in upper end of the left femur.

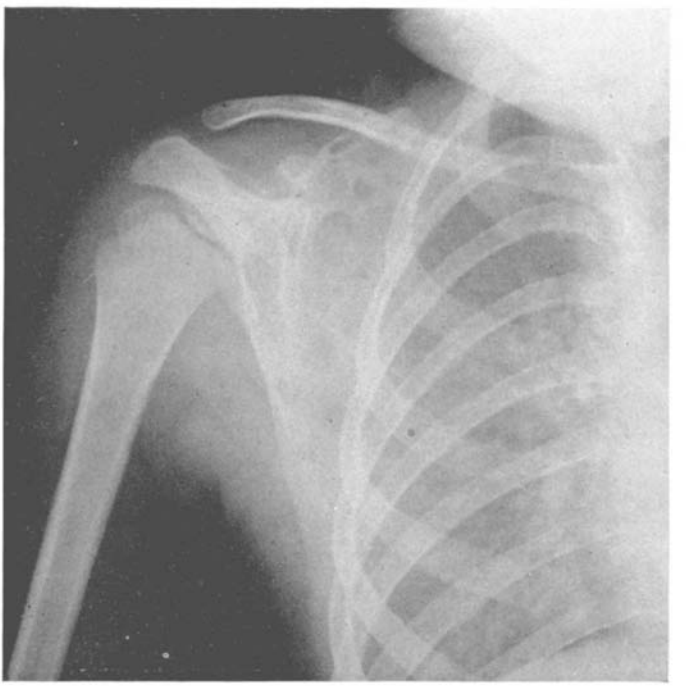


FIG. 6.

Case I. Radiograph of the right scapula to show a "honeycomb" type of lesion.

The appearances were consistent with a diagnosis of eosinophilic granuloma.

The blood picture showed a red cell count of 5·17 millions/cc., and hæmoglobin of 77 per cent. or 11·4 grams/100 ml., a colour index of 0·74, a total white cell count of 8,000 and the differential count was Neutrophils 68 per cent., Eosinophils 2 per cent., Lymphocytes 25 per cent., Monocytes 5 per cent.

The following report (53/6312) was given on the biopsy by Dr. J. H. Mercer: "This is a secondarily infected granuloma showing a tremendous reticuloendothelial hyperplasia with foci of heavy eosinophilic infiltration. There are areas of surface necrosis with growth of secondary organisms. There can be no doubt from this biopsy that the condition belongs to the group, Eosinophilic Granuloma, Letterer-Siwe and Hand-Schüller-Christian disease." (See Figs. 10 and 11.)

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FIG. 7.

Case I. Radiograph to show expanding lesions of 2nd and 4th left ribs.

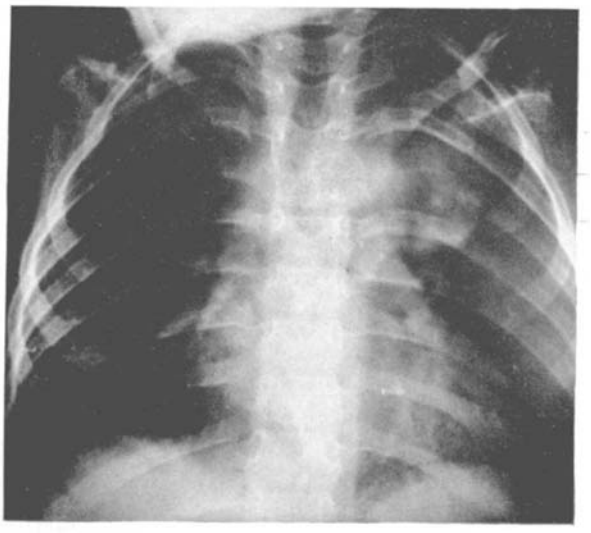


FIG. 8.

Case I. Radiograph of the thoracic spine demonstrating a lesion which involves 4th and 5th thoracic vertebrae.

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On November 19th, 1953, Mr. C. J. L. Thurgar of the Radiotherapy Department agreed that a course of treatment should be given.

A dose of 400r was given to each mastoid and directed towards the pituitary fossa. In view of the frequent bed-wetting an insidious diabetes insipidus was considered but not proved (the specific gravity of the urine never fell below 1015).

On December 7th, 1953, the child was discharged. There was no improvement in his hearing but the facial weakness was less. The child was much better. A blood examination showed that the eosinophils had now risen to a total of 4 per cent.



FIG. 9.
Case I. The cystic lesion in the left femur.

On January 5th, 1954, the mother thought the child much better. Fluid intake and output were considered to be usual in amount. His walking had also improved but he now held the right shoulder stiff. The left postaural wound had healed over and the meatus was stenosed. The right ear appeared cleaner but had not healed completely and the meatus was severely stenosed. He was given 400r to his right scapula.

On February 2nd, 1954, right arm movements were satisfactory. On the whole the child has been better and speech improved. The boy's general health was better. However, the mastoid wounds had been slightly moist and some granulations had reappeared. The facial palsy showed no improvement.

During the next few weeks the child complained of right costal and subcostal

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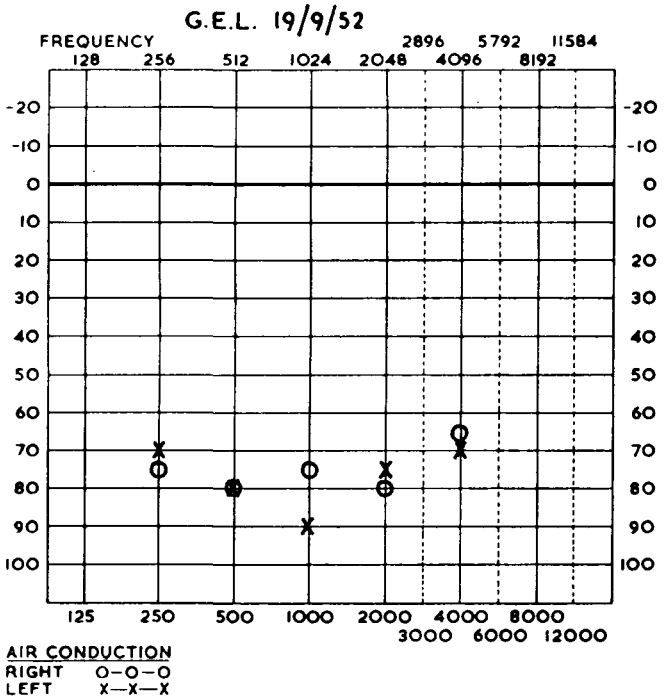
pain extending into the right groin. In March 1954 additional lesions were demonstrated in 4th and 5th thoracic vertebrae (Fig. 8). There were also generalized lymphadenopathy, hepatomegaly and splenomegaly; the ears remained unimproved. In May 1954 the lesion in the left femur (Fig. 9) and those in the temporal bones were treated by radiotherapy.

Case II. G.E.L., æt. 3, Male. 799/2

This child was first seen in April, 1952 with a five months history of cystic changes in, and a pathological fracture of, the neck of the right humerus. (Fig. 11.) A biopsy report (52/2205) by Dr. Mercer suggested the diagnosis of eosinophilic granuloma (Fig. 12).

Both humeri and right fibula became involved and were treated by radiotherapy.

In August 1952 the boy was noticed to be deaf. His general condition however was improving.



Audiogram 1.

Radiologically there was mottling of both lung fields (Fig. 14). The skull roentgenograms showed no lesions of the vertex but extensive areas of destruction of the base of the left petrous temporal with destruction of the semicircular canals and involvement of the middle ear ; there was also a suspicious area in the right petrous temporal (Fig. 15).

The differential white cell count, plasma proteins and serum cholesterol were

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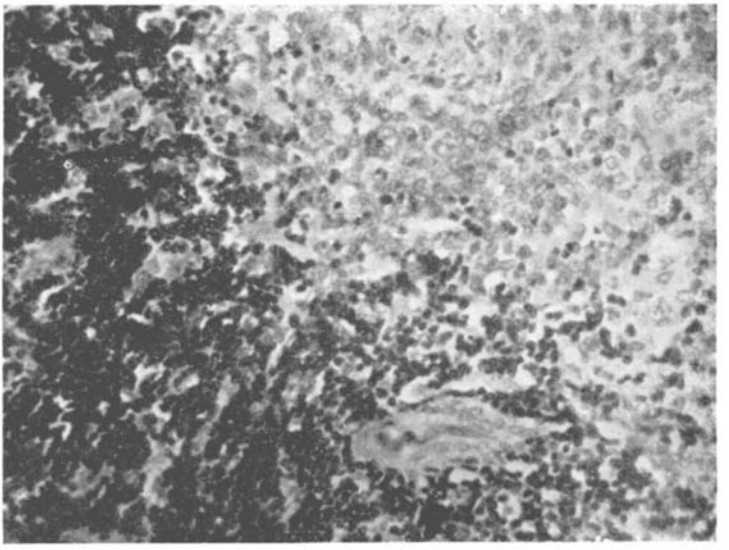


FIG. 10.

Paraffin section of the granulation tissue from the mastoid. This area shows the sheets of histiocytes infiltrated by eosinophils (darker stained cells) (Hæmatoxylin and Eosin × 100).

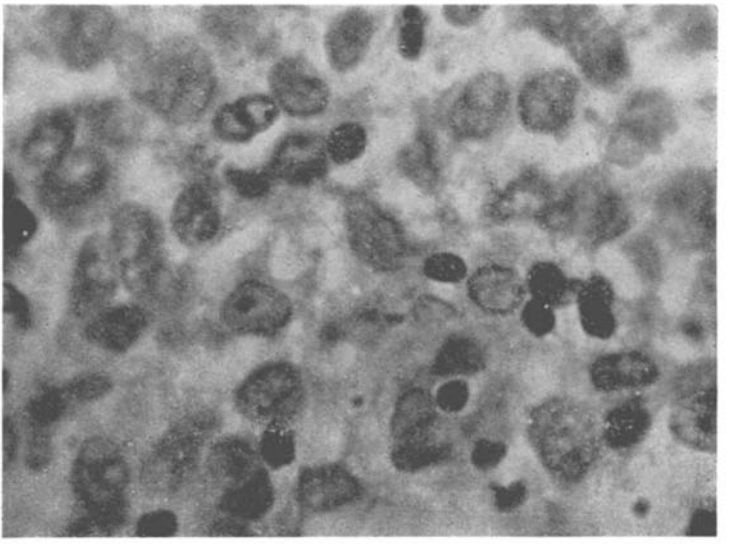


FIG. 11.

Case I. A higher powered view of the same slide as Fig. 10.

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FIG. 12.
Case II. Radiograph of the right humerus to show the cystic changes.

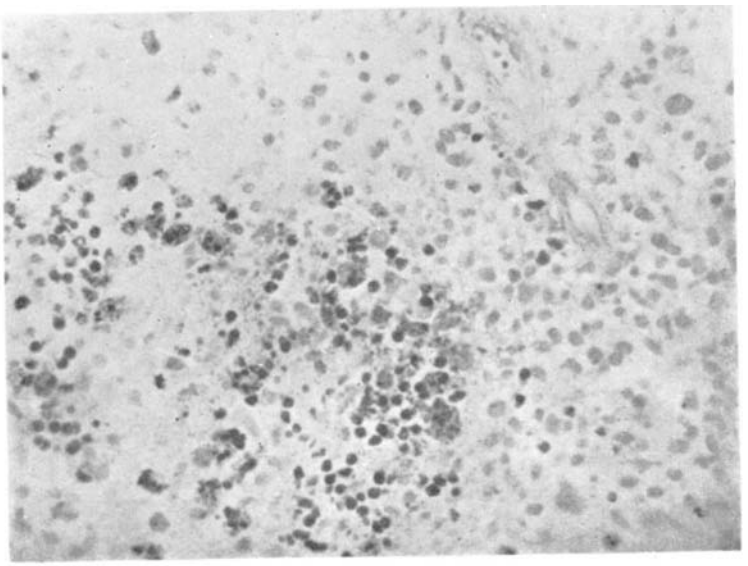


FIG. 13.
Case II. Paraffin section of the granulation tissue obtained from the neck of the humerus (× 100). Compare with Figs. 10 and 11.

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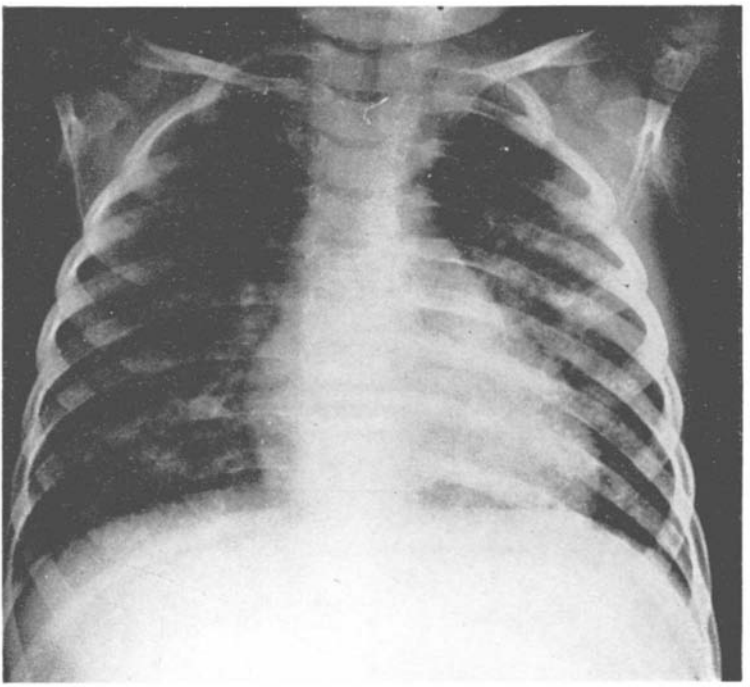


FIG. 14.
Case II. Radiograph of the chest to show mottling of both lung fields.

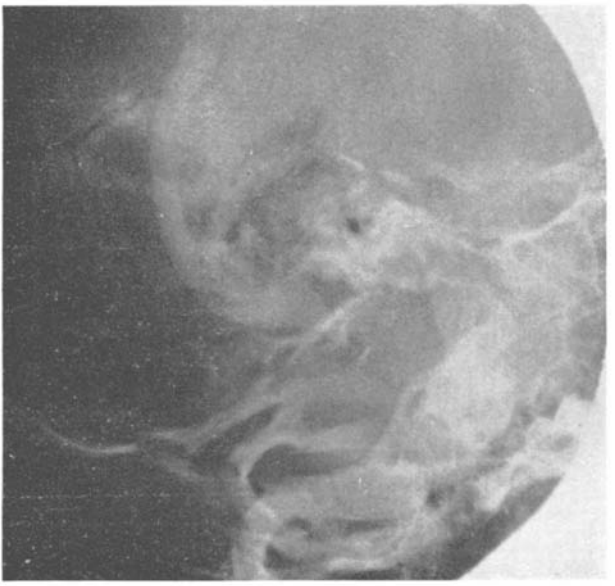


FIG. 15.
Case II. Lateral view of the left mastoid temporal bone showing the destructive lesion.

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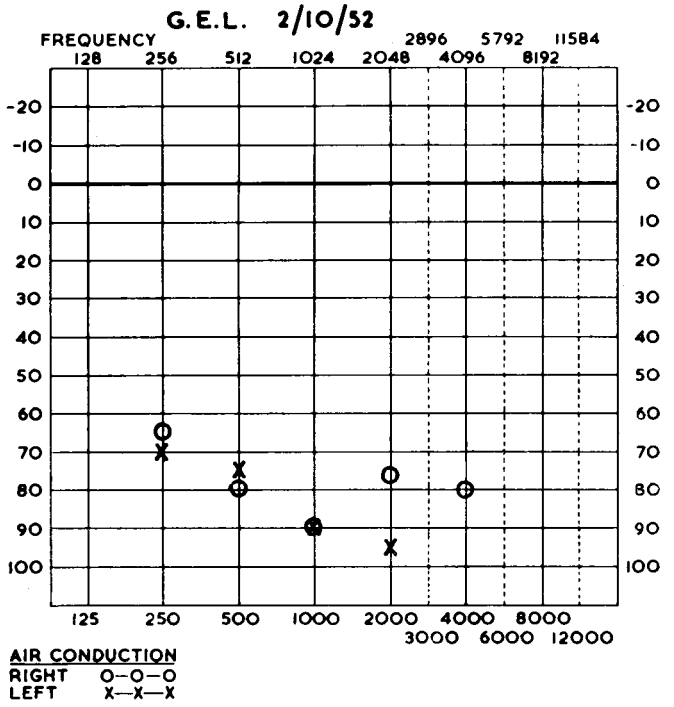


FIG. 16.
Case II. A lateral radiograph of the right mastoid temporal bone.

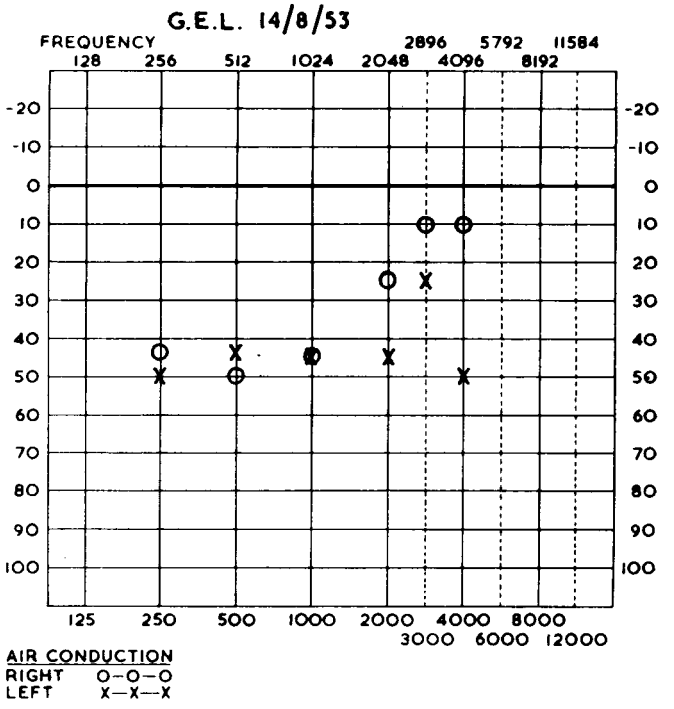


FIG. 17.
Case II. Submento-vertical view to show the lesions in both temporal bones.

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Audiogram 2.



Audiogram 3.

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normal, and a positive Mantoux reaction was obtained at a dilution of 1 in 1,000. The first audiogram was recorded. Towards the end of September, 1952, a dose of 1136r was given to the lateral aspect of each side of the head. Within one month, a second audiogram was obtained and a definite lesion could be demonstrated radiologically in the right ear (Figs. 16 and 17), although the boy did not complain of pain.

By the end of October, 1952, the hearing had improved. Radiologically within five months the mastoid lesions appeared less extensive and the degree of improvement in the hearing had been maintained (see audiogram 3). However, in May, 1953, he developed a pathological fracture of the right fibula.

In July, 1953, a swelling developed in the right side of neck and the boy had a husky voice. There was a hard swelling $2\frac{1}{2} \times 3$ cms. of limited mobility adherent to the right side of the larynx. Unfortunately the larynx was not examined.

During the next two weeks his voice improved but a slight enlargement of lymph nodes in all the superficial glandular areas was noticed. Diabetes insipidus developed in August, 1953. Radiotherapy directed against the pituitary was ineffective and an attempt has been made to control the lesion by Pitressin. The boy is still under observation and is now having no aural troubles but the diabetes insipidus is still a problem.

Case III. A.L., æt. 1-4/12, Male. 51/53.

This child's mother noticed a swelling behind the right ear in November, 1952. Over a period of 6 weeks there was no obvious increase in size, and there was no response to penicillin therapy. A postaural incision was made, but no pus was found and a biopsy was taken.

23.12.52. Dr. J. Tregellon reported from Darlington Memorial Hospital as follows: "The specimen consists of sheets of undifferentiated cells, somewhat resembling reticulum cells, which are actively invading and destroying the neighbouring fibrous and muscular tissue. Some of the cells are trinucleate or multinucleate and eosinophils are literally scattered throughout. This lesion is considered to be a reticulosis primarily arising in a post-auricular lymph node. The recent rapid increase in size and extensive invasion of the cranial bones strongly suggest that we should at least consider this a locally malignant condition."

The chest roentgenogram showed no abnormality but an extensive bone defect in the right squamous temporal and parietal bones immediately behind the petrous portion was demonstrated radiologically.

The child was admitted to the Babies' Hospital, Newcastle, on February 7th, 1953. At that time there was a firm swelling about 6×6 cm. behind the right ear. The centre of the lesion felt fluctuant and the overlying skin for about 2 cm. in diameter was red and smooth. There was also a fullness in front of the ear. One tender upper deep cervical lymph node could be palpated on the right and the spleen was felt $\frac{1}{2}$ inch below the costal margin. The right tympanic membrane was obscured by the distortion of the external auditory canal. The left tympanic membrane was considered to be normal. The blood cholesterol, the blood calcium, serum and phosphates, and plasma protein were all within normal limits.

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On February 9th a dosage of 600r was given to the right mastoid area.

By May, 1953, the child's general condition had improved and the swelling had largely subsided. The spleen was still felt below the costal margin, and although both the tonsillar lymph nodes were palpable they were no larger. However, a radiograph of the mastoid showed a destructive lesion on both sides.

Early in June, 1953, a swelling appeared round the right ear, mainly in front and above. The boy was obviously suffering pain and there was a seropurulent aural discharge from which the hæmolytic streptococcus was cultured. Systemic penicillin therapy was undertaken and a further course of radiotherapy (600r) was given to the right mastoid. Within two weeks the swelling was hardly noticeable. However on July 27th, 1953, the child returned with a swelling above and behind the right ear and also a history of pain and discharge from the left ear. The boy's temperature was 101°F. A foul smelling seropurulent discharge was seen in the right external meatus and granulation tissue was observed in the left ear from which there was a fœtid discharge. The left mastoid process was tender, the tonsillar glands enlarged, and the spleen was palpated ½ inch below the costal margin. Systematic penicillin therapy was recommenced and a dose of 600r given to the left mastoid.

Hæmolytic streptococcus and *Staphylococcus aureus* were cultured from the aural discharge.

A month later the right ear had dried up but there was no change in the left ear and the temperature varied from 102°F. in the evening to 97°F. in the morning. A biopsy of the granulations in the left external auditory canal was taken.

Dr. Mercer's report (53/5130) on the granulation tissue read: "There is surface necrosis with colonies of secondary bacterial invaders. A typical suppurative surface reaction is seen. In the deeper tissues there are clusters of eosinophils with typical histiocytes. This is one of the group: Eosinophilic Granuloma, Letterer-Siwe or Hand-Schüller-Christian Disease."

In mid-September, 1953, acid-fast bacilli were demonstrated in the aural discharge and the Mantoux was strongly positive. By October 15th, 1953, the child had gained 2 lb. and no further confirmatory evidence of tuberculosis was obtained. The left ear had now ceased to discharge and the drumhead appeared only opaque, but a diffuse swelling had developed again on the right side extending from the outer canthus of the eye to behind the pinna.

A dose of 940r was given to the right mastoid and parotid regions in 8 treatments.

By November, 1953, the swelling had completely resolved, the child looked much better and the ears were dry.

Since then radiological evidence of a pulmonary infiltration has been found.

Case IV. J.T., æt. 18/12, Male. 5205/50.

This boy was first seen in October, 1950, by the Department of Child Health with a history of coughing and loss of weight. At that time he was also noticed to be limping. A pin-point papular rash extended over the back and small purpuric spots were present over the abdomen and clavicular regions. At rectal examination a smooth mass could be felt in the left ischium. The spleen was ½ inch below the costal margin. Over the occipito-parietal region a soft cystic mass was felt.

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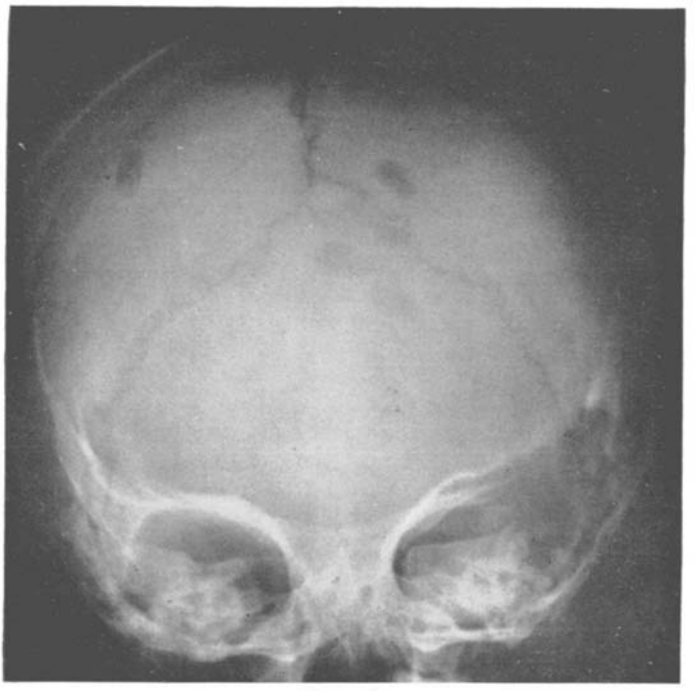


FIG. 18.
Case IV. Antero-posterior view of the skull to show several punched-out lesions and large lesion which displaced the left orbit.

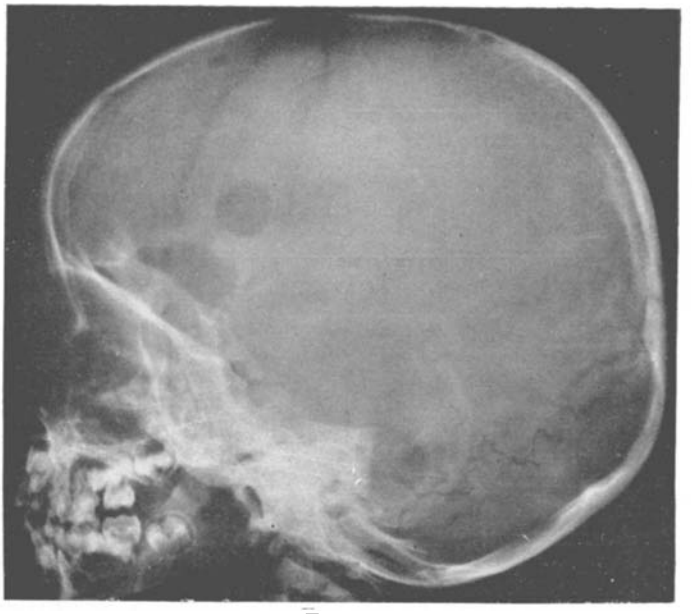


FIG. 19.
Case IV. Lateral view of the same skull as Fig. 18. Notice in particular the orbital les

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An expanding and destructive lesion in the left ischium and three clearly defined defects in the left parietal region of the skull were demonstrated radiologically. The Mantoux test was negative at a dilution of 1 in 1,000. The boy's hæmoglobin was 83 per cent. but the differential white cell count and serum cholesterol were normal.

The diagnosis of eosinophil granuloma was made by a biopsy, Dr. Mercer's report (5L/7145) states: "The granulation tissue shows sheets of histiocytes, foci of eosinophils, a few small multinucleated giant cells, and some histiocytes contained hæmosiderin and fat. This is a case of Eosinophilic Granuloma or Letterer-Siwe Disease."

In November, 1950, a peribronchial infiltration was seen in a radiograph.

After treatment by radiotherapy the ischial lesion improved but later the lung lesion also required treatment by radiotherapy.

All was progressing well till March, 1951, when the child presented with a proptosis of the right eye, a discharging right ear with several lesions of the parietal region. The lesion producing the exophthalmos can be seen in Figs. 18 and 19.

There was an irregular defect ½ inch diameter in the right mastoid process which is tender on pressure. The external auditory canal was filled with sticky brown debris and a good view of the tympanic membrane was not obtained.

With penicillin therapy the ear lesion cleared up leaving a tympanic membrane which lacked lustre.

Radiotherapy (500r) was also given to the whole skull.

The child continued to improve but was not seen for 3 months and was later known to have died at home. An autopsy was not obtained.

Case V. D.T., æt. 3-2/12, Female. 975/53.

9.6.53. This child presented with difficulty in walking and glands in neck, axilla and groin.

A biopsy of a cervical lymph node was seen by Dr. Mercer, who reported that it showed the kind of reticulum cell change which one encounters in cases of Letterer-Siwe, or Hand-Schüller-Christian disease. Radiologically lesions were demonstrated in the calvarium, mastoid, pelvis, right femur, dorso-lumbar vertebrae and ribs. A further biopsy of a rib confirmed the diagnosis.

No clinical evidence of a mastoid lesion appeared before the child's death occurred. An autopsy was not obtained.

Case VI. G.W.W., æt. 13, Male. 615/48.

This patient was seen by Mr. Watts in April, 1948, with a slight pain in a lump which had been present for 6 weeks over the vertex of the skull. The swelling had been incised but no pus found.

An incision was made over the tumour, and a clot was evacuated from a round defect in the skull. A biopsy was taken of the margins of the bony defect.

Dr. Mercer considered the histological appearances of the tumour as compatible with a diagnosis of Eosinophilic Granuloma.

A dose of 1,000r was given in 5 treatments during May, 1948. No further lesion has presented to date.

The patient joined the Army in 1952 and has remained well.

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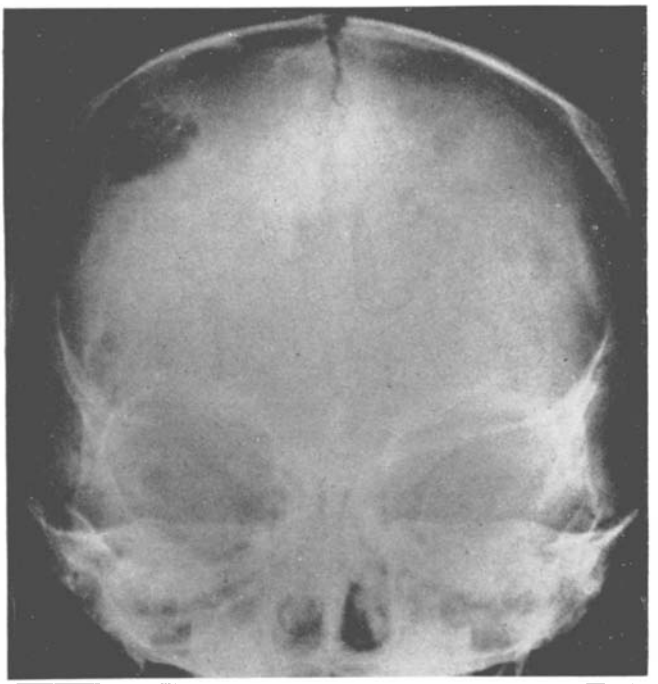
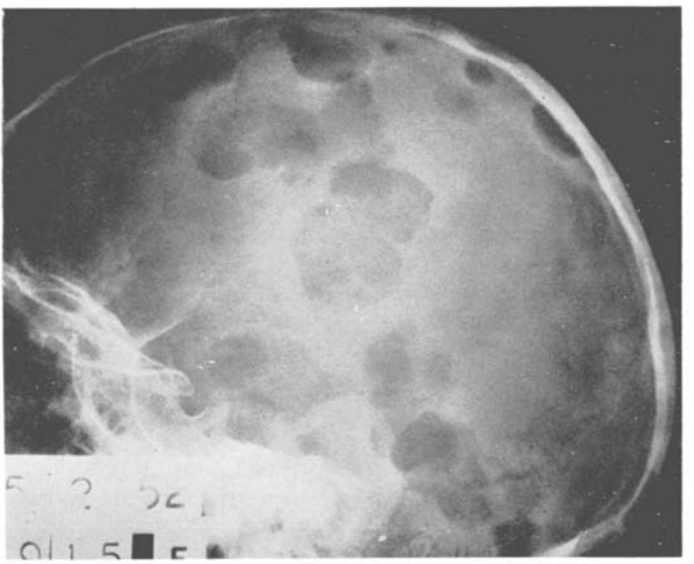


FIG. 20.
Case VII. Antero-posterior radiograph of the skull to show a punched-out lesion in the right parietal region.



Case VII. Lateral view of skull at a later date to show the number of lesions which developed.

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Case VII. K.W., æt. 1-7/12, Female. 2023/51.

This young girl was seen by the E.N.T. Department with a history of left recurrent otitis media in March, 1951. This settled with penicillin therapy and has given no trouble since. However, although a swelling of the forehead was noticed, it was not possible to obtain satisfactory radiographs. In May, 1951, the child attended the Child Health Department with a history of a parietal swelling which had varied in size and position for 6 months (Fig. 20).

Since then this girl has had numerous lesions involving the skull, long bones and mandible, vertebrae, the pelvis, ribs, etc.

Fig. 21 demonstrates the number of calvarial lesions which were present and shows how easily the squamous temporal bone may be involved.

Case VIII. N.B., æt. 4. Admitted 25/9/50.

This boy presented with a tender parietal swelling in May, 1950 (Fig. 22). He also complained of headache. His skull lesions varied in appearances over a period of 2 years. In April, 1952, the presence of diabetes insipidus was noticed and treatment with Pitressin begun. This treatment has been continued, but the control of the diabetes insipidus has been very difficult.

Case IX. R.G., æt 11, Male.

This patient was referred to Mr. F. McGuckin by Mr. K. H. Dalrymple with a history of recurrent earache from August 1953 until February 1954, when his mother noticed a small growth in the external auditory meatus. He began to be deaf also at this time. An exploratory mastoidectomy was carried out by Mr. Dalrymple in March 1954, and soon after operation he developed a right facial weakness, his deafness became increased and he developed diabetes insipidus. The mastoid cavity rapidly refilled with granulation tissue, and a biopsy showed this to be eosinophil granuloma.

From these case histories alone it can be seen that the ear lesion may be the presenting symptom or that the ear lesion may develop during the course of the disease or that it may be an accidental finding during a routine examination.

Dingley (1952) suggested that the lesion begins in the squamous temporal region and spreads to the mastoid. However, lesions are here presented which demonstrate that the lesion may originate in either the squamous or petrous temporal bones.

Otological Symptoms and Signs

The disease is most common in childhood but it does occur in adults (Schuknecht and Perlman, 1948). If the patient is very young he may not complain of pain, but usually either a lump appears in the neighbourhood of the pinna or there may be a serous or blood-stained otorrhœa or deafness alone.

On examination, a soft fluctuant swelling with ill-defined edges may be felt. Granulations may be seen in the external auditory meatus, or there

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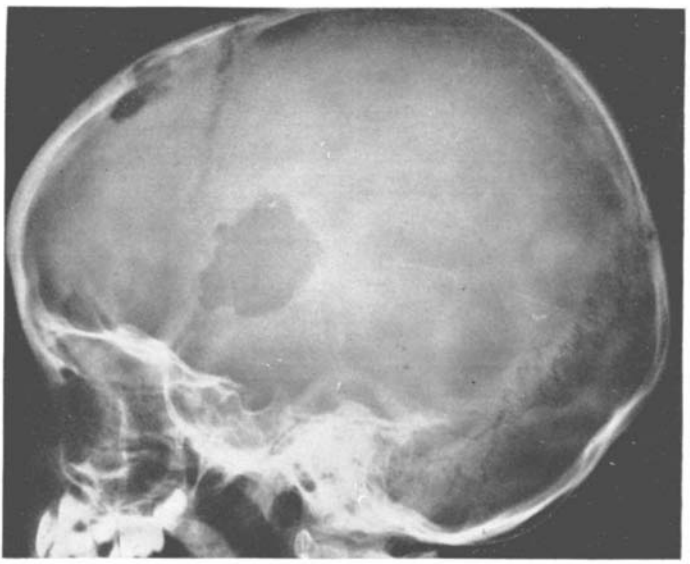


FIG. 22.
Case VIII. Lateral radiograph of the skull to show a large punched-out lesion.

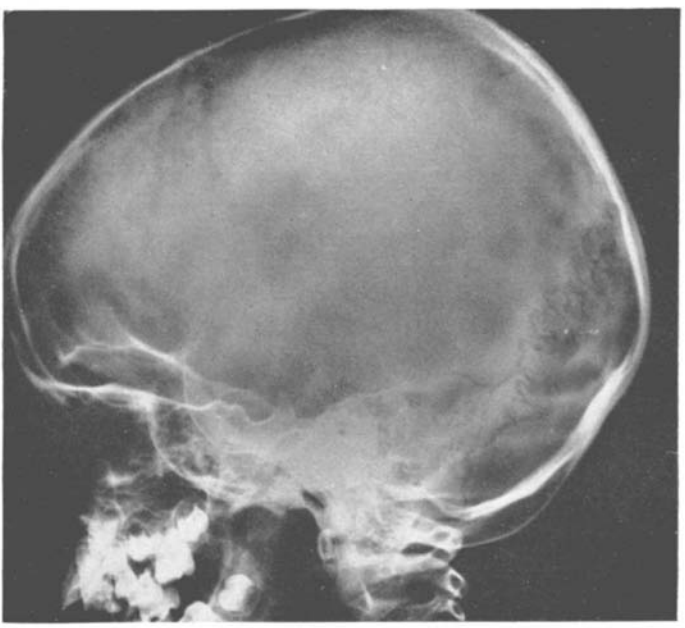


FIG. 23.
Case VIII. The same lesion as in Fig. 22, after radiotherapy.

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may be a stenosis of the external auditory canal, or as in Ponseti's (1948) case a granulomatous swelling may be seen coming through the skin of the roof of the external auditory meatus. In two of these cases the postaural swelling was incised for a suspected postaural abscess complicating mastoiditis. Essentially this is a granular lesion from the outset, and these granulations recur rapidly after removal.

However, the child is often surprisingly well in spite of the frightening local signs. The lesion may have extended far enough to produce deafness (Cases I and II) and its consequent speech defect, or to injure the facial nerve (Case I).

Blood Picture

An eosinophilia of 6 per cent. to 10 per cent. may or may not be present. The blood cholesterol, the serum phosphates and calcium, and the serum protein are all usually within normal limits. A secondary hypochromic anæmia may be present but this is of no diagnostic value.

Radiological Picture

Radiographs of the mastoid (Figs. 4, 5, 6, 15, 16 and 17) may show gross disorganization of the whole petrous temporal and parts of the petrous temporal may appear separated from other portions. A punched-out lesion in the squamous temporal would be almost diagnostic. The degree of disorganization of the temporal bone makes one suspect this type of lesion but a tuberculous mastoiditis must be excluded.

Biopsy

The only certain method of reaching a diagnosis is by means of a biopsy. This biopsy should be adequate, and a small piece of granulation tissue is probably inadequate, for the specimen may not show all the characteristic features of the disease. The only difficult specimen submitted to the pathologist for diagnosis was a biopsy of granulation tissue from the external auditory canal.

Differential Diagnosis of the Ear Lesion

The question of tuberculous mastoiditis was raised on two occasions. In case (I) the diagnosis was provisional and made upon the clinical appearance alone by two people partly confused by a suspicious chest lesion, and in case (III) because an alcohol acid-fast bacillus was found in a smear.

When the lung tissue is also involved by an eosinophilic infiltration, it radiologically resembles a tuberculous lesion. However, radiographs of the skeleton and the involvement of other organs help in reaching a clinical diagnosis. Multiple metastases in bone, can usually be excluded by the age of the patient and appearances of the lesion. Radiological appearances

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help to distinguish the lesion from an infective type. However, the final diagnosis is entirely dependent upon histopathology.

The Skeletal Lesions

Skeletal lesions commonly produce the presenting symptoms and signs, but often a radiological study of the skeleton will often reveal other silent lesions. A study of these patients confirms the findings of Farber and Green (1942) in that the flat bones (i.e., ribs, pelvis, calvarium, etc.) are those most commonly involved. The appearances of the lesion in the radiograph may not be characteristic, thus we find a single or multiple punched-out areas in the skull (Figs. 18, 21), expansion of the ribs (Fig. 7), a cyst in a long bone (Fig. 9), a honeycomb appearance (Fig. 6), or a collapsed vertebrae (Fig. 8). There is a tendency to spontaneous fracture of the long bones, particularly those which are weight bearing. Bone lesions may show spontaneous healing (Farber and Green 1942, Lichtenstein and Jaffe 1944), or heal after radiotherapy (Figs. 22, 23).

Other Methods of Presentation

Any one of the numerous lesions may be the presenting symptom. Thus, for example, we find patients arriving with a limp, inability to raise an arm, a spontaneous fracture, a swelling of the skull or long bones or even a papular rash (which is due to an infiltration of the skin by the pathological cells), etc.

The Course of the Illness

Letterer-Siwe disease is usually a fairly rapid illness terminating in death, having a febrile course with splenomegaly, hepatomegaly, lymphadenopathy, a secondary hypochromic anæmia, skeletal lesions, and often a purpuric rash which is quite marked before the approach of death. Secondary bacterial infections often occur during this illness.

The eosinophil granuloma if not a solitary lesion is more prolonged as demonstrated by these case histories but the distribution of the lesions is similar, and the histopathology is the same. However, deterioration in the patient usually coincides with diffuse involvement of the soft tissues, e.g., lymphadenopathy, hepatomegaly and splenomegaly.

Hand-Schüller-Christian syndrome is usually more chronic still. Often a Letterer-Siwe disease or eosinophilic granuloma may show during the course of the illness, exophthalmos, diabetes insipidus and calvarial lesions. It must be stressed that the Hand-Schüller-Christian syndrome is but one variety in which there are widespread calvarial lesions displacing the orbit or involving the pituitary.

No one of these diseases is a clear-cut clinical entity and varieties are seen which blend with one another.

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Pathology

Macroscopically eosinophil granuloma is most commonly a granular lesion, which feels velvety, and sometimes yellow streaking can be seen. It can be present as a chocolate cyst with granulating walls.

Histologically there are sheets of histiocytes or reticulum cells with a finely or coarsely granular cytoplasm and the area is infiltrated often by large numbers of eosinophils which may collect in follicles. Lymphocytes and plasma cells are quite commonly seen whilst foreign body giant cells may be present. Large areas may undergo necrosis, and hæmorrhages are sometimes seen. If the lesion has reached the surface of the body secondary infection is present. When foam cells are present, the lipoid concerned is cholesterol.

Flori and Parenti (1937), Glanzmann (1940), and Wallgren (1940), regarded Letterer-Siwe disease and the Hand-Schüller-Christian syndrome as different manifestations of one pathological entity.

Farber (1941), Farber and Green (1942), Lichtenstein and Jaffe (1944), and Ponseti (1948) consider that foam cells only occur in the late stage of healing when fibrosis is also present, and believe that this is the stage represented by the Hand-Schüller-Christian syndrome. In other words the scarring, bone healing, and foam cells present in the Hand-Schüller-Christian syndrome (lipogranulomatosis) are regarded as a late manifestation of eosinophilic granuloma. However, Symmers (1952) among others still has some doubt about this.

Treatment

The general view is that each lesion should be treated by radiotherapy in a dosage of 400-1,000r. However, many lesions heal spontaneously and it is better to reserve radiotherapy for those foci causing symptoms, particularly when painful. In Newcastle, the multiple lesions are usually treated to make the patient more comfortable, since the prognosis is poor.

Prognosis

The outlook in a solitary granuloma may be excellent (Case VI) but when speaking to the patient's relations, a very guarded prognosis must be given for this single lesion may only be a local manifestation of a more generally disseminated disorder. This fact is demonstrated by this series of cases. In the acute febrile case with diffuse involvement of the soft organs the prognosis is poor and if a similar diffuse involvement should appear during a predominantly skeletal disease, one can be fairly sure of rapid deterioration. When the lesion is more chronic and typical of the Hand-Schüller-Christian disease, the prognosis may be better (Frazer, 1935).

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An individual lesion may not show a satisfactory response to radiotherapy and this applies particularly in the presence of diabetes insipidus which may be due to involvement of the nervous tissue in the stalk of the pituitary or the region of the third ventricle.

Summary

Eight cases are presented, these being a sample of a larger series. They are recorded primarily to illustrate the otological aspects of Eosinophil Granuloma, Letterer-Siwe disease, and the Hand-Schüller-Christian syndrome.

The local symptoms, signs, the general picture and course of the illness are described.

The clinical evidence suggests that the three diseases are varieties of but one disorder.

Treatment by radiotherapy is reserved in this Infirmary for the relief of pain and making the patients more comfortable.

Prognosis should always be guarded for the behaviour of the lesion in any one individual patient cannot be forseen.

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