Recent investigations have added to our means of establishing the true diagnosis of pernicious anæmia. Until recently the cardinal laboratory features in pernicious anæmia were the characteristic blood picture, megaloblastic marrow and histamine-fast achlorhydria.

The serum vitamin B_{12} level in our patient was abnormally low; this estimation may bring to light examples of neurological disease due to vitamin B_{12} deficiency: this is amplified by the clinical picture resembling that of the patients reported by Jewesbury (1954).

Absolute achlorhydria was confirmed by the augmented histamine test meal, and the most important feature, absence of intrinsic factor production, was confirmed by the Schilling test carried out before and after giving the patient intrinsic factor.

The patient responded fully to vitamin B_{12} therapy.

Summary

Pernicious anæmia is recorded in a patient aged 24 years, presenting chiefly with neurological manifestations.

The rarity of this disease in young patients is pointed out and reference is made to the literature. The importance of precise diagnosis aided by newer techniques is stressed owing to the necessary life-long substitution therapy required.

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HYPERTROPHIC PULMONARY OSTEOARTHROPATHY ASSOCIATED WITH PULMONARY METASTASES REMOVED SURGICALLY

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CLUBBING of the fingers and toes of the most advanced type, associated with thickening of the bones of the carpus and tarsus, painful swollen joints, and with periosteal thickening of the long bones of the limbs, is a well-recognized complication of many chest diseases. This degree of clubbing or, as it is more usually called, hypertrophic pulmonary osteoarthropathy (H.P.O.A.), is found most commonly in cases of bronchial carcinoma, where the incidence in a large series was up to 2% (Semple and McCluskie, 1955). H.P.O.A. has also been observed in association with pulmonary metastases of many kinds arising from primary neoplasms outside the chest. Metastases in the lungs arising from primary osteogenic sarcomata are more often accompanied by the development of H.P.O.A. than is spread from other non-pulmonary primaries (Mendlowitz, 1942; Gibbs, Schiller and Stovin, 1960).

The case to be described is that of a young girl

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of 17 years who presented with incapacitating symptoms of H.P.O.A. She had had an osteogenic sarcoma of leg removed with a good result two years before. The generalized arthropathy developed over six months and caused complete immobility with severe pain. Localized pulmonary metastases were found and resected with immediate and complete relief of her symptoms, which did not recur in spite of the development of further pulmonary and other metastases four months later.

Various forms of treatment have been used for the relief of H.P.O.A. including steroids, radiotherapy, nitrogen mustard and gold, but surgery to the lung lesion affords the most certain relief (Semple and McCluskie, 1955; Flavell, 1956) and was chosen in this case because of the localization of the metastases and the youth of the patient.

Case History

Our patient was first seen in the Orthopædic Department on August 28, 1957, at the age of 15 years. At that time she complained of a 'burning' type of pain in the region of the left ankle of three months' duration. This pain disturbed her sleep and caused her to limp. She had also noticed some dyspnœa on effort of recent onset and she had lost a few pounds in weight.

Examination revealed a slight swelling of the left lower leg, not involving the ankle. This swelling was warm and tender and appeared to be bony in origin. Movements of the ankle and knee were full and painless. No other abnormalities were detected on general examination. In particular it was noticed that there was no finger or toe clubbing.

An X-ray (Fig. 1) of the affected parts showed an area of bone-destruction of the lower end of the tibia associated with a layered type of periosteal reaction. The lowest part of the lesion showed elevation and breaking-through of the periosteum with bony spicule formation radiating into the soft tissues on the posteromedial aspect. The appearances were consistent with a malignant bone tumour, probably an osteosarcoma. A biopsy of this tumour was done on August 29, 1957. This comprised a mass of yellowish grey material which, on microscopy, was shown to consist of an anaplastic neoplasm. Some parts were almost completely undifferentiated but others showed some indication of chondroid and osteoid differentiation. It was considered that these features indicated a highly malignant variety of osteogenic sarcoma. After decalcification of the specimen both the anaplastic and differentiated ingredients were well demonstrated.

On September 5, 1957, a mid-thigh amputation of the left leg was performed. Over the lower end of the tibia was a projecting soft mass 2 x 1.5 x 0.8 cm., lifting the periosteum and extending to 3 cm. above the tip of the medial malleolus. The specimen removed at operation showed a spindle-shaped thickening of the lower third of the shaft of the tibia with appearances which were considered to be those of an osteogenic sarcoma.

Her immediate post-operative progress was uneventful. Chest X-rays done in September and December 1957 were both normal. However, in December 1959, she developed pain and swelling affecting the right ankle, knee, both elbow and wrist joints and several joints of the fingers. At about that time she noticed the onset of increased sweating affecting particularly the palms, axillae and sole of the right foot. X-rays of the left elbow, right knee, tibia and fibula and ankle were all normal. The symptoms and arthropathy increased during the succeeding months and she was readmitted to the Royal Hospital, Sheffield, for further investigation on August 1, 1960. There was some impairment of appetite, and weight loss of about one stone had occurred during the previous two years. For the previous six months she had had mild dyspnœa on exertion and a slight non-productive cough. There had been no hæmoptysis.

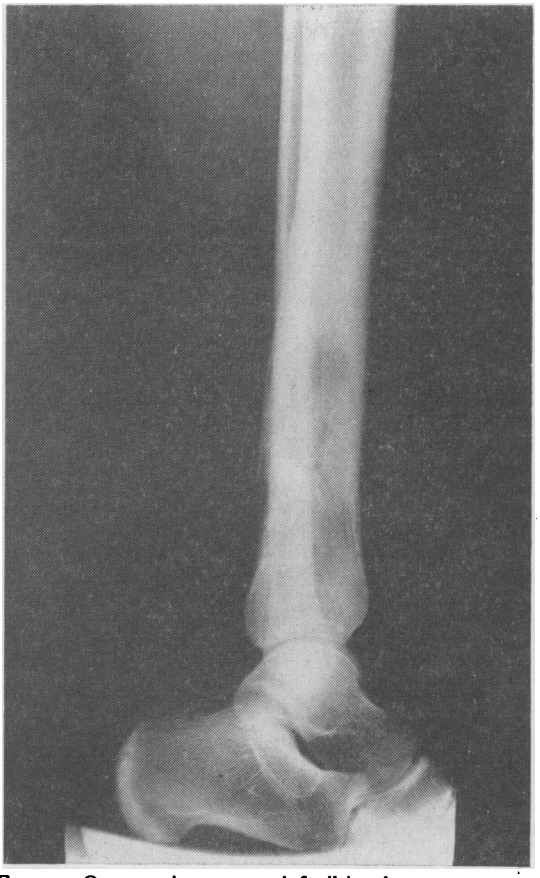

FIG. 1.—Osteogenic sarcoma, left tibia. August 27, 1957.

On examination she was a pale young woman weighing 109 lb., with obvious clubbing of the fingers and toes and with tender periarticular thickening of several interphalangeal joints, both wrists and the right ankle. There was a considerable effusion into the right knee joint. The elbows were swollen and the left one contained some fluid. The palms, axillæ and right sole were moist. Auscultation of the chest demonstrated crepitations at the left base.

The left mid-thigh stump was satisfactory. The remainder of the general examination was normal. While she was in hospital there was a low-grade remittent pyrexia of up to 100°F. A chest X-ray (Fig. 2) on August 4, 1960, showed what appeared to be two rounded metastases in the left lower lobe. X-rays of several bones showed osteoporosis around the right wrist and both elbows, and affecting the medial aspect of the head of the right tibia. There was periosteal thickening of the lower end of the right radius, also above the right medial femoral condyle and just above the medial malleolus of the right ankle. Radiographs of the

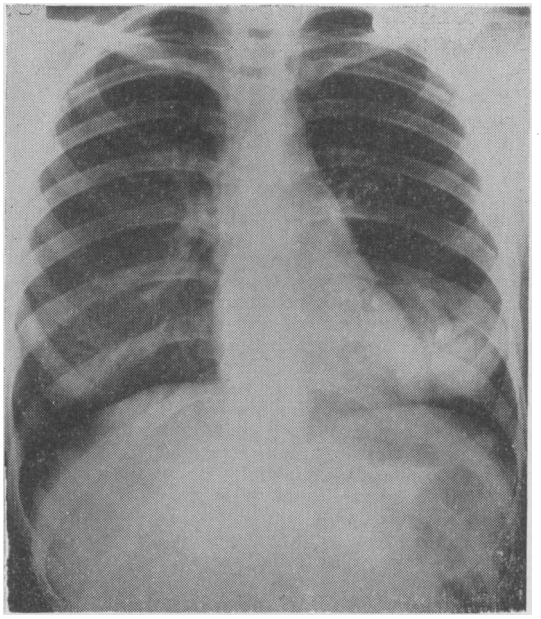

FIG. 2.—Metastases, left lower lobe. August 4, 1960.

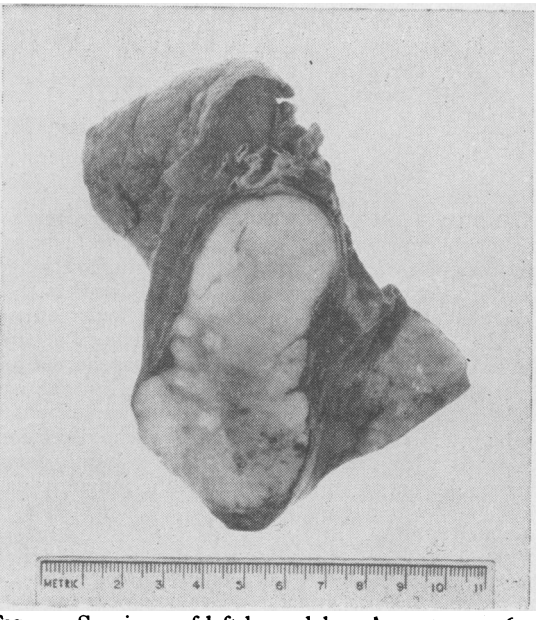

FIG. 3.—Specimen of left lower lobe. August 22, 1960.

fingers showed 'tufting' of the terminal phalanges of two of the fingers. All these appearances were consistent with the diagnosis of hypertrophic osteoarthropathy.

Investigations. Hb 80% (11.8 g./100 ml.); r.b.c. 3.8 m./c. mm.; w.b.c. 9,000/c. mm.; differential white cell count, normal; E.S.R. 78 mm./hr. (Westergren).

In view of the localized nature of the metastases and the severity of the symptoms due to the arthropathy she was transferred to the thoracic surgical unit at Sheffield Royal Infirmary for a thoracotomy. This was performed on August 22, 1960, and a large hard mass was found in the posterior and lateral basal segments of the left lower lobe coming out to the surface of the lung but not invading the chest wall. A left lower lobectomy was performed and several glands dissected out from the hilum of the lung (Fig. 3).

Histological examination showed appearances consistent with a metastatic sarcoma, but there was no evidence of tumour in the lymph nodes.

Post-operative recovery was uneventful; immediately after the operation the patient reported loss of pain in the previously affected joints and within seven days all swelling and tenderness had disappeared. After four weeks the patient had gained weight and was free of pain, and there was possibly a slight reduction in the clubbing.

Four months after the lobectomy metastases began to appear in the right supraclavicular region and in a further three months they reappeared in the chest and were treated with radiotherapy. During this period clubbing persisted, but there was no return of pain or swelling in her joints.

Summary

Hypertrophic pulmonary osteoarthropathy developed in a patient of 17 years associated with pulmonary metastases from an osteogenic sarcoma of leg removed two years before.

The symptoms of arthropathy were very severe and, as the metastases were localized, they were removed surgically. A complete remission of the arthropathy occurred, and there was no reappearance of joint symptoms when further metastases developed.

We are grateful to Dr. J. L. Jago who referred the patient for treatment, and to Dr. T. E. Gumpert under whose care she was admitted to the Royal Hospital, Sheffield. We are indebted to Mr. F. W. Taylor, Royal Hospital, for the records of orthopædic treatment; to Mr. A. W. Fawcett, Royal Infirmary, Sheffield, for the thoracic surgical details; also to the Departments of Pathology in both hospitals and the Photographic Department at the Royal Hospital.

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