INTRATHORACIC HETEROTOPIC BONE MARROW SIMULATING A NEOPLASM—REPORT OF A CASE

By Y. S. Lee and N. E. Wong

SYNOPSIS

A case of massive intrathoracic heterotopic bone marrow is reported. The patient, a Chinese woman aged 39 years, was found to have a symptomless mass in the thorax during a routine radiological examination. She was operated on with a mistaken diagnosis of intrathoracic neoplasm. The true nature of the mass was established by histological examination of the resected specimen. After the operation patient developed jaundice, and was found to be anaemic. The spleen was enlarged and there was a history of previous cholecystectomy. Haematological investigations showed that patient had hereditary spherocytosis. The literature was reviewed and the salient points of this rare condition were outlined.

INTRODUCTION

During the prenatal period several locations such as the yolk-sac, blood vessels, liver, spleen, thymus, lymph-nodes and bone marrow are successively the sites of formation of blood cells. One by one these organs lose their haemopoietic function, until eventually the red marrow remains the sole haemopoietic organ during postnatal life. These sites however still retain their haemopoietic potentialities and are capable of activity if sufficiently stimulated under conditions in which the red marrow is unable to cope with the demand either as a result of a need to increase production due to excessive haemolysis or as a result of insufficient marrow tissue due to tumour destruction, myelofibrosis or osteopetrosis. The spleen, liver and lymph-nodes are the usual sites involved in extramedullary haemopoiesis; at times the kidneys, adrenals and broad ligaments may participate (Braunan, 1927). These foci of extramedullary haemopoiesis are as a rule microscopic in character. Occasionally large tumour-like nodules of heterotopic bone marrow are encountered; these have been reported in the falx cerebri and kidney (Braunan, 1927), suprarenal (Collin, 1932), retroperitoneum (Blaisdell, 1933; Lyall, 1935; Dodge and Evans, 1956) and the thorax.

Reported below is a case of intrathoracic heterotopic bone marrow simulating a primary neoplasm in the thorax. The nature of the mass and the underlying haemolytic disorder were not realised until after surgery was performed.

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CASE REPORT

The patient, a Chinese woman aged 39 years, was found to have a mass in the thorax at a routine chest X-ray taken on 16.10.69 during an anti-tuberculosis campaign. The radiograph (Fig. 1) showed a well circumscribed rounded opacity bulging out from the right border of the heart. A right lateral radiograph (Fig. 2) showed that the mass was in the posterior mediastinum in line with the vertebral column. She was apparently well and without any complaints. There was a past history of cholecystectomy in 1959. A primary thoracic neoplasm was suspected and the patient was submitted for operation on 26.11.69. A right thoracotomy incision was made and the 4th rib resected. Exploration revealed a dark spongy mass 2·5 cm. in diameter in the posterior mediastinum which at the time of operation was suspected to be a haemangioma. The mass was excised and the chest closed and drained.

Pathology Report

Intrathoracic Mass: Specimen consisted of three irregular pieces of dark haemorrhagic tissue having the appearance of an organised blood clot. The largest piece measured $4 \times 2 \times 1$ cm. Microscopically the tissues were composed essentially of bone marrow elements with a predominance of the erythrocytic series. A varying amount of adipose tissue was seen. In some areas a fibrous capsule was present. Stainable iron was present in large amount in the bone marrow tissue and in the fibrous capsule. The histological features were that of a heterotopic bone marrow (Figs. 3 and 4).

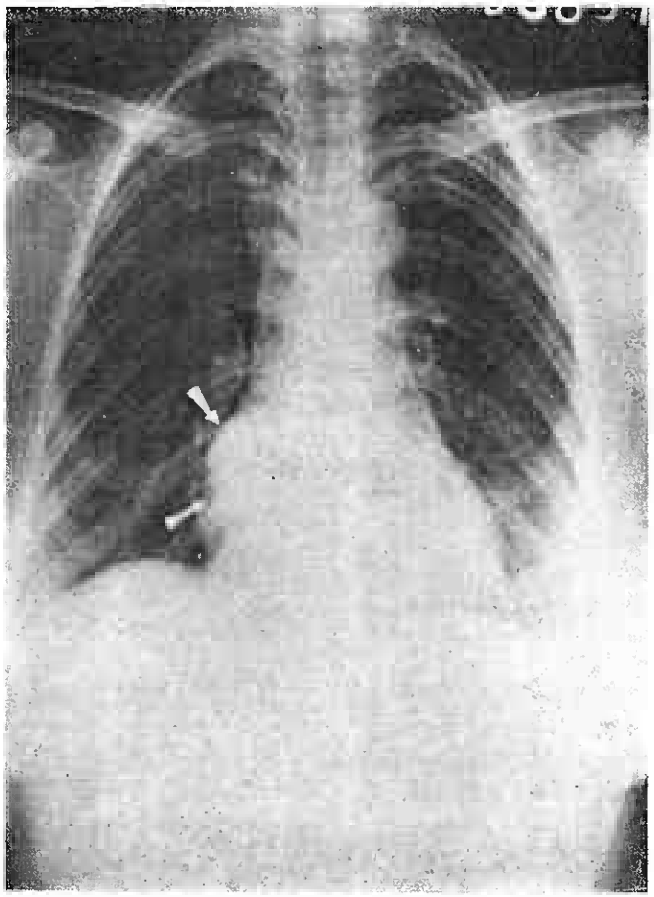

Fig. 1. Radiograph of the chest (A-P view) showing a rounded opacity (arrowed) bulging out from the right cardiac border.

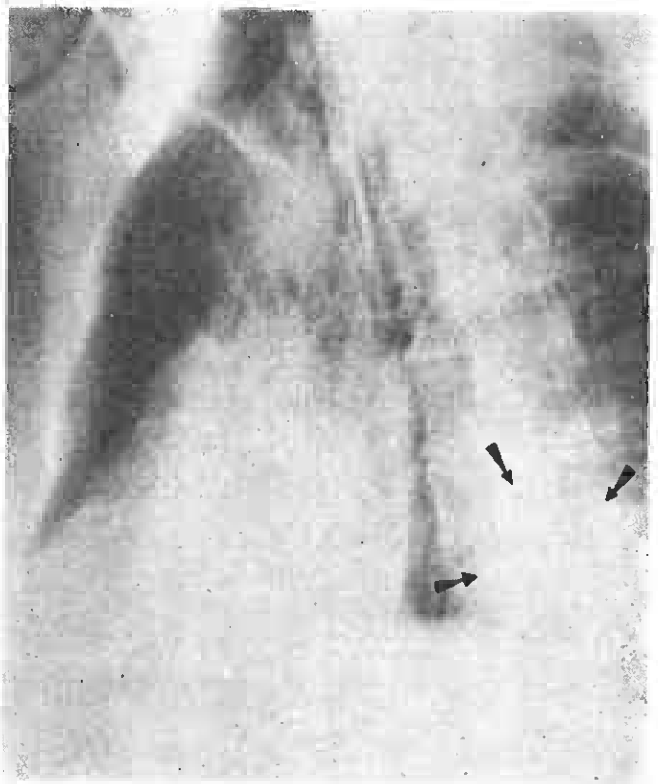

Fig. 2. Radiograph of the chest (right lateral view) showing the opacity (arrowed) in the posterior mediastinum.

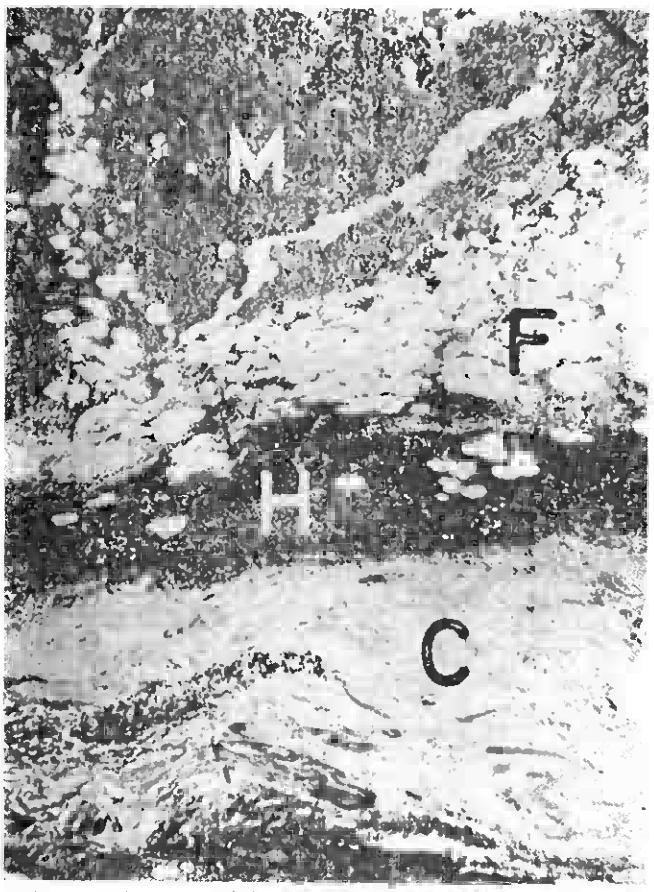

Fig. 3. Histology of the intrathoracic mass showing marrow tissue (M), adipose tissue (F), haemorrhage (H), and a fibrous capsule (C). H + E × 45.

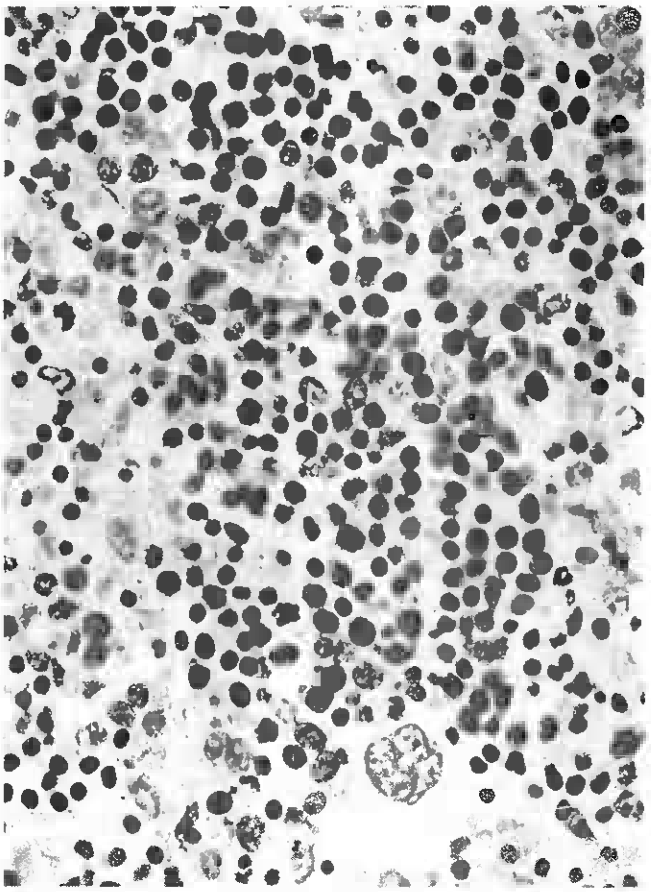

Fig. 4. Higher magnification of the marrow tissue showing the various marrow elements with a predominance of the erythrocytic series. H + E × 500.

Post-operatively the patient was noticed to be jaundiced. Laboratory findings on the second day were as follows:— Serum bilirubin 3·5 mgm.%; Hb. 9·0 gm.%; TWC 15,000/c.mm.; neutrophils 74%, lymphocytes 19%, monocytes 6% and eosinophils 1%; Platelets 100,000/c.mm. The peripheral blood smear showed a mixed picture of well haemoglobinised and hypochromic cells with slight anisocytosis and poikilocytosis. There were a fair number of darkly stained microcytes. No white cell precursors were seen.

Two days later, the serum bilirubin rose to 6·1 mgm.%. Other laboratory findings were:— Hb. 7·6 gm.%; TR 3·0 million/c.mm.; reticulocyte count 15%; MCV 80 cu.u.; MCHC 32%; RCV 24%; MCH 25 ugm.; Peripheral blood smear showed normochromic red blood cells, and many densely stained microspherocytes. TWC 16,000/c.mm. with neutrophils 80%, metamyelocytes 2%, myelocytes 2%, lymphocytes 10% and monocytes 3%; there was a slight shift to the left. Platelets were normal. Direct Coomb's test was negative.

A diagnosis of hereditary spherocytosis was made. Patient recovered from the operation and was discharged on 8.12.69.

One year later patient was admitted for an elective splenectomy. On this occasion, she complained of slight breathlessness and palpitation on walking fast. Physical examination revealed slight anaemia. No jaundice was detected. The spleen was firmly enlarged and was felt 4 cms. below the left costal margin. Haematological investigations then showed Hb. 10·8 gm.%; TWC 11,500/c.mm. with normal differential count. Reticulocyte count was less than 1%. Platelets 215,000/c.mm. Splenectomy was performed on 27.11.70. Patient recovered well from the operation and was discharged on 5.12.70.

Pathology Report

Splenectomy Specimen: The spleen was congested and grossly enlarged measuring 15 × 9 × 5 cm. Microscopically numerous erythrocytes were seen in the cords of Billroth and the sinusoids were relatively empty. Iron pigments were present in large amount in the pulp and trabeculae. The histological features were consistent with hereditary spherocytosis.

REVIEW OF LITERATURE

Twenty-one cases of massive heterotopic bone marrow have been reported in the literature (Guizetti, 1912; Saleeby, 1925; Rich, 1927; Plonskier, 1930; Dawson, 1931; Hartfall and Stewart, 1933; Hunter, 1933; Covey, 1935; Gleave, 1936; Ask-Upmark, 1945; Paraf, Deroix and Caroli, 1957; Foster, 1958; Knoblich, 1960; Coventry and Labree, 1960; Hanford, Schneider and MacCarthy, 1960; Papavasiliou and Sfikakis, 1964). The following is a brief review of the salient points.

Almost all the cases occurred in adults over 20 years of age; the only patient below this age was an eighteen day old infant. The oldest patient was a woman aged 81 years. Where the sex was recorded, eleven were male and seven female.

The heterotopic bone marrow masses did not give rise to symptoms. Their presence was discovered either at necropsy or by radiography during life. The patients presented themselves in three different ways:—

(a) with signs and symptoms of a haemolytic anaemia,

(b) with other illnesses; the features of haemolytic anaemia were either absent, minimal or present but overlooked, or

(c) without any complaints;—the intrathoracic opacity having being detected by routine X-ray examination of the chest.

Some form of anaemia, notably haemolytic anaemia, was present in the vast majority of cases. There were 5 cases of acholuric jaundice (Rich, 1927; Dawson, 1931; Hartfall and Stewart, 1933; Gleave, 1936 and Ask-Upmark, 1945), 4 of spherocytosis (Coventry and Labree, 1960; Hanford *et al*, 1960, Present case), 3 of thalassaemia major (Papavasiliou and Sfikakis, 1964), 1 of thalassaemia minor (Knoblich, 1960), 1 of erythroblastosis (Covey, 1935), 1 of osteitis fibrosa cystica with anaemia (Saleeby, 1925) and 3 of anaemia unspecified (Plonskier, 1930; Hunter, 1933). There were only two cases (Saleeby, 1925; Foster, 1958) where haematological disorders were reported to be absent. Saleeby's case however was questioned, and rightly so, by Ask-Upmark (1945) on the grounds that as the bone marrow was not examined and as the patient had splenomegaly and gall-stones, the possibility of an acholuric jaundice could not be excluded.

Largely due to the frequent association with haemolytic anaemia, cholelithiasis and other gall-bladder diseases were common especially among the older patients. There were 9 cases of gall bladder diseases of which 6 had gall-stones mainly of the pigment variety.

The location of the heterotopic bone marrow deposits in the thorax is characteristic. Invariably they were situated paravertebrally in the posterior mediastinum; they were occasionally unilateral but more often bilateral. The majority were situated at the lower thorax above the diaphragm. The size varied from numerous small nodules to large masses over 10 cm. in diameter. Masses as large as the size of two fists have been described (Knoblich,

1960). They were often described as soft, reddish or purplish, incompletely encapsulated masses and likened to organised blood clots, spleen or bone marrow. Yellowish fatty tissue were occasionally made out grossly. Histology invariably revealed bone marrow elements with varying degree of fibrous stroma, fatty tissue and iron pigments.

Plain radiographs of the chest often showed single or multiple well-outlined round or oval shadows located behind and often bulging out of the cardiac borders. The superimposition of the masses often gave a lobulated appearance but a segmental arrangement was sometimes present. Tomographic studies would show that the masses were located posteriorly in the costovertebral angle adjacent to the vertebral bodies and the proximal parts of the ribs. The underlying bones were not eroded (Papavasiliou and Sfikakis, 1964).

The bone marrow masses grew very slowly in size in the presence of continued stimulus. Knoblich (1960) described a case where the circumscribed lobulated densities in the radiograph of the chest increased markedly in size over a period of 14 years. Similarly Coventry and LaBree (1960) described a right-sided mass faintly visible behind the heart shadow which over a period of 8 years had grown well beyond the right cardiac border to form a mass about 8 cms. in diameter, accompanied by smaller rounded nodules in the left side of the chest. To date no spontaneous regression in the size of the "tumour" has been observed.

Since the vast majority of cases were associated with an underlying haemolytic anaemia, there has been general agreement that the demand for excessive haemopoiesis is the aetiological factor responsible for the extramedullary haemopoietic deposits in the thorax. It appeared that the presence of a chronic haemolytic anaemia had provided the necessary conditions facilitating the deposition in the paravertebral spaces, via the intercostal veins, of bone marrow tissue which could then grow in response to the continued demand for haemopoiesis (Cone, 1925; Ask-Upmark, 1945). In the rare instance where no stimulus for excessive haemopoiesis was present, the possibility of a neoplastic growth has been proposed, and the term myelolipoma has been used (Foster, 1958).

DISCUSSION

The occurrence of large masses of heterotopic bone marrow in the thorax is rare. With the more frequent use of X-rays, it is likely that more cases will be detected during life. The significance of these masses lies in the fact that by virtue of their size and location, their rarity and consequent a lack of awareness of the condition, they have often been mistaken for primary neoplasms in the thorax, such as carcinoma of lung, lymphoma and neurogenic tumours. It is of practical importance to differentiate these conditions, as the correct diagnosis of heterotopic bone marrow will save patients from unnecessary operations. Furthermore these masses are often an indicator of an underlying chronic haemolytic process which may be latent and easily overlooked.

It is concluded therefore that any case of symptomless mass occurring in the posterior mediastinum paravertebrally, the possibility of it being heterotopic bone marrow must be considered. The presence of an associated haemolytic blood disorder, a family history of haemolytic disease, splenomegaly and cholelithiasis or gall-bladder disease are supportive evidence in favour of the diagnosis. Conversely, the diagnosis of a heterotopic bone marrow deposit in the thorax is an indication for investigating the haemopoietic system to exclude a haemolytic disorder.

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