Summary

The effects of intravenous injection of 25–50 mg. of promethazine hydrochloride have been studied in six cases undergoing cardiac catheterization. No significant changes occurred in the systemic blood pressure. One case showed a slight rise in pulmonary artery pressure. Pulmonary blood-flow showed little change in four cases, an increase in one, and a slight decrease in one. The heart rate increased in all cases.

The small circulatory changes associated with a satisfactory hypnotic effect suggest that promethazine is a suitable drug for the premedication of cardiac cases.

We are indebted to the technical staff of the Institute of Cardiology for assistance in making these observations.

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CARCINOMA OF THE BRONCHUS WITH BENCE JONES PROTEINURIA

BY

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Since the first description by Henry Bence Jones (1848) of the substance which now bears his name, interest has continued in the nature of Bence Jones protein. Its association with conditions other than multiple myelomatosis has only rarely been reported. Geschickter and Copeland (1928), from their own experience and a review of the literature, collected 26 cases of Bence Jones proteinuria in diseases other than multiple myelomatosis. Nine of these cases had skeletal metastatic tumours. Copeland (1931) reported three cases of carcinoma of the breast with skeletal metastases in which Bence Jones proteinuria was demonstrated. There have been few reports in recent literature, and Snapper (1949), from his own experience, believed Bence Jones proteinuria to be almost pathognomonic of multiple myelomatosis.

The two cases reported here are cases of carcinoma of the bronchus, confirmed at necropsy, in which Bence Jones proteinuria was demonstrated. An additional interesting feature was the sternal marrow of the first of these cases, which showed a "myeloma-like" picture.

Case 1

A man aged 74 had been for some time in poor health, complaining of anorexia and general malaise. Two months before admission to hospital he had noticed an exacerbation of his chronic cough with the production of a moderate amount of purulent sputum. Two weeks before admission his condition had deteriorated and he had developed feverishness and a sore throat. There was no relevant family or previous medical history. On October 6, 1952, he was admitted to Crumpsall Hospital, Manchester, under Dr. M. D. Milne. Examination revealed an emaciated ill man, sweating slightly. His temperature was 100.2° F. (37.8° C.), pulse 112 and regular, and B.P. 120/65. His heart was normal. There were diminution in expansion, dullness to percussion, and diminished air entry over the right lower lobe. The oral mucosa was inflamed. There was no hepatomegaly or splenomegaly and no lymphadenopathy.

Investigations.—Urine : S.G., 1012 ; Fehling's, Benedict's, and Rothera's tests were negative. Testing for albumin revealed a moderate amount of Bence Jones protein. The methods for detection of Bence Jones proteinuria outlined by Jacobson and Milner (1944) were used both in this and in the following case. X-ray examination of the chest showed right-lung collapse together with a large cavity with a fluid level, the appearances being those of a breaking-down neoplasm. Antero-posterior and lateral views of the skull showed no abnormality. Blood : Hb, 8.5 g. ; white cells, 13,300 (polymorphs 84%, lymphocytes 10%, monocytes 6%). The sputum was negative for tubercle bacilli. Serum urea was 54 mg. per 100 ml., serum protein 5.5 g. per 100 ml. (albumin 2.8 g., globulin 2.7 g.), serum calcium 7.5 mg. per 100 ml., serum inorganic phosphate 2.6 mg. per 100 ml.

Sternal Marrow.—The marrow smear showed an average cellularity and a normoblastic erythropoiesis. The striking feature was the preponderance of plasma cells, which formed about 40% of the nucleated cells. Many were atypical, having two and occasionally three nuclei. In addition many reticulum cells were present. The picture was thought to represent the reaction of the marrow to malignant infiltration, though clumps of tumour cells were not demonstrated and sections of marrow fragments gave no diagnostic assistance.

Clinical Course.—Treatment with antibiotics failed to alleviate a short downhill course, and the patient died on December 10.

Necropsy Findings.—The right lung weighed 2,100 g. A large growth arising from the right main bronchus had extended throughout most of the right lung. Areas of necrosis, dilated bronchi containing pus, and a right-sided empyema were present. Both kidneys and the right adrenal contained tumour secondaries. Microscopy of the primary and secondary tumours showed an anaplastic oat-celled carcinoma.

Case 2

A man aged 40 had been for three months in poor health associated with loss of weight and lack of energy. He complained of dyspnoea and a non-productive cough ; there was no haemoptysis. One brother and a sister had died of pulmonary tuberculosis. His previous medical history was not relevant. On March 6, 1953, he was admitted to Crumpsall Hospital, Manchester, under Dr. R. W. Luxton. Examination revealed a pale ill man ; temperature 98° F. (36.7° C.), pulse 88 and regular, B.P. 130/80. His heart was normal. Trachea to right, diminution in expansion, percussion note and air entry over both bases. The liver was enlarged 2 in. (5 cm.) below the costal margin ; the spleen was just palpable ; there was no lymphadenopathy.

Investigations.—Urine : S.G., 1020 ; Fehling's, Benedict's, and Rothera's tests were negative. Testing for albumin revealed a moderate cloud on boiling and with sulphosalicylic acid. Subsequent investigation revealed in addition to albumin the presence of a moderate amount of Bence Jones protein. X-ray examination of the chest showed partial consolidation of the right middle lobe, the appearances suggesting a neoplasm. The patient's condition precluded further radiological examination. Blood : Hb, 11.5 g. ; white cells, 11,000 (polymorphs 73%, lymphocytes 12%, eosinophils 3%, basophils 1%, monocytes 6%, myelocytes 5%) ; normoblasts, 3 per 100 white cells. The sputum was negative for tubercle bacilli. Serum proteins, 5.7 g. per 100 ml. (albumin 2.6 g., globulin 3.1 g.) ; serum alkaline phosphatase, 17 King-Armstrong units per 100 ml. Unfortunately, specimens of urine and serum were several weeks old when submitted for electrophoresis and, although kept frozen solid, did not give satisfactory electrophoretic patterns.

Sternal Marrow.—The marrow smear showed a depression of erythropoiesis associated with the presence of many undifferentiated cells resembling reticulosarcoma or anaplastic carcinoma. Clumps of tumour cells were not demonstrated, nor did section of marrow fragments give additional information.

Clinical Course.—Deterioration was rapid; the patient developed purpura, haemoptysis, and epistaxis, and died on March 19.

Necropsy Findings.—The right lung weighed 1,010 g. The bronchus to the right middle lobe was occluded by a mass of whitish growth 3 by 2 cm. in diameter. The remainder of the right lung and the left lung were not involved in growth. The liver weighed 5 kg. and showed widespread secondary deposits, as did the pancreas. Microscopy of primary and secondary tumours showed an oat-celled carcinoma. Section of the sternum revealed metastatic carcinoma.

Discussion

The main interest of the two cases is that they provide further unequivocal instances of the occurrence of Bence Jones proteinuria in secondary carcinomatosis. Both were cases of bronchial carcinoma of oat-cell type accompanied by secondary deposits in bone. Study of previously reported cases of Bence Jones proteinuria in skeletal secondary carcinomatosis does not indicate any special association with bronchial carcinoma.

Case 1 further illustrates that multiple myelomatosis may on occasion be simulated by secondary carcinoma if undue reliance is placed on the finding of Bence Jones proteinuria together with the presence of a high percentage of plasma cells in the marrow smear. That carcinoma cells infiltrating marrow can arouse a plasma-cell response is well known, and several recent papers have emphasized the occurrence of a "myeloma-like" marrow reaction in such cases. Rohr and Hegglin (1936), Nordenson (1940), Stöger (1941), and Delcourt (1946) have all reported this association. Coste *et al.* (1948) described a case under the heading "Pseudomaladie of Kahler," while Marchal and Mallet (1948) reviewed the subject under the heading "Plasmacytose Cancereux." Hardisty (1952) published a further case in which metastatic breast cancer gave a marrow picture indistinguishable from that of myelomatosis.

The possibility that multiple myelomatosis and carcinoma of the bronchus may have coexisted in these two cases requires consideration. In both cases microscopical examination of post-mortem material showed generalized carcinomatosis. In addition to the histological study of the primary tumour, sections were taken in Case 1 of adrenal, kidney, and sternum, and in Case 2 of liver, spleen, kidney, sternum, and vertebrae. In each case the pathology was typical of secondary carcinoma, with no histological evidence to support a diagnosis of multiple myelomatosis.

The validity of methods for the detection of Bence Jones protein has occasioned much discussion. Snapper (1949), in a brief review, said that the careful examination, under controlled conditions of temperatures, of precipitation and solution affords the most suitable method for the routine examination of urine for this substance. The methods outlined by Jacobson and Milner (1944) and recommended by Snapper were followed in the examination of the above cases. In each case a substance fulfilling the criteria laid down by these authors was demonstrated. Temperatures of precipitation were from 50 to 55° C., whilst the precipitate was completely redissolved at a temperature of 100° C.

It is interesting to note the increase in serum globulin in both these cases. Such an increase was reported by Delcourt (1946) in a case of metastatic abdominal cancer in which the globulin was 3.8 g. per 100 ml. Coste *et al.* (1948) describe a case of breast cancer in which the globulin was also 3.8 g. per 100 ml. In their case the myelogram showed that plasma cells formed 80% of the nucleated cells. The sternal marrow of Case 1 had the characteristic appearance associated with multiple myelomatosis, and this case adds further weight to the growing opinion of the non-specific nature of such a marrow picture.

Summary

Two cases of carcinoma of the bronchus with Bence Jones proteinuria are reported.

The simulation of multiple myelomatosis is commented upon.

Alternative explanations of the findings are discussed. The literature is briefly reviewed.

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ACUTE SUPRARENAL FAILURE

BY

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The occurrence of acute suprarenal failure in cases of Addison's disease is not uncommon, but in cases in which previous adrenal insufficiency was unsuspected it is not very usual. The following case is reported because of its interest, as there were practically no signs or symptoms of suprarenal failure until within five days of the patient's death.

Case Report

A man aged 30 was seen on September 8, 1953, with a history of loss of weight for one year (approximately 1 st.—10.9 kg.), lassitude, some dizziness, and a feeling of faintness for the last three months. He had previously had a tuberculous lesion of the left knee, which had responded well to treatment, there having been no evidence of any pulmonary lesion at that time. In view of the lassitude and loss of weight, the possibility of reactivation of the knee or of a pulmonary tuberculous lesion was considered. There was no evidence of active disease in the knee either clinically or radiologically, this being confirmed by an orthopaedic surgeon, but an x-ray examination of his chest showed a minimal lesion at the left apex. The clinical findings were negative apart from limitation of range of movements of the left knee. His blood pressure was 130/85, he had no sputum to test, but his stools did not contain tubercle bacilli. The rapid onset of further symptoms prevented gastric lavage from being done. His E.S.R. at this time was 20 mm. in the first hour (Westergren).

It was thought that the loss of weight and the lassitude were probably accounted for by the tuberculous lesion in the chest, although at the time it was felt that the lesion was not sufficient to cause such toxic symptoms. The patient was put on to streptomycin, 1 g. twice a week, P.A.S., 12 g. daily, and isoniazid 150 mg. twice daily. Forty-eight hours after starting this regime vomiting began, but his general condition appeared to be good. Vomiting continued the following day (September 20), and as this was thought to be probably due to the P.A.S. that drug was stopped. On September 21 his general condition rapidly deteriorated; he became dehydrated, felt thirsty, had marked oliguria, and his blood pressure had dropped considerably, being only 95 systolic, the diastolic pressure not being readable. His alkali reserve was 24 vols. CO₂ and his chlorides 450 mg. per 100 ml. as sodium chloride. His blood urea was 100 mg. per 100 ml.