Case Report

GASTRIC PLASMACYTOMA (OR LYMPHOMA) FOLLOWED BY CHRONIC MYELOID LEUKAEMIA: A RARE LYMPHO-MYELO-PROLIFERATIVE DISORDER

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The comprehensive terms 'lympho-proliferative disorders' and 'myelo-proliferative disorders' are strongly favoured by such authorities as Dameshek[1] and Rebuck.[2] This case report is presented as an example of an interesting and very rare transition of a 'lympho-proliferative disorder' to a 'myelo-proliferative disorder'.

In 1956 a 23-year-old man had a gastric plasmacytoma (or lymphoma), and in 1963 was found to have chronic myeloid leukaemia. His case history was presented to Mr. N. Tanner, F.R.C.S. during his visit to Somerset Hospital in 1963.[3]

CASE HISTORY

Plasmacytoma (or Lymphoma) of Stomach in 1956

The patient. A 23-year-old man was admitted to the medical wards of Somerset Hospital on 29 February 1956, complaining of pain in the left groin and thigh for 4 days. On questioning he stated that he had experienced burning epigastric pain immediately after meals, relieved by fluid, for 'a few years', accompanied by loss of weight. Exertional dyspnoea was present for 1 year. On examination, the abnormalities noted were pallor, a firm splenomegaly of 3 fingerbreaths, and signs of thrombophlebitis in the left groin and thigh.

Investigations. Hb. was 6 G/100 ml.; WBC 12,650/cu.mm. (neutrophils 58%, lymphocytes 40%, eosinophils 2%); faecal occult blood positive; bone-marrow smear showed iron-deficiency; barium meal showed an abnormal appearance of the stomach and lymphosarcoma was suggested.

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Operation. The anaemia was corrected by blood transfusions. Laparotomy was performed on 30 April by Mr. J. A. S. Marr. Large smooth-walled masses were palpable in the stomach wall, and the major procedure of total gastrectomy and splenectomy was performed.

Macroscopically, the mucosa of the proximal two-thirds of the stomach was grossly thickened and hypertrophic and thrown into large almost polypoid folds. The large folds of mucosa measured up to 2·5 cm. in height (Fig. 1). (The speci-

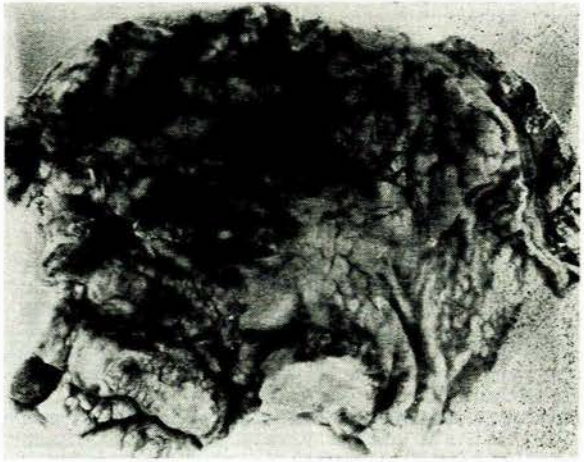

Fig 1. Macroscopic appearance of stomach. Large polypoid folds.

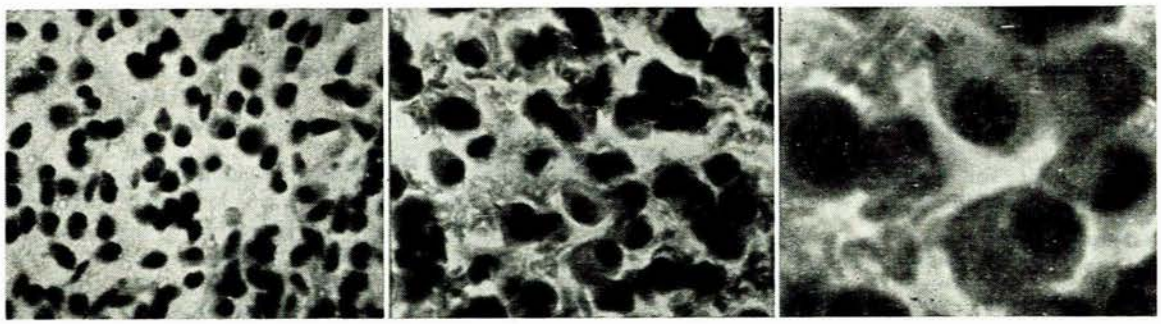

Fig. 2 *Fig. 3* *Fig. 4*

Figs. 2 - 4. Microscopic appearance of stomach (different magnifications). Many cells have eccentric nuclei. Some nuclei have a 'cart-wheel' appearance.

men has been kept in the Pathology Museum, University of Cape Town.)

Histological report. 'The mucosa overlying the thickened folds is thin and atrophic. The underlying submucosa is heavily infiltrated by masses and sheets of cells, and it is this infiltration which is responsible for the naked-eye appearances. The cells are also infiltrating the muscularis and the subserosa to a variable degree in different sections. The predominant cell has an eccentric nucleus and bears a superficial resemblance to a plasma cell. Many have basophilic cytoplasm and a typical "cartwheel" arrangement of nuclear chromatin, and must be regarded as plasma cells (Figs. 2 - 4). However, a large number of the cells, and in places by far the predominant type, are large, with a well-defined cytoplasmic border, and a large nucleus with a more open chromatin pattern. Thus it is apparent that the massive infiltrate of cells in the submucosa and other coats consists of all gradations from typical plasma cells to the larger reticulum-type of cell described above.'

The conclusion was that it was a neoplasm. The precise nomenclature was difficult but on cytological grounds it was best labelled a plasmacytoma. Another possibility was that it was a lymphoma which was closely imitating a plasmacytoma histologically.

A number of lymph nodes, measuring up to 2 cm. in diameter, were present along the greater curvature. Numerous plasma cells were present, but the normal architecture was preserved, and the picture was that of reactive, rather than neoplastic nodes. The spleen weighed 240 G, and histologically showed reactive changes.

Progress. When this histological report was known the patient was carefully re-examined for signs of multiple myelomatosis and none were found. Skeletal X-ray pictures, urine, and bone marrow were normal. Serum albumin was 4·6 G/100 ml., serum globulin 2·8 G/100 ml., and serum calcium 9·6 mg./100 ml.

He was not given irradiation or cytotoxic drugs, and was discharged on 2 July 1956, weighing 100 lb. Thereafter he resumed work.

Megaloblastic Anaemia in 1958

He was re-admitted on 14 September 1958, complaining mainly of swelling of the feet, dyspnoea on exertion, tiredness, and dizziness for 1 year. His weight was 110 lb.

Investigations. Hb. was 5·5 G/100 ml.; the bone marrow was megaloblastic and the reticulocyte count was 20% of the red cells after administration of 200 μg. of vitamin B_{12} intramuscularly.

There were no signs of multiple myelomatosis. The urine contained no albumin. Skeletal survey was negative. Serum albumin was 4·9 G/100 ml.; serum globulin 2·5 G/100 ml.

The diagnosis of post-gastrectomy megaloblastic anaemia was made, and ever since he has received 100 μg. of vitamin B_{12} intramuscularly every month at medical outpatient department.

Chronic Myeloid Leukaemia in 1963

The dizziness became worse after August 1962. He was re-admitted for a few days on 17 August 1963, mainly to determine whether any signs of multiple myelomatosis had developed. Haematological examination showed the surprising presence of chronic myeloid leukaemia. The sternum was slightly tender. He weighed 125 lb.

Investigations. Hb. was 10·8 G/100 ml.; WBC 104,000/cu. mm. (neutrophils 40%, lymphocytes 12%, basophils 23%, eosinophils 4%, monocytes 4%, myelocytes 7%, metamyelocytes 10%). A haematologist reported that 'the blood smear resembles that of chronic myeloid leukaemia. The whole myeloid series are represented, from a few blast cells to many myelocytes and segmented neutrophils, basophils and eosinophils. There are many nucleated red cells and numerous platelets' (Fig. 5). The bone marrow is replaced by a spectacular proliferation of myeloid cells, chiefly promyelocytes and myelocytes. Megakaryocytes are greatly increased, too, but the red series is relatively overshadowed. The picture strongly supports the diagnosis of chronic myeloid leukaemia.'

The patient was unable to accept prolonged hospitalization and the recommended treatment until re-admission was precipitated on 27 October 1963 by the onset of painful priapism, pyrexia, and joint pains—especially in the right shoulder and left hip. He now weighed 117 lb.

Investigations. Hb. was 12·9 G/100 ml.; WBC 120,000/cu.mm. (neutrophils 41%, metamyelocytes 6%, myelocytes 5%, promyelocytes and blasts 3%, eosinophils and precursors 6%, basophils and precursors 17%, lymphocytes 21%): platelets 1,625,000/cu.mm. The smear showed many normoblasts.

The priapism was attributed to thrombosis of the corpora cavernosa which were swollen and tender in the perineum.

On 6 November pus was aspirated from the right shoulder joint. No organism was isolated and blood culture was negative, but pyaemia appeared to be the correct diagnosis. Subsequently lytic lesions developed in the left acetabulum and head of the femur.

Treatment and progress. Therapy was thus required, not only for the chronic myeloid leukaemia, but also for priapism

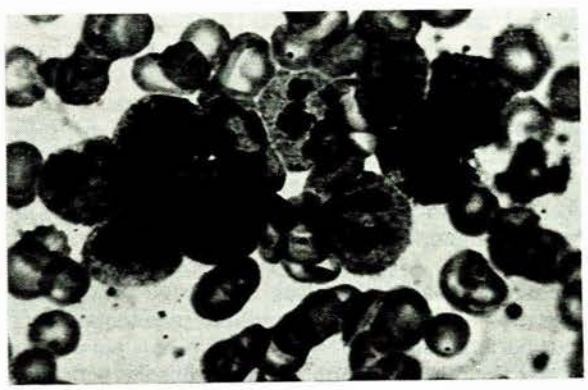

Fig. 5. Peripheral blood showing chronic myeloid leukaemia.

and pyaemia. Anticoagulant therapy with phenindione was administered from 27 October 1963 until 23 January 1964. Antibiotic therapy consisted of intramuscular methicillin (later replaced by oral isoxazolyl penicillin), oral ampicillin, and oral phenoxymethyl penicillin for approximately 10 weeks. During this time the priapism, pyrexia, and joint pains gradually subsided, but impotence subsequently resulted.

The chronic myeloid leukaemia was treated with 6 mg. of busulphan daily, from 2 November 1963 with a gratifying haematological result. The busulphan was discontinued at the end of December 1963, after the WBC count had fallen below 10,000/cu.mm.

During February 1964 anaemia increased and he was given 4 pints of blood. On 25 February, Hb. was 12·3 G/100 ml.; WBC 3,680/cu.mm.; platelets 74,000 per cu.mm.

The clinical and haematological outcome was satisfactory. The patient has remained well during 1964 and has resumed work. Blood counts during June and October 1964 indicate that the peripheral blood has become normal (Table I).

TABLE I. NORMAL BLOOD COUNTS FOLLOWING TREATMENT

Date	*Hb.*	*PCV*	*WBC*	*N*	*B*	*E*	*L*	*M*	*Platelets*	*Smear*
30 July.. ..	15	42	13,500	54	1		43	2	200,000	
1 October ..	15·6	47	12,700	58	1	3	36	2		normal
29 October ..	13	43	12,000	55	1	1	29	3	350,000	normal

DISCUSSION

This patient's case history from 1956 to 1963 contains items of great interest and rarity.

Plasmacytoma of the stomach was found at total gastrectomy in 1956. Wintrobe[4] states that extramedullary plasma cell tumours have been followed by generalization of the disease with bone involvement at variable intervals of time following discovery of the extramedullary tumour. Multiple myelomatosis was not apparent in this case in 1956 and had not appeared 7 years later. Ende *et al.*[5] quoted Hellwig's review of gastric plasmacytomata, and described a case of their own treated by subtotal gastrectomy and irradiation. There was no evidence of bone lesions or other laboratory findings associated with multiple myelomatosis at the time, or at follow-up examination 8 months later.

The alternative histological diagnosis of this case was an unusual lymphoma of the stomach. Bockus[6] states that when the stomach is involved by a lymphoma it is often the primary site of the disease, although generalized involvement may become clinically apparent late in the course of the disease. The macroscopic appearances of the stomach in this case resemble descriptions and illustrations of lymphoma of the stomach.

Many authorities, e.g. Wintrobe[4] and Rebuck[2] stress the well-recognized instances in which lymphoma has developed into leukaemia. When this occurs, it is almost always lymphatic leukaemia. Links and transitions between members of the 'lympho-proliferative disorders' and members of the 'myelo-proliferative disorders' are very much rarer. Hornbaker described 2 cases of giant follicular lymphoblastoma terminating in acute myeloid leukaemia.[7] Rebuck quotes one such rare example—a 76-year-old woman with lymphoma in the neck, followed by generalized dissemination, and a year later by acute granulocytic leukaemia. At autopsy, acute granulocytic leukaemia was confirmed, and there was no vestige of the original lymphoma.[2] Two cases of multiple myelomatosis have been reported, one of whom had concurrent polycythaemia vera and the other concomitant myelofibrosis with myeloid metaplasia,[8] and the authors also refer to other case reports of multiple myelomatosis associated with polycythaemia or with myelofibrosis.

This case report appears to be unique, namely, the sequence of a gastric plasmacytoma (or lymphoma) followed by *chronic* myeloid leukaemia. The gastric lesion was noted in 1956 after symptoms had been present for 'a few years'. The chronic myeloid leukaemia was noted in 1963, but it is not certain in which year it actually developed. Custer[2] expounds the concept that neoplastic proliferation may 'remain pure as to cell type from the outset, may become composite, or may alter completely during the course of the disease'. This case of 'lympho-myelo-proliferative disorder' supports this concept.

Parts of the chapters on lymphomas and leukaemias make gloomy reading, so it is encouraging to be able to present a patient who has survived 8 years after total gastrectomy for plasmacytoma (or lymphoma), and whose chronic myeloid leukaemia, noted 7 years later, is in remission 1 year after busulphan therapy. Wintrobe[4] states that remissions in chronic myeloid leukaemia treated with busulphan have been maintained for as long as 2 years, the longest intervals usually occurring in patients with a leucocyte count below 10,000/cu.mm. when the therapy was stopped, as in this case.

SUMMARY

1. A 23-year-old male had a total gastrectomy for gastric plasmacytoma in 1956. The alternative histological diagnosis was an unusual gastric lymphoma.
2. Post-gastrectomy megaloblastic anaemia was noted in 1958 and responded to vitamin-B_{12} therapy, which has been maintained.
3. In 1963 the patient was examined for evidence of either multiple myelomatosis or generalized lymphoma. Neither was found. Instead, chronic myeloid leukaemia was detected.
4. This sequence of pathological changes appears exceedingly rare. It provides an example of transition from a lympho-proliferative disorder to a myelo-proliferative disorder and supports the views of those who stress the overlapping relationships. It is called a 'lympho-myelo-proliferative disorder'.
5. The blood count is normal 1 year after busulphan therapy for chronic myeloid leukaemia.

I should like to thank the Medical Superintendent, Somerset Hospital, for access to the case notes of the patient whom I clerked in 1956, and for permission to publish. I am indebted to Drs. A. Landau, E. Dowdle, I. Bouchier, M. Horwitz, O. Meyers and B. Myers, and to several medical officers who have looked after the patient for 8 years. I am grateful to the Pathology Department, University of Cape Town, for the 1956 report, and to Prof. C. J. Uys for comments in 1963. Much work was done by Dr. R. S. Mibashan and technicians in the Haematology Laboratory, Groote Schuur Hospital. Mr. I. O'Reilly, Mr. G. McManus, Dr. J. B. King, Dr. R. I. Samson, and the Department of Clinical Photography, Groote Schuur Hospital, provided the photographs. Finally, there would not have been a case report but for Mr. J. A. S. Marr's major surgery in 1956.

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