BIBLIOGRAPHY

- Braude, A. I., Williams, D., Sieminski, J., and Murphy, R. (1953). *A.M.A. Arch. Intern. Med.*, 92, 75.
 Fremont, R. E., Luger, N. M., Surks, S. N., and Kleinman, A. (1954). *A.M.A. Arch. Surg.*, 68, 44.
 Gilmour, T. E. W. (1955). *British Medical Journal*, 2, 1248.
 Kurland, G. S., and Malach, M. (1952). *New Engl. J. Med.*, 247, 383.
 Luger, N. M., Kleinman, A., and Fremont, R. E. (1951). *J. Amer. med. Ass.*, 146, 1592.
 Miller, A. J., Shifrin, A., Kaplan, B. M., Gold, H., Billings, A., and Katz, L. N. (1953). *Ibid.*, 152, 1198.
 Moyer, J. H., Skelton, J. M., and Mills, L. C. (1953). *Amer. J. Med.*, 15, 330.
 Ritchie, H. D. (1956). *British Medical Journal*, 1, 371.
 Shanahan, E. F. (1955). *Brit. J. Anaesth.*, 27, 31.
 Skelton, J. M., Mills, L. C., and Moyer, J. H. (1952). *Fed. Proc.*, 11, 391.
 Wise, R. I., Shaffer, J. M., and Spink, W. W. (1952). *Proc. cent. Soc. clin. Res.*, 25, 961.

REPORT OF TWO SIBLINGS DIAGNOSED AS CASES OF ACUTE LYMPHATIC LEUKAEMIA

BY

MARY E. CARTER, M.B., B.S.

House-Physician, St. Mary's Hospital, London

The cases described below concern a brother and sister in both of whom acute lymphatic leukaemia was diagnosed during life. In the sister the disease followed a classical course to an early death, but in the brother, although he too died after a short illness, certain unusual features were noted during life and at necropsy. This report is presented because of the rarity of familial leukaemia and because of the interest of the case of the brother.

Case 1

The patient, a housewife aged 38, was admitted to West Middlesex Hospital early in March, 1950, because of pallor, generalized pains and weakness developing during the last three months, epistaxes, and the passage of blood clots per vaginam apart from normal menstruation. There was nothing relevant in the past history. Results of blood examination on March 3 were: haemoglobin 53% (Haldane); R.B.C. 2,390,000 per c.mm. Total white cell count not available, but differential count showed polymorphs 12%, lymphocytes 71%, prolymphocytes 9%, and nucleated R.B.C. 8%.

Clinical examination revealed a pale woman with bilateral subconjunctival haemorrhages and suborbital bruising, petechiae, and bleeding gums. There was no lymphadenopathy, but spleen and liver were each enlarged to two fingerbreadths and were tender; two small haemorrhages were noted in the left optic fundus. Blood pressure was normal, the urine clear, and the temperature 99.6° F. (37.55° C.). Blood examination on March 10 showed: haemoglobin 34%; R.B.C. 1,200,000 per c.mm.; W.B.C. 50,700 per c.mm. (polymorphs 2.5%, lymphocytes 77%, lymphoblasts 20%).

The patient's condition rapidly deteriorated, with epistaxes, haematemesis, and melaena, and she died in cardiac failure on March 17, 1950.

Case 2

This patient, a brother of Case 1, aged 31, was admitted to King Edward Memorial Hospital, Ealing, on July 5, 1955. He had first complained of lumbar pain, with swollen inguinal and axillary lymph nodes, eight weeks previously, and at that time was thought to be suffering from glandular fever. There was no history of past illness. On June 8 a blood count revealed: haemoglobin 94%; W.B.C. 6,000 per c.mm. (polymorphs 10%, lymphocytes 89%, monocytes 1%), some large and atypical lymphocytes being similar to those seen in glandular fever.

Two weeks later severe gingivitis and some petechiae on the left arm developed. Cervical and submandibular

lymph nodes swelled and he became pyrexial. On June 24 the blood count was: haemoglobin 78%; W.B.C. 7,000 per c.mm. (polymorphs 56%, lymphocytes 36%, monocytes 4%, eosinophils 3%). No atypical "glandular fever" cells noted.

On his admission to hospital on July 5 the patient was pale and had visibly enlarged cervical and submandibular lymph nodes. There were no abnormalities in the cardiovascular or respiratory system. The tip of the spleen was just palpable, but the liver was not enlarged. There was

FIG. 1.—Case 2: Sternal marrow smear on admission to hospital. (×180.)

generalized lymphadenopathy, also generalized petechiae becoming confluent over chest and abdomen. Temperature was 101° F. (38.3° C.). Blood picture on admission: haemoglobin 57%; R.B.C. 4,400,000 per c.mm.; W.B.C. 3,400 per c.mm. (atypical non-granular immature cells 27%, neutrophils 6%, lymphocytes 67%); platelets 166,000 per c.mm. On sternal marrow puncture large numbers of primitive leucocytes (blast cells) and a very few normal elements were found (Fig. 1). Blood was transfused repeatedly, but no remission occurred. In view of the low total leucocyte count the patient was not given radiotherapy, or any drugs, apart from sedatives. He steadily became weaker, and on July 26 a severe throat infection with monilia occurred which did not respond to treatment.

By August 1 the lymph nodes had rapidly decreased in size and then remained so. Clinically the spleen did not appear to enlarge further. A swinging temperature—98°–101° F. (36.7°–38.3° C.)—was maintained throughout the illness. A blood count on July 27 showed: haemoglobin 70%; W.B.C. 2,400 per c.mm. (lymphoblasts 20%, polymorphs 14%, lymphocytes 64%, monocytes 2%); and on July 30: haemoglobin 57%; W.B.C. 1,400 per c.mm. (differential count as before). The blood picture continued to deteriorate, and on August 10 the figures were: haemoglobin 25%; W.B.C. 800 per c.mm. (lymphoblasts 8%, polymorphs 6%, lymphocytes 84%, monocytes 2%). The patient died two days later.

Comment

There is no other family history of leukaemia, but the father and a brother and sister, who are alive and well, state that the patients' maternal grandfather died of a "rare disease." Their mother was said to have died "at the menopause," and she lost three infants before the birth of the two patients and the surviving brother and sister, the cause of their death being unknown.

Unfortunately no post-mortem examination was held on the woman. The following is taken from the necropsy report (Dr. W. S. Killpack) on her brother: "Emaciated

young adult male, slightly jaundiced. **Cardiovascular System:** Heart as a whole, dilated; pericardium healthy, no haemorrhages; myocardium very pale but fairly firm; endocardium healthy; vessels healthy. **Respiratory System:** Lungs very bulky due to oedema; numerous emphysematous bullae in right upper lobe; extensive congestion of lower lobes, ? also interstitial haemorrhage; no pneumonia found. Air passages: Some frothy mucus present; thrush membrane on epiglottis and vocal cords. Pleurae dry; fibrin over left lower lobe. **Alimentary System:** Tongue clear; extensive thrush membrane on pharynx. Oesophagus dilated with almost cylindrical, firm thrush membrane. Stomach dilated, healthy. Small gut: a few ulcers up to 1 cm. diameter in terminal ileum. Large gut: similar ulcers with membrane in caecum and descending colon. Liver (2,200 g.): normal pattern; cut surface rather brown. Gall-bladder distended with watery bile. Pancreas healthy. **Urogenital System:** Kidneys (320 g.) generally pale, marked cloudy swelling, number of pin-point haemorrhages. Bladder healthy. Genital organs healthy. Spleen (170 g.): cut surface congested, normal pattern. Lymph nodes: all groups enlarged to about twice normal size except those on lesser curvature of stomach, which were firm and greatly enlarged. Bone marrow uniformly pink and creamy. Adrenals oedematous; complete lipid depletion. Thyroid healthy."

The histological report is as follows. Sternal marrow practically acellular; oedematous young connective tissue with small collections of lymphocytes and plasma cells and histiocytes; occasional groups of undifferentiated cells (Fig. 2). Spleen: Extramedullary haematopoiesis and siderosis without fibrosis; widespread infiltration by histiocytes (? reticulum cells), many multinucleate; undifferentiated cells here also scattered in small groups. Kidney: small focus of proliferating histiocytes or reticulum cells,

FIG. 2.—Case 2: Appearance of sternal marrow smear post mortem. (×180.)

with some new connective-tissue formation. Lung: oedema and "monocytic pneumonia." Oesophagus: monilial oesophagitis. Liver: some fatty change; no obvious infiltration.

Discussion

The interesting features of the brother's case were the rapid regression of the enlarged lymph nodes, and the change in the sternal marrow from being full of proliferating primitive cells to being virtually empty of everything but connective tissue. The enlarged submandibular and cervical nodes were very prominent at the time of his admission and subsequently. Their size diminished rapidly, literally overnight, so that by the morning of August 1,

1955, his face had resumed its normal contours. What had happened during the course of a few hours to the cellular or other tissues responsible for these swellings? And what had happened to the cells crowding the marrow cavity? Two possible diagnoses might be considered: (1) atypical reticulum-cell sarcoma with bone-marrow depression; and (2) acute lymphatic leukaemia with atypical termination. But both seem rather unlikely, for in effect there was little sign of either condition at necropsy, especially in the histological sections. No record of a similar case has been found, and it is considered that no recognized diagnosis can be applied to the present case. The case perhaps illustrates the point made by Marshall (1956), that "owing to the effects of specialisation in peripheral blood and bone marrow studies there is still a tendency to regard leukaemia as a separate disease entity instead of as a symptom in a number of neoplastic reticular tissue proliferations."

The rarity of familial leukaemia is shown by a comparison between the number of cases reported in the literature and the total number of deaths from leukaemia, which in England and Wales alone averages over 2,000 a year, the figures for 1952, 1953, and 1954, as given by the Registrar-General in his quarterly returns, being respectively 2,043, 2,121, and 2,160. By contrast there have been only about 110 cases of familial leukaemia reported in the world literature since the first descriptions of leukaemia in 1845 (Virchow; Bennett; Craigie). The first authenticated case of familial leukaemia which Videbæk (1947) allows was described by McGavran in 1922 and included in Petri's 1933 review.

Videbæk's appears to be the last review of the literature on familial leukaemia to have been published; this author found 82 leukaemic subjects in all age groups belonging to 37 different families, in none of which was there consanguinity. Since its publication, so far as I can ascertain, another 28 unquestionable cases in 12 families (excluding cases without supporting laboratory evidence) have been reported (Frech, 1948; Riel, 1948; Barbiet *et al.*, 1949; Smith and Horne, 1950; Anderson, 1951; Bieber, 1951; Debré *et al.*, 1951; Portmann and Robinson, 1951; Reilly *et al.*, 1952; Stobbe and Taeschner, 1952; Ward *et al.*, 1952).

Summary

The cases of a brother and sister diagnosed in life as suffering from acute lymphatic leukaemia are reported, with a discussion of certain unusual aspects of one of the cases. Both patients died.

Brief reference is made to cases of familial leukaemia reported in the world literature.

I wish to thank Dr. J. W. Litchfield, under whose care Case 2 was admitted, for permission to publish. Case 1 was under the care of the late Dr. J. A. Torrens. I would also thank Dr. W. S. Killpack (who performed the necropsy in Case 2) and Dr. R. R. Wilson for their opinions on the bone-marrow smears and necropsy sections, and am greatly indebted to Dr. R. R. Wilson for help in preparing the article.

REFERENCES

- Anderson, R. C. (1951). *Amer. J. Dis. Child.*, **81**, 313.
- Barbiet, J., Guillermet, J., and Morel, P. (1949). *Lyon méd.*, **182**, 379.
- Bennett, J. H. (1845). *Edinb. med. surg. J.*, **64**, 413.
- Bieber, A. (1951). *Riv. Clin. pediat.*, **49**, 161.
- Craigie, D. (1845). *Edinb. med. surg. J.*, **64**, 400.
- Debré, R., Bernard, J., and Buhot, S. (1951). *Bull. Soc. méd. Hôp. Paris*, **67**, 183.
- Frech, H. C. (1948). *J. med. Ass. Ga.*, **37**, 183.
- McGavran, C. W. (1922). *Amer. J. med. Sci.*, **164**, 545.
- Marshall, A. H. E. (1956). *An Outline of the Cytology and Pathology of the Reticular Tissue*. Edinburgh.
- Petri, S. (1933). *Acta path. microbiol. scand.*, **10**, 330.
- Portmann, U. V., and Robinson, W. H. (1951). *Cleveland Clin. Quart.*, **18**, 33.
- Reilly, E. B., Rapaport, S. I., Kart, N. W., Mills, H., and Carpenter, G. E. (1952). *Arch. Intern. Med.*, **90**, 87.
- Riel, L. (1948). *Kinderrztl. Prax.*, **16**, 148.
- Smith, J. F., and Horne, J. N. (1950). *St. Thom. Hosp. Rep.*, **6**, 255.
- Stobbe, H., and Taeschner, H. (1952). *Z. ges. inn. Med.*, **7**, 736.
- Videbæk, A. (1947). *Acta med. scand.*, **127**, 26.
- Virchow, R. L. K. (1845). *N. Notiz. Geb. Natur- u. Heilk.*, **36**, 151.
- Ward, J. E., Galinsky, I., and Newton, B. L. (1952). *Amer. J. hum. Genet.*, **4**, 90.