LIPODYSTROPHIA PROGRESSIVA AND TEMPORARY HYDRONEPHROSIS

BY

P. B. S. FOWLER, D.M., M.R.C.P.*Assistant Physician, Charing Cross Hospital*

If the association of two diseases in a patient is not fortuitous their relationship to each other may throw light on the aetiology of one or both diseases. Lawrence's (1946) study of a woman with lipodystrophia progressiva and insulin-resistant diabetes supports the concept of two types of diabetes mellitus and suggests the simple explanation that the elderly obese person develops diabetes because she is unable to convert any more carbohydrate into fat.

In this paper the association of temporary hydronephrosis with lipodystrophia progressiva is reported and the renal disorders which have been described with this disease are reviewed. It is suggested that in some of the case reports the renal changes may have been similar to those present in the patient described here.

Gross hydronephrosis can develop in a week and disappear completely if the obstruction is removed early enough, and the term "temporary hydronephrosis" has been used to describe these transient changes (Fowler and Frankel, 1947).

Ellis (1951), writing about lipodystrophia progressiva, mentions the association of this condition with renal disease. He makes a brief reference to the occurrence of oliguria in Gerhartz's case (1916). The daily urinary output of this patient was 400–1,100 ml., and it is difficult to believe that this is a significant oliguria. Klien (1921) reports on a patient with lipodystrophy and mentions polyuria. Recently a patient with this disease was shown at the Royal Society of Medicine (Tizard, 1954), and the summary of the case included the information that "she is said to drink and void excessive quantities of fluid." The glucose-tolerance test in this patient was normal, but full urinary investigations including a pyelogram had not been done. Following the paper by Lawrence (1946) on the association of lipodystrophy and diabetes, any patient with lipodystrophy complaining of thirst and polyuria may be examined for further evidence of diabetes mellitus only, as happened to our patient, when studied for a short period at another hospital.

In 1932 two cases were reported in which lipodystrophia progressiva and uraemia occurred in the same patient. They were both thought to have had chronic nephritis, but in neither did the diagnosis appear likely, nor was it confirmed. They both had unusual clinical features in common with the patient described in the present paper.

Horton and Emmett (1932) report the case of a woman of 61 with a history of increasing nausea for one year with occasional attacks of vomiting. The patient was alert, and physical examination was essentially negative except for lipodystrophy affecting the legs. There were no symptoms or signs suggesting uraemia. On admission the blood urea was 400 mg. per 100 ml. After five weeks on a diet containing 25 g. of protein and 3–4 litres of fluid daily, the blood urea fell to 60 mg. per 100 ml. It was stated that pus cells, grade III, were present in the urine, but no mention of urine culture was made. The renal lesion was diagnosed as chronic

diffuse glomerulonephritis after the possibility of polycystic kidneys had been considered and dismissed, as no enlargement of the kidneys could be found on abdominal palpation.

Berger (1932) reported the case of a woman aged 26 who developed lipodystrophy at the age of 3½ years. Pyelitis occurred at 6 and another attack a year later. At the age of 19 the blood pressure was found to be raised and albumin was present in the urine. A diagnosis of acute exacerbation of chronic nephritis was made. Following a severe reaction to vaccination, the patient for a short time passed into uraemic coma. During the next seven years she remained well, and clinical examination at the end of this period was essentially negative except for the lipodystrophy. The blood urea was then 21 mg. per 100 ml.

Igersheimer (1948) described the case of a patient who had lipodystrophia progressiva, bilateral hydronephrosis with aberrant renal arteries, and other congenital abnormalities.

Case Report

The patient was the youngest of four children. Her parents and siblings were healthy. At the age of 2½ years she had scarlet fever and was in bed for three months with subsequent "kidney trouble." She had several attacks of sore throat until tonsillectomy at the age of 5. Between the ages of 5 and 9 she remained well except for mild attacks of measles, chicken-pox, and rubella. In 1950, at the age of 9, she was referred to the out-patient department with a ten-day history of abdominal pain and nausea. Her doctor wrote that she was "very lethargic and looked cadaverous."

She presented with the typical appearance of lipodystrophia progressiva with the so-called "death's head" and circumoral wrinkling on speaking or smiling. Loss of subcutaneous fat was symmetrical and complete down to the pelvic girdle, where there was an abrupt change. Below this level subcutaneous fat was present in normal but not excessive amounts. Her weight was 3 st. 10 lb. 4 oz. (24.2 kg.). Examination was otherwise negative. In view of the recent illness further investigations were done: a Mantoux test, which was negative; E.S.R., 4 mm. in the first hour; Hb, 98%; W.B.C., 5,000; and x-ray examination of the chest, normal. No investigation of the urinary system was done at this time except for a routine examination of the urine, which contained no abnormal constituents. The mother was told that improvement in the child's appearance was unlikely, but that she would remain healthy.

In September, 1951, fifteen months later, the mother, anxious for something to be done to improve the child's appearance, took her to a London teaching hospital, where she was an in-patient for fifteen days. In the case summary on her discharge it was noted that the child "was said to be rather thirsty." The glucose-tolerance test was normal. No special urinary-tract investigations were done. It was concluded that she was "a case of lipodystrophia progressiva unassociated with evident endocrine disorder."

In February, 1952, four months later, the child was admitted to Bromley Hospital with a history of repeated vomiting for five days, and abdominal pain and red urine for three days. The temperature at the onset had been 103° F. (39.4° C.) and there had been repeated rigors, dysuria, and frequency. On examination she showed the features of lipodystrophy unchanged from when she was first seen twenty months previously. The child now looked toxic and dehydrated, with a dry furred tongue. The pulse was of poor quality and the rate 100 before admission. In hospital the rate was at first about 90, later rising on occasion to over 120. The temperature settled to 99° F. (37.2° C.) and for the next three weeks there was a low-grade pyrexia up to 99.5° F. (37.5° C.). During the fourth

week the temperature fell and was normal for the remaining three weeks in hospital. For the first few days tenderness was present in the right loin. There was no tenderness in the left loin or over the bladder. The B.P. was 120/80, and, with the exception of the urine, the remainder of the physical examination was negative.

The urine on admission was scanty and contained a very heavy cloud of albumin. There were numerous red cells, pus cells, and isolated cellular casts. Catheter specimens of urine were sterile. Five days after admission the blood urea was 330 mg. per 100 ml.; W.B.C., 19,000, with 80% polymorphs; E.S.R., 25 mm. in the first hour.

Four days later the blood urea was still 320 mg. per 100 ml. and oliguria persisted. The Bull-Borsh regime was then started, and the blood urea fell to 183 mg. per 100 ml. after a further five days and in the next fortnight to 40 mg. per 100 ml. The child's condition improved with the fall in

the blood urea. An intravenous pyelogram, when the blood urea had fallen to normal, showed bilateral hydrocalicosis, hydronephrosis, and hydroureter more marked on the right (Fig. 1). Cystoscopy showed no abnormality. The child was discharged from hospital on April 9, weighing 4 st. 6 lb. (28.1 kg.), and returned to school one month later.

During her stay in hospital there was striking mental instability, the child being one moment aggressive and abusive and the next exceedingly timid. This was in marked contrast to her mental state when her condition improved, her personality then becoming stable and pleasant. The mental changes appeared to be a manifestation of uraemia, improving as the blood urea fell.

When seen in the out-patient department three months later she was free of symptoms, was feeling well, and had won the high jump at school. No abnormal constituents were found in the urine, the intravenous pyelogram showed only slight bilateral hydronephrosis and hydroureter affecting mainly the right side.

Her progress was watched in the out-patient department and she continued to remain well until fourteen months later. While on holiday she was admitted on August 13, 1953, to the Royal County Hospital, Ryde, with a history of vomiting, abdominal pain, headache, and dark urine for four days. The urine contained large amounts of albumin, many pus cells, and red blood cells with a moderate amount of granular and cellular casts. The B.P. was 130/80, E.S.R. 47 mm. in the first hour, and Hb 90%. The blood urea was 73 mg. and later rose to 109 mg. per 100 ml. Before transfer back to Bromley Hospital the blood urea had fallen to 28 mg. An intravenous pyelogram (Fig. 2) showed little change from that done one year previously, but there was marked improvement as compared with the first x-ray films taken soon after the most severe uraemic episode. On discharge from hospital on October 12 she was free of symptoms and her general condition was satisfactory, although there was still a moderate albuminuria.

When seen in the out-patient department in March, 1954, she was feeling well. The B.P. was 140/80. The urine contained 0.5 g. of albumin and a moderate number of red cells and pus cells. The blood urea was 32 mg. per 100 ml. and the urea clearance (Van Slyke) 54%. An E.E.G. in November showed no abnormality.

Discussion

In retrospect, it appears likely that the first illness in June, 1950, was due to incipient or transitory uraemia and that she has therefore been in renal failure three times. The nature of the kidney trouble at 2½ years old is unknown.

Although the equanimity of most patients with lipodystrophy emphasizes their mental stability, psychological disturbances have occurred in a number of patients. Warin and Ingram (1950) reported two such cases and reviewed other instances of this association. The presence with lipodystrophy of mental disorder due to organic disease of the brain lends some support to the theory that this disease results from a lesion in the central nervous system. In our patient the mental changes were due to uraemia, and, although in none of the case reports was mental change attributed to this cause, renal and other organic disease may pass unrecognized when presenting with mental symptoms (Stokes *et al.*, 1954).

In this child the three attacks of uraemia were clearly due to the hydronephrosis. The cause of the uraemia in the patients with lipodystrophy described by Horton and Emmett (1932) and Berger (1932) was obscure. In Berger's patient it seems improbable that an acute exacerbation of chronic nephritis had caused uraemia when seven years later the patient was in good health and the blood urea 21 mg. per 100 ml. Intravenous pyelography, which might have shown a hydronephrosis, was not done in either of these two patients. This technique had not been introduced at the time Gerhartz (1916) and Klien (1921) described their cases.

FIG. 1.—Intravenous pyelogram done on March 26, 1952.

FIG. 2.—Intravenous pyelogram done on October 9, 1953.

Renal failure did not occur in Igersheimer's (1948) patient with lipodystrophy and hydronephrosis. Igersheimer maintained that lipodystrophy is due to a defect of the mesenchyme and described various mesenchymal abnormalities in his patient. He reviewed other published cases to support his view. The hydronephrosis in his patient was believed to be due to an aberrant renal artery. This was found at operation and cut. A subsequent intravenous pyelogram showed no change from the appearance before operation.

Igersheimer summarily dismisses the nervous, endocrine, and other causes suggested for lipodystrophia progressiva. The different hypotheses concerning aetiology have been fairly reviewed by Ellis (1951). There is much evidence to suggest that lipodystrophy may result from a lesion in the central nervous system (Warin and Ingram, 1950).

Besides that of associated mesenchymal defects or mere chance, there is another possible explanation for the occurrence together of uraemia and lipodystrophy. Lesions of two closely related areas of the brain, anterior to the hypothalamus, may be responsible for trophic changes and uraemia, both of these effects occurring if both areas are involved. Evidence that the cause of lipodystrophy may lie in a lesion related to the hypothalamus is found in the diencephalic syndrome (Russell, 1951), where profound wasting is a prominent feature. In Tizard's patient (1954) the profound wasting was a true lipodystrophy with disappearance of subcutaneous fat and no muscle-wasting. Dr. Russell, who saw this child, thought it likely that she had a diencephalic lesion. Evidence that trophic changes and uraemia can be due to lesions in closely related areas anterior to the hypothalamus is furnished by McLardy (1950). After prefrontal leucotomy, trophic changes with gross wasting and uraemia have often been described. These complications of the operation usually occur when the incisions go too far back (Freeman, 1953). McLardy has shown that prefrontal leucotomy can be followed by uraemia or trophic changes, depending upon which of two areas is damaged. Injury to posterior area 47 of the orbital cortex leads to uraemic death, and the severance of connexions between the caudate nucleus and Brodmann's (non-granular) cortical areas 8 and 6 is concerned with the trophic fatalities. The immediate cause of renal failure in McLardy's series of uraemic deaths is not known, but he mentions the work of Cort, who claimed to reproduce Trueta's renal shunt mechanism in cats by electrical stimulation of the cortex of area 13.

If renal failure in lipodystrophy is due to a lesion in the central nervous system, this could be caused by abnormal function of the autonomic innervation of the urinary tract, producing hydronephrosis, or of renal cortical arterioles, producing a Trueta shunt effect. Besides the evidence of the present case, hydronephrosis as a functional disorder of the urinary tract is common in man. The rare cortical necrosis of the kidney during pregnancy is the only disease which may be comparable to Trueta's shunt mechanism in the experimental animal.

Lesions affecting autonomic centres are responsible for diverse vegetative effects, including uraemia. The common idiopathic hydronephrosis with no organic obstruction may be due to disease of the central nervous system involving an autonomic centre regulating the function of the renal tract.

Summary

A case of lipodystrophia progressiva, temporary hydronephrosis, and recurrent uraemia is described.

The occurrence of renal disease with lipodystrophy is reviewed. The association of the two diseases may be fortuitous; the result of a mesenchymal defect; or the result of a lesion of adjacent centres in the central nervous system, responsible for the renal and trophic changes.

Evidence is submitted that a lesion anterior to the hypothalamus may be responsible for these changes.

My thanks are due to Dr. N. S. Plummer for permission to publish this case and for his helpful criticism.

REFERENCES

- Berger, E. H. (1932). *Med. Clin. N. Amer.*, **15**, 1431.
 Ellis, R. W. B. (1951). *British Encyclopaedia of Medical Practice*, 2nd ed., **8**, 146. Butterworth, London.
 Fowler, P. B. S., and Frankel, E. (1947). *British Medical Journal*, **1**, 887.
 Freeman, W. (1953). *Arch. Neurol. Psychiat.* (Chicago), **69**, 640.
 Gerhartz, H. (1916). *Munch. med. Wschr.*, **63**, 823.
 Horton, B. T., and Emmett, J. L. (1932). *Med. Clin. N. Amer.*, **15**, 1505.
 Igersheimer, W. W. (1948). *Amer. J. Dis. Child.*, **75**, 206.
 Klien, H. (1921). *Munch. med. Wschr.*, **68**, 206.
 Lawrence, R. D. (1946). *Lancet*, **1**, 724, 773.
 McLardy, T. (1950). *J. Neurol. Neurosurg. Psychiat.*, **13**, 106.
 Russell, A. (1951). *Arch. Dis. Childh.*, **26**, 274.
 Stokes, J. F., Nabarro, J. D. N., Rosenheim, M. L., and Dunkley, E. W. (1954). *Lancet*, **2**, 862.
 Tizard, J. P. M. (1954). *Proc. roy. Soc. Med.*, **47**, 128.
 Warin, R. P., and Ingram, J. T. (1950). *Lancet*, **2**, 55.

MALIGNANT GRANULOMA OF THE NOSE

BY

MAXWELL ELLIS, M.D., M.S., F.R.C.S.

Surgeon to the Royal National Throat, Nose, and Ear Hospital, London; E.N.T. Surgeon to the Central Middlesex Hospital

The condition known as malignant granuloma of the nose is uncommon and almost invariably fatal. The chief purpose of this report is to present a unique result—a treated case which has remained healed for over five years. The secondary purpose is to present another case of a different and unusual type.

Only five cases of recovery appear in the literature, but closer examination of the case records and subsequent history reveals inconsistencies. Woods's case (1921) healed locally after interstitial irradiation, but the patient died within two years, of generalized sarcomatosis. The diagnosis of the original lesion must therefore be suspect. In the case of M'Arthur and Dew (1925) the local lesion healed after three doses of deep x rays, but the patient died four years after the last dose from what was called "miner's phthisis." No necropsy was permitted, and Stewart (1933) quotes a letter from M'Arthur in which the possibility of pulmonary sarcomatosis was envisaged. Schütz (1938) records eight cases, in one of which spontaneous resolution occurred, but the account is too brief to be entirely acceptable. Hoover (1941) describes an admittedly atypical case which apparently healed after excision of the granulomatous area followed by antisyphilitic treatment.

An exhaustive survey of the literature by Williams (1949) failed to reveal any cases of survival other than those cited above. His discussion of the pathology is most instructive, particularly in assessing a link with periarteritis nodosa and with certain types of hypersensitivity reactions. Following upon this paper, Williams and Hochfilzer (1950), Moore *et al.* (1951), and Woodburn and Harris (1951) have had some success with cortisone and A.C.T.H., but the follow-up period recorded is too short for appraisal.

Finally, Sneddon and Colquhoun (1952) claim a cure with chlortetracycline ("aureomycin") and chloramphenicol, but the patient died a year or so later, and, furthermore, the precise nature of the lesion was never identified by biopsy. They considered the lesion to be staphylococcal in origin, but no other case has been recorded in which the local lesion healed with antibiotics (Breckenridge *et al.*, 1954).