Meeting November 17 1960

Cases

Lipoid Proteinosis (Urbach-Wiethe) (Hyalinosis cutis et mucosæ)

M A Cowan MB MRCP (for H R Vickers MD FRCP)

M B, aged 43. Housewife.

History: Inability to cry at birth, and subsequent hoarseness. 12 years of age: development of lesions of left shoulder, neck, and elbows. 1956: diagnosed as having akinetic epilepsy, controlled by Epanutin. 1958: referred to ENT Department with hoarseness, and from there to Department of Dermatology. Had increased tendency to bruise with a positive tourniquet test and menorrhagia. Corticosteroid therapy for eight months with improvement of voice, skin lesions and disappearance of bruising tendency. August 1960: painless swelling of left submandibular gland for one month. Hoarseness and skin lesions have slowly progressed since onset except during corticosteroid therapy. No history of consanguinuity, but her mother has diabetes mellitus.

Clinical findings: Diffuse non-scarring alopecia, particularly of occipital region. Face waxy and wrinkled with a mauve atrophic patch of right side of forehead, pearly bead-like lesions of margins of upper eyelids and fissured infiltrated plaques of angles of mouth. Tongue normal. Yellowish follicular papules with perifollicular atrophy of neck and upper arms. Hyperkeratotic plaques of both elbows with warty excrescence on the left. Infiltrated lesion of left shoulder and gluteal cleft. Infiltrations of pharynx. Considerable thickening of both vocal cords with pallor, scarring and some proliferation posteriorly.

Investigations: Blood count, platelets, bleeding time, capillary microscopy, urine, Wassermann and Kahn, plasma proteins, blood lipoid phosphorus, normal.

Skull X-rays: Bilateral bean-like calcification in temporal lobes, probably medial to posterior horns of lateral ventricles.

Electro-encephalogram: normal.

Biopsies of skin and larynx histologically similar. They show clumps of hyaline, PAS positive material in the dermis with perivascular and periglandular deposition. (The perivascular material appears to be replacing the mucous membrane.) The elastica is degenerate and reticulin absent in these areas. Thick fragmented clumped areas of elastic outside the hyaline material.

Comment: This patient presents a classical picture of lipoid proteinosis with a new feature of increased bruising tendency. The histological findings so far as they go, support the hypothesis that this is an infiltrative rather than a degenerative condition.

Dr H R Vickers: I first saw this patient some three years ago and she was referred to me from the ENT Department. I thought that she probably had pseudoxanthoma elasticum but the correct diagnosis was made by the pathologists on the biopsy from the skin of the side of the neck. I mentioned this case in my Watson Smith lecture.

Dr G B Dowling: According to Scott & Findlay (1960) who have studied the literature very fully this may well be the first case to be presented in Great Britain. These authors have recently collected 27 South African cases and they point out that like two other inherited diseases, porphyria and pseudoxanthoma elasticum, the incidence in relation to population is very high indeed. The South African cases have occurred in 18 white families of whom 17 bear Africaans surnames, and 1 coloured family. They believe that the anomaly was probably imported from Germany at an early stage of the white settlement in South Africa.

In a personal communication Dr Findlay has informed me that none of the South African cases, of which the first was reported in 1948, has died.

REFERENCE

Scott F P & Findlay G H (1960) *S. Afr. med. J.* 34, 189

Dr C D Calnan: Last week I saw a severe example of this condition in Professor Orbaneja's clinic in Madrid. The patient was a child of about 8 or 9 and the whole of her face showed intense reddish yellow infiltrate. It is possible that light had something to do with it.

Professor J T Ingram: I saw Urbach's original case in Vienna in 1935. There was a positive family history. I understand there is no family history in this case? The condition is described in a recent book by Fleischmayer.

Dr J J Jacobson: We see quite a number of these cases in South Africa: the pathologist's report always makes the diagnosis very soon. They include very young children, and often there is a familial pattern.

Psoriasiform Dermatosis associated with Bizarre Metabolic Abnormalities

Maurice Garretts MRCP (for Professor C E Dent)

S A M, female, aged 12. Schoolgirl.

History: This girl was referred to University College Hospital by Dr Patrick Montgomery, to whom we are most grateful for the opportunity to

study this patient. She had knock-knees when aged 2, and at this time she suffered from infantile eczema. Since the age of 4 she has had dry and scaly patches on her skin, and these became a severe eruption six months ago. One year ago she had two epileptiform convulsions for which she was given phenobarbitone. She was sent to see Dr Montgomery six months ago with a rash which was thought to be psoriasis, and at this time the signs of latent tetany were elicited and she was referred to the Metabolic Unit at University College Hospital for further study. She was then regarded as a possible case of eruption associated with hypocalcæmia.

Clinical findings: There was a widespread eruption consisting of psoriasiform plaques 2–4 cm in diameter, mainly on the trunk. In addition there were large areas over the upper trunk and back showing the most pronounced follicular hyperkeratosis (Fig 1). The Chvostek sign was easily

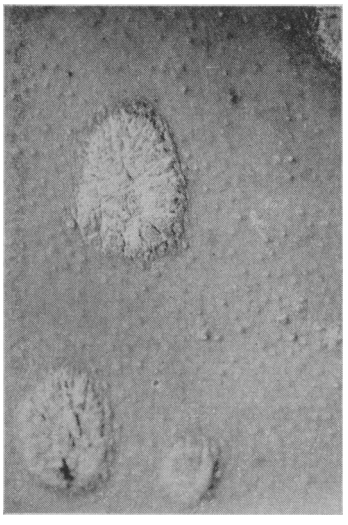

Fig 1 *Case S A M: skin below shoulder, taken in horizontal position, showing psoriasiform plaques and follicular hyperkeratosis. The largest plaques measured about 4 cm in diameter*

elicited. There was bilateral genu valgum with intermalleolar separation of 4 in. She was on the 16 percentile for height. She was plump and healthy otherwise.

Investigations: Serum calcium 4·9, phosphorus 9·6 mg%. Phosphatase 42 K-A units. Electrolytes normal. Urea 18 mg%, urea clearance 114%. Twenty-four-hour urine calcium 14 mg, phosphorus 619 mg. Urine S.G. range 1004–1020. Glucose tolerance test: slightly flat curve obtained. Fat balance 98% absorption. Xylose absorption test normal. Vitamin A absorption normal. Dark adaptation test impaired, compatible with mild vitamin A depletion (Dr G Arden). Fasting vitamin A level 90 and 130 i.u./100 ml (low normal). EEG: widespread high voltage activity in a wide range of frequencies.

Skin biopsy (Dr A Jarrett): The histology of the follicular lesions shows a parakeratotic intrafollicular keratinization. The psoriasiform plaque-like lesion showed a diffuse parakeratosis with a thickened epidermis and is indistinguishable from psoriasis. However, these lesions are quite different in their development. In psoriasis the follicles are the last region to be affected by the parakeratotic process, whereas in this case they are the first to show the change. This strongly suggests that the lesions in this case are those of a primary avitaminosis A of the skin.

Comment: The investigations yielded very puzzling results. Because she presented with latent tetany and an eruption closely resembling that seen in vitamin A deficiency, it was tempting to consider that she might have steatorrhœa with tetany, considered by some to be due to inability to absorb vitamin D and the follicular hyperkeratosis of phrynoderma due to the inability to absorb vitamin A. Her history of knock-knees together with poor linear growth suggested mild rickets. The rickets was not gross enough to show any clear X-ray changes, but the high alkaline phosphatase was very suggestive. In addition to these factors she had an eruption similar to that associated with vitamin A deficiency, but occurring in the presence of only low normal plasma vitamin A levels. Her diet was normal and there was an adequate intake of vitamins A and D. We assumed that she must have occult steatorrhœa, or else something very complicated which we had not heard of before. The interpretation of her condition was further complicated by her gross biochemical hypoparathyroidism, which undoubtedly explained her tetany and probably her epilepsy of one year ago.

She was put on a fat balance regime and during this time we confirmed that she had abnormal dark adaptation, as in a mild case of vitamin A deficiency. The skin biopsy material was found to be consistent with that diagnosis, and we are most grateful to Dr A Jarrett for carrying out the histological studies.

She had an abnormal EEG tracing and all other tests of renal function and electrolytes &c. were normal. The fat balance came back normal. While we recovered from the surprise, further tests of renal phosphate threshold were made and these fully confirmed a high threshold typical of hypoparathyroidism.

Recently we have recorded cases of skin disease in which the rash was directly related in severity and onset to the serum calcium level (Dent & Garretts, 1960). These cases were in the main eczematous. It was nevertheless planned to treat this girl with vitamin D only in order to see how far improvement in her serum calcium level might affect her skin as well as her tetany. After giving a loading dose of dihydrotachysterol (DHT), she was put on a maintenance dose of 2 mg/day. She responded rather slowly and her calcium level slowly rose to normal, while the phosphorus fell, this latter being shown to be due to a fall in her renal phosphate threshold to nearly normal. This response is quite typical of that which occurs in hypoparathyroidism. During this time her phosphatase level fell, thus confirming that her raised phosphatase was due to rickets and not to a hepatic cause.

During the period of treatment with DHT her skin definitely became worse, thus confirming that the eruption was not due to hypocalcæmia. It was, however, interesting to note that local treatment during this time of a small scaly patch with vitamin A (50,000 i.u./ml), resulted in a definite improvement of the eruption where the vitamin A oil was applied. There was no improvement of another scaly patch treated with the solvent oil only.

It was next decided to discover her response to vitamin A while her serum calcium level was maintained at normal levels with appropriate maintenance doses of DHT. A vitamin A absorption test was first of all carried out and this showed normal results, a further point against the possibility of steatorrhœa. She was then given vitamin A 50,000 i.u. daily by mouth, and there was little doubt that her skin began to improve, especially on the trunk, after two weeks' treatment. First the follicular lesions disappeared and later the large psoriasiform lesions began to improve, shedding their scales and leaving normal skin underneath. Her dark adaptation test became normal.

Since her EEG was still abnormal after raising her serum calcium level to normal, she was presumed to have an underlying irritable focus which had been triggered off to produce epilepsy by the low serum calcium. It was decided to stop her phenobarbitone.

She was discharged from hospital on May 29, 1960, and she was sent out taking 2 mg daily of DHT, and as we were impatient the dose of vitamin A was raised to 250,000 i.u. daily. On follow up her plasma calcium was satisfactorily maintained at normal with DHT. A close watch was kept on her plasma vitamin A levels. They had not risen one month afterwards so the dose was increased to 750,000 i.u. daily. Her skin was quite normal at this stage, although there were still marked psoriasiform patches in her scalp. On October 3, 1960, she presented the features of vitamin A intoxication with a very high plasma level of vitamin A. The vitamin A was stopped and she has not been put back on it. Her calcium, phosphorus and phosphatase levels remain satisfactory and she has had no further tetany or epilepsy.

Professor C E Dent: I wish to support Dr. Garretts' remarks to the effect that the patient had, associated with the dermatosis, clear evidence of hypoparathyroidism, of mild rickets and signs of vitamin A deficiency. We controlled her treatment closely in our Metabolic Ward. Her response to vitamin D was that of the state of hypoparathyroidism; her plasma calcium rose, the phosphorus fell and the renal clearances showed an abnormally low clearance before and a normalization after the vitamin D was given. The evidence for rickets was in her history of knock-knees and high plasma alkaline phosphatase levels, which latter became normal as the vitamin D was given in doses sufficient to control the hypoparathyroidism. The signs of vitamin A deficiency comprised the clinical signs of the dermatosis and the skin histology which was consistent with this diagnosis. Of further importance was the result of loading with large doses of vitamin A, no other change of treatment occurring; her dark adaptation became normal and the dermatosis improved in the most spectacular manner. This latter is now beginning to return since we have temporarily stopped the vitamin A.

Clearly the signs of vitamin A and D deficiency in this child (if you accept this evidence) have arisen in the presence of normal dietary intakes of these vitamins. The child appears, therefore, to have a higher than normal requirement since supplementation by large doses has corrected the deficiencies. The simplest plausible mechanism for this is presumably a metabolic disturbance in the body leading to excessive rate of destruction of the vitamins, or to an inability to act properly on their target organs. The same disorder may well have caused her own parathyroid hormone to be ineffective, and it would be most fascinating if eventually there could be discovered a common pathway of metabolism of these three factors, so essential to normal development. This patient is presented in the hope of stimulating such thoughts, and perhaps to direct future research along these lines. We have not yet come across a similar patient in the literature. It is relevant to point out, however, that there are already known to be many complicated syndromes in which apparently disordered function of the parathyroid glands (hypo- or hyper-) is associated with other metabolic defects.

We are in the course of preparing a fuller paper on this child for publication elsewhere.

REFERENCE

Dent C E & Garretts M (1960) *Lancet* i, 142

Dr I B Sneddon: We have a similar case in a woman of 51, who eleven years ago had a total thyroidectomy. Within weeks she developed widespread psoriasis and

this was associated with a low serum calcium as her parathyroids had been removed at operation. The psoriasis varies directly with the level of serum calcium, clearing if it returns to normal.

She has also had an epileptiform attack and an abnormal EEG when her serum calcium has been low.

Dr H R Vickers: I well remember the case described by Dr Sneddon since she was under my care when I was in Sheffield. I saw a second similar case three years ago who was referred to me by Professor Witts. He was a man with very widespread psoriasis which followed thyroidectomy and he was found to have hypoparathyroidism with low serum calcium. He was treated with calciferol, the serum calcium returned to normal and the psoriasis cleared. I would like to discuss the local application of vitamin A, since vitamin A in an ointment base will act as a keratolytic agent and beneficial results when used on scaling skin may be due not to any specific action of vitamin A but to the non-specific keratolytic effect.

Hyperkeratotic Follicular Plugging with Alopecia Totalis

R D Sweet MRCP

Male aged 61.

Has had a dry skin all his life with scaling on the extensor aspects of arms and legs.

Family history: Negative. 8 sibs all unaffected.

History: Thyroidectomy 1942: Cerebral thrombosis 1954 from which he has recovered completely, apart from some minor trouble with his speech.

Three years ago he developed a hypostatic eczema on his right lower leg which became severe just under two years ago, and at that time he probably had some papular eczema on his back. Since then the skin of his trunk has appeared ichthyotic also.

One year ago the sides of his face and temple regions of the scalp began to be affected, as at present, and the whole picture became fully developed within two or three months. He does wonder, however, whether further areas are gradually becoming involved lately.

Six months ago, in the course of a fortnight, he lost all the hair from his scalp, eyebrows, eyelids, nostrils and beard. There was marked associated formication. He had not previously noticed any thinning of his hair in the temporal regions, and he previously had a thick crop of grey hair.

On examination: He has a mild, but definite generalized ichthyosis. The palms and soles are normal. He presents the typical appearances of alopecia totalis, and in addition, on the sides of the scalp and face, and to a lesser extent the centre of the face, there is gross follicular plugging reminiscent of the appearances seen in chloracne.

Chest X-ray: Nothing abnormal noted. *Blood count:* Normal. *W.R.:* Negative. *Serum cholesterol:* 187 mg/100 ml.

Histology: (Biopsy: skin of L cheek). The section shows patchy hyperkeratosis, the granular layer being reduced to a thin line. Follicular plugging is a conspicuous feature, and there are many small deformed hair follicles, but they are not forming hairs. Sebaceous glands are large and numerous. A very slight chronic inflammatory reaction is present in the dermis.

Comment: Taken alone this man's striking follicular hyperkeratosis with plugging is unusual enough, but the association with alopecia totalis must be unique. Before either of these conditions occurred his skin had become ichthyotic, apparently as an aftermath of a generalized hypostatic eczema.

Has this man four independent skin conditions, or is there some relationship between them?

An ichthyotic skin might well be more prone to follicular hyperkeratosis, even late in life, or both conditions might result from some undiscovered metabolic disturbance. The hair loss is equally complete where the follicles are hyperkeratotic and where they are not.

When workers in a factory develop chloracne, the severity of the lesions is directly proportional to the amount of exposure to the fumes responsible, and no predisposition of certain types of skin has been recorded.

Dr I B Sneddon: I should have thought there was a possibility that this was a reticulosis. I have seen a similar follicular eruption as a pre-mycotic condition before, but this does not explain the alopecia.

Dr Louis Forman: Did he have contact with paraffin or mineral oil?

Dr R D Sweet: His job is dismantling unwanted naval wireless sets and other small items. I could not convince myself that his condition was anything to do with his work. Three other men who work with him were not affected. He had earlier used brilliantine on his hair when he had flowing white hair.

Dr M Garretts: I wondered whether this could be a case of ulerythema sycosiforme, but the fact that the hair loss preceded the appearance of the eruption makes this idea unlikely.

Dr B C Tate: Have any vitamin A studies been carried out on this man?

Dr R D Sweet: No.

Dr P R Montgomery: What about the exclusion of myxœdema in this case?

Dr J Savage: Before the discussion started I passed the time looking at Marshall's new book, and there is a picture in that of a similar facial condition due to the use of brilliantine.

REFERENCE
Marshall J (1960) Diseases of the Skin. Edinburgh and London