ACQUIRED ICHTHYOSIS IN HODGKIN'S DISEASE

BY

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Involvement of the skin by either specific or non-specific lesions is a common finding in Hodgkin's disease. In a study of 156 cases Epstein and MacEachern (1937) found that 53.2% showed skin changes. A rare and interesting change is that of acquired ichthyosiform atrophy. It simulates congenital xerodermia so closely that it can be overlooked unless it is appreciated that the eruption has not been present since infancy. Ronchese (1943) first described the onset of an ichthyosiform atrophy of the skin in a patient with Hodgkin's disease eleven months before the patient's death and while he was apparently in good health. Since then Glazebrook and Tomaszewski (1944, 1947) have reported the skin change in association with cases of Hodgkin's disease and lymphosarcoma, Welch and Epstein (1952) in a case of Hodgkin's disease, and Forman (1953) in a case of reticulosarcoma. It is probable that the complication occurs more frequently than the scanty reports suggest, as it was present in the four following cases.

Case 1

A man aged 48, a steelworks gas-producer, some five months before admission began to feel weak and ill, and complained of a pain in the right loin which spread round to the abdomen. He vomited occasionally and was troubled with morning diarrhoea, sometimes three to four loose stools after rising. There had been a weight loss of several stones in the preceding year. On several occasions in the preceding months he had been confined to bed with attacks of so-called "flu." For two months before admission to hospital he noticed that his skin had become dry and scaly (Fig. 1) but not irritable. He was adamant that he had never had a skin abnormality before this.

On examination he appeared wasted, and the skin of the whole body and face showed a dry ichthyotic change. The ichthyosis was indistinguishable from a congenital ichthyosis, though at the time no special attention was paid to whether it spared the flexures. Enlarged glands were detected in the left supraclavicular region and in the left axilla. The spleen was enlarged a handbreadth below the costal margin. Gland biopsy showed Hodgkin's disease. Histological examination of the skin showed only hyperkeratosis and atrophy. There was no sign of an infiltrate. Dark-adaptation tests gave results within normal limits.

FIG. 1.—Case 1. Showing well-marked ichthyosiform change in the skin of the arm.

The patient was included in the M.R.C. trial of R.48 and at first seemed to benefit from treatment, the glands and spleen diminishing in size. Coincident with this improvement the ichthyosis became less pronounced.

Five months later he was readmitted for transfusion, and his ichthyosis was then worse than it had been originally. He was readmitted on several occasions in the next two years, but contact with him was eventually lost. He is presumed to be dead.

Case 2

In August, 1953, I was asked to see a 52-year-old man in the Sheffield Royal Hospital, under the care of Dr. T. E. Gumpert. He had been admitted six days previously with a five-weeks history of severe diarrhoea, which had come on suddenly when on holiday in Germany and which had not been controlled with sulphaguanidine. For several weeks previous to the onset of diarrhoea he had felt listless and tired. Soon after the start of the diarrhoea the skin of his face felt tight and drawn and the skin of his body became dry and scaly.

On examination the skin of the chest and trunk was dry, was slightly erythematous, and showed large leafy scales; the facial skin seemed to be tightly stretched and was desquamating. On the limbs the appearance was identical with a moderate degree of congenital ichthyosis, though there was no sparing of the flexures. No enlarged lymphatic glands were found, or any abnormality on palpation of the abdomen.

At this stage the tentative diagnosis was a chronic dysenteric infection, and the skin change was ascribed to dehydration. Culture of stools, however, revealed no pathogens, and agglutinations were negative for salmonella. Sigmoidoscopy revealed only inflamed and oedematous mucosa, and a barium enema gave normal results. A blood count showed: Hb, 68%; red cells, 3,200,000; white cells, 4,400 (normal differential); platelets, 32,000. Marrow examination was inconclusive. The only other really positive finding was some enlargement of the hilar glands seen on a chest x-ray film and tomogram.

The course of the illness was one of uninterrupted deterioration. The haemoglobin and platelets fell, and extensive purpura developed shortly before the patient died, one month after admission. A tentative diagnosis of Hodgkin's disease, based on the ichthyotic skin change, the discovery of the enlarged hilar glands, and the course of the illness, was reached before his death.

Necropsy.—The relevant findings were enlargement of the glands at the base of the neck and in the mediastinum. These showed a grey uniform cut surface and were rather soft. The lungs and bronchi were not involved. Many whitish nodules were present in the omentum, which was almost devoid of fat; in the wall of the jejunum and in the wall of the ileum were firm masses made up of nodules aggregated together. They were firmer and more rubbery than the mediastinal glands. The aortic glands, and particularly those in the portal fissure and around the pancreas, were enlarged and firm. The liver showed a whitish mottling and at one point appeared to be infiltrated. The spleen was small and fibrotic. On macroscopic examination there was still some doubt about the nature of the nodules in the jejunum and ileum, which resembled carcinomata. Histological examination showed that there were deposits of sclerosing Hodgkin's disease in all coats of the bowel. The lymph nodes from the portal fissure, and the liver and spleen, showed recognizable Hodgkin's disease. The mediastinal nodes were less characteristic, and in some areas resembled an undifferentiated malignant neoplasm. The pathologist, Dr. J. L. Edwards, was confident, however, that only one pathological condition was present—Hodgkin's disease. Section of the skin showed similar findings to the first case—hyperkeratosis, with atrophy of the remainder of the skin elements and no evidence of infiltration in the dermis.

Case 3

An old-age pensioner of 67 had suffered for two years from an eczematous eruption on the feet and ankles. Some four months before he attended hospital he had developed hard painless lumps on the skin of the shoulders and chest. He had not lost weight nor did he feel unwell.

On examination a well-marked ichthyosiform change was present on the skin of the face, trunk, and limbs. This did not spare the flexures. He was uncertain how long the dry scaliness had been present, but was sure it was of recent onset. Multiple skin tumours of firm consistency and a reddish-purple colour, varying in size from a pea to a golf

FIG. 2.—Case 3. Showing multiple skin tumours on the trunk.

ball, were present over the shoulders, chest, upper abdomen, and thighs. Enlarged glands were found in the neck and the supraclavicular axillary and inguinal regions. The liver and spleen were not palpable. Skiagrams of the chest showed no mediastinal glands. Marrow puncture and blood count revealed no abnormality.

In view of the ichthyotic change, the nodules were presumed to be due to Hodgkin's disease rather than

secondary carcinomata, and this was substantiated by the histological findings of a reticulosarcoma of Hodgkin's type.

Case 4

An 85-year-old woman complained of painless lumps appearing on the back of her neck some two months previously. After discovering those lumps she had noticed others on the trunk.

Examination showed a dusky-red nodular tumour on the back of her neck and another below her left ear. Less obvious smaller nodules were present over the left parotid region and the trunk. No enlarged lymph nodes were found, nor was there demonstrable enlargement of liver and spleen. On the trunk was a mild generalized ichthyosis which she said was of recent onset. The nodules were obviously either secondary carcinomatous deposits or some form of reticulosis. The presence of the ichthyosis suggested the likelihood of the latter, and histological examination of a neck nodule showed a reticulosis of mycosis fungoides type. The nodules failed to respond to radiotherapy or triethylene melamine, and she died two months after admission to hospital.

The significant findings at necropsy were nodular plaques of greyish-white tissue on the lateral thoracic wall and on the lung beneath the pleura. The mediastinal lymph nodes were enlarged. More neoplastic nodules were present on the peritoneal surface of the small and large intestine and in the tail of the pancreas, and the mesenteric lymph nodes were massed together and enlarged. Another greyish-white mass was seen to surround the pelvis, ureter, and inferior pole of the right kidney, and more were present on the posterior wall of the uterus and in the broad ligaments. The liver and spleen showed no macroscopic change. Sections from the affected organs showed deposits of large pleomorphic neoplastic cells characteristic of a reticulosarcoma.

Discussion

In the present series of cases no light has been thrown on the mechanism of production of this curious skin change, but it seems probable that it falls into the group of non-specific skin changes, a great variety of which are known to occur in Hodgkin's disease and allied reticuloses.

In Case 1 the ichthyosis did improve during a remission of the Hodgkin's disease whilst under treatment with R.48, and

this suggests a close association between the presence of Hodgkin's tissue and the skin change. Similar improvement was reported by Welch and Epstein when their patient was given x-ray therapy. Vitamin A was being given at the same time, so there is also a possibility that this played some part in the improvement. A disorder of vitamin A metabolism due to liver damage was suggested by Glazebrook and Tomaszewski as the cause of ichthyosis, but in Forman's case blood vitamin A studies were normal, and in my Case 1 dark-adaptation tests were normal.

If the ichthyotic change were due to liver damage alone one would expect to find it in other types of severe liver disease, and such is not the case. Also, it does not occur in association with secondary carcinomatous damage to the liver.

The onset of the ichthyotic change occurs early in the course of the disease and before there has been any appreciable wasting, so that mere inanition is not the cause.

From a practical point of view acquired ichthyosiform atrophy is a rare change, but it may be of value when the diagnosis of Hodgkin's disease is in doubt, as in Case 2. It is not easily differentiated from congenital ichthyosis, though my impression is that the acquired type affects the trunk and face more than the limbs, and, also, it does sometimes involve the flexures, which are usually spared in the congenital variety. Histologically there is no difference.

The onset of an ichthyotic eruption in an adult should certainly initiate a search for an underlying lymphoblastoma.

Summary

Four cases of an acquired ichthyosis associated with Hodgkin's disease and reticulosarcoma are described. The importance of investigating cases of acquired ichthyosis for underlying Hodgkin's disease or lymphoblastoma is stressed.

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The Victoria Cross awarded to Surgeon-Major Edmund Baron Hartley in 1879 was acquired for the record sum of £300 by the Royal Army Medical Corps when it came up for auction in London on March 17. Hartley, the son of a Devonshire doctor, was born in 1847 and qualified from St. George's Hospital in 1874. He then became district surgeon in Basutoland. In 1877 he joined the Cape Mounted Rifles as surgeon, becoming principal medical officer in the following year, and subsequently colonel in command of the Cape Medical Corps. He served in several campaigns during the Zulu war of 1877-9, and in the Boer War. He was decorated with the Victoria Cross for the conspicuous gallantry he displayed on June 5, 1879, in attending the wounded under fire at the unsuccessful attack on Morosi's Mountain, Basutoland. Other awards to Hartley included in the sale were the Cape General Service Medal with three bars (only thirteen other recipients of this medal and three bars are known), the Queen's South Africa Medal with three bars, and the King's South Africa Medal with two bars. He was appointed C.M.G. in 1900; he died on March 20, 1919, in his seventy-second year.