FOETAL VACCINIA

BY

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This paper presents a case of vaccinial infection in the foetus, the second known to have occurred.

Generalized vaccinia in the foetus has been recognized only once before. Lynch (1932) described a prematurely born child showing clinical and pathological features very similar to the present case. Lynch made a thorough survey of the literature on foetal skin disease, especially on foetal variola, in order to establish his diagnosis of foetal vaccinia. He discovered 47 reports of variola in the foetus but no previous instance in which vaccinia was recognized. Others (Vignes, 1942) also failed to find any report of foetal vaccinia, and Ballantyne (1902) in his classical monograph on foetal disease stated that 'an infant has never been born carrying a vaccination pustule upon its skin, as a result of the vaccination of the mother'. We have been unable to trace any record of a case of foetal vaccinia since Lynch's report.

Lynch quoted 11 reports of single cases described as foetal variola without variola in the mother, including one by Jenner. In three of the reports the author did not state that the mother had been in contact with a case of smallpox. In none of the cases was the possibility considered that the foetal disease might be due to vaccinia though in several it was mentioned that the mother was recently vaccinated. It seems possible that at least some of these may have been unrecognized instances of foetal vaccinia.

Clinical Record

Between March 26 and April 1, 1950, 18 cases of smallpox occurred in the vicinity of Glasgow. This outbreak caused considerable alarm among the local population and in consequence nearly half a million people were vaccinated during the first three weeks of April (Laidlaw and Horne, 1950). One of these was an unmarried woman aged 19 years who was working on a farm in Lanarkshire. She was about three months pregnant at the time of vaccination and she had never been vaccinated before. She developed a severe primary vaccination reaction with a large area of redness and induration and with considerable general upset of health so that she could not do her work for two or three days. Eleven weeks later she was spontaneously delivered of a live premature infant, who was thus of about six months' gestation.

She had given birth to a normal healthy child 18 months before the present child was born. With the exception of the vaccination reaction she had been perfectly well during the pregnancy and she had a normal puerperium without fever or abnormal lochia. After delivery she and her child were admitted to Strathclyde Infectious Diseases Hospital, Motherwell, where her blood Wassermann reaction was found to be negative; a blood culture was sterile, and a blood white cell count was normal.

The child was examined three and a half hours after delivery. He was a cold, hydropic premature infant and was whining feebly. About 25% of the body surface was covered with multiple, discrete and confluent, circular and umbilicated, greyish white, sodden lesions, with no surrounding erythema. The child's blood was sterile on culture and blood Wassermann and Kahn reactions were negative. He died 15 hours after birth.

Necropsy Findings

A necropsy was performed five hours after death. The body was that of a premature male infant weighing 1,090 g. and estimated to be under seven months' gestation. The skin lesions were extensive. That over the left side of the face was circular, centred at the inner third of the zygomatic arch and extending anteriorly to the middle of the eyelids on that side and posteriorly to the pinna and tragus. The edges were scalloped and raised. The skin of the lesion was light in colour and necrotic. Underneath it was some caseous material on a granulation foundation. The necrotic part was easily removed. Similar lesions were seen on the outer aspects of both arms and to a lesser extent on the forearms. There was a small patch on the upper inner aspect of the right thigh and a large asymmetrical lesion covered most of the back from the neck to the level of the first lumbar spine. Smaller oval lesions were present over the epigastrium and in the midline of the abdomen above the umbilicus. There were no lesions

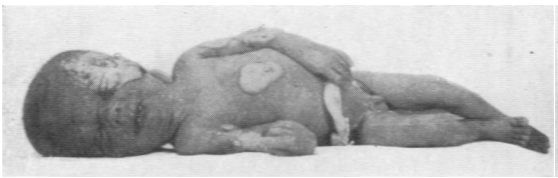

FIG. 1.—Frontal view of infant showing the cutaneous lesions.

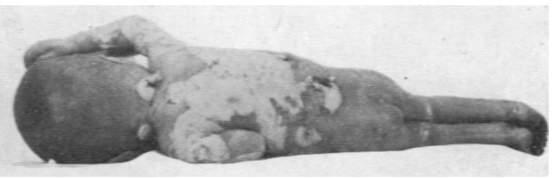

FIG. 2.—Back view to show the greater extent of the cutaneous lesion when compared to the front.

on the palms or soles or round the anus (Figs. 1 and 2).

Many blocks from the skin were made and cut. There was massive necrotic cellulitis with some fibrosis in the corium and re-epithelialization at the centre of the lesion (Fig. 3). Most of the deeper necrotic foci were strikingly limited to the hair follicles (Figs. 4 and 5). The skin epithelium was either completely denuded or thickened with long prolongations into the corium. The cellular reaction was mainly mononuclear in type similar to that seen in other virus infections, but large numbers of eosinophils were also seen. No bacteria were observed in Gram-stained sections. Tissue stained for virus bodies by Lendrum's (1947) phloxin-tartrazine method showed highly refractile eosinophil inclusion bodies (Fig. 6). The umbilical cord was attached and healthy and histologically normal.

The brain was primitive. No gyri had been formed and its total weight was 123 g. There was an extensive ventricular haemorrhage which had originated from the veins lying between the thalamus and the lentiform nucleus. A block was made from the cerebral hemisphere including the middle part of the ventricle and others from the thalamus, pons, cerebellum and medulla. Sections from these showed normally developing brain and no virus bodies were detected.

The mouth was clean and the larynx and trachea were normal. The lungs were poorly expanded and the pleural surfaces were normal. On cutting the right lung a firm white area, 1 cm. in diameter with an indefinite margin, was found in the lower lobe posteriorly, and next to it beside a small bronchus was a smaller red focus. Elsewhere no lesion was found. Histologically there was considerable atelectasis and many alveoli contained amniotic debris and so-called vernix membranes. Next to a small bronchus there was a lesion with a massive necrotic centre, in which calcium could be demonstrated by Von Kossa's method, bounded by granulation tissue (Fig. 7). No bacteria were seen in sections stained by Gram's and Ziehl Neelsen's methods. Lendrum's phloxin-tartrazine method showed aggregations of virus particles identical with those seen in the skin.

The thymus appeared normal to the naked eye but microscopically large numbers of eosinophils were seen mainly in the connective tissue septa. The heart was normal, weighing 5 g., and its histology was normal. The oesophagus, stomach and intestines presented no abnormality but there was a moderate infiltration of eosinophils into the epithelium of the colon. The spleen weighed 6 g. and the liver 70 g.; they were within normal limits of size, shape and colour, and both of these organs histologically presented a picture of extensive haemopoiesis compatible with the age of the foetus. No virus bodies were recognized. The gall bladder and ducts were normal. The adrenals were normal. The pancreas appeared normal; histologically, haemopoiesis was present and the impression was formed that eosinophil myelocytes were relatively increased. The kidneys were of equal size weighing 11 g. together. No lesion was seen by the naked eye, and histologically there was extensive haemopoiesis. A section through the end of a rib showed normally developing bone and marrow.

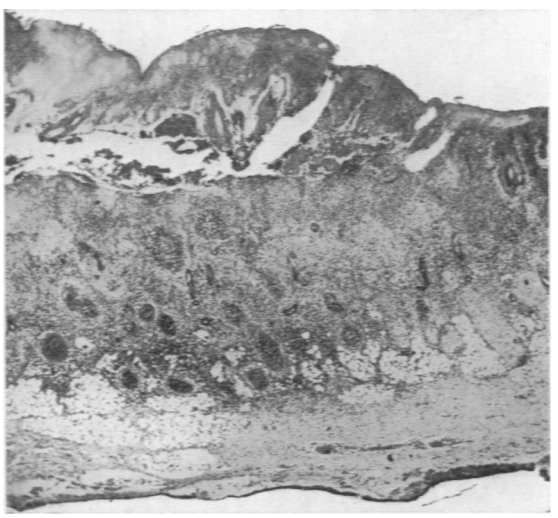

FIG. 3.—Section of skin lesion to show the necrotic cellulitis, re-epithelialization at the centre of the lesion and the necrosis of the hair follicles. Haemotoxylin and eosin × 20.

Discussion

It is claimed that the clinical and pathological features in this case justify the diagnosis of generalized foetal vaccina. The mother is known to have reacted strongly to the vaccination and the systemic upset must have been considerable to force her to take to bed in the spring-time, because she was a strong, healthy woman employed as a farm labourer. She bore a large recent vaccination scar on the left shoulder.

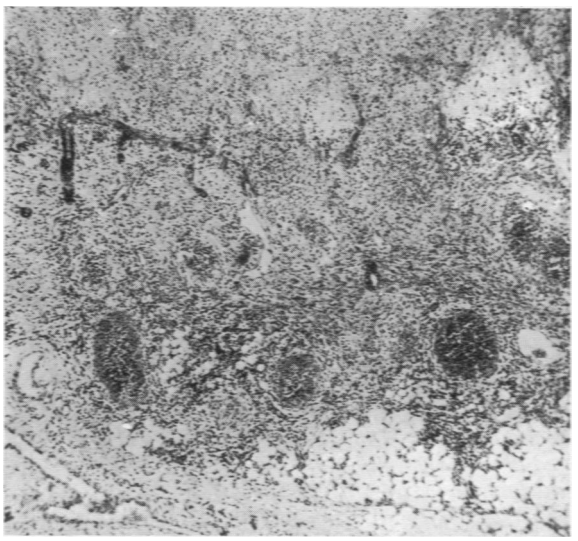

FIG. 4.—Higher power view of the corium to demonstrate the surface necrosis and the hair follicle lesion with early re-epithelialization. Haematoxylin and eosin · 40.

Successful vaccination is accompanied by viraemia and from this woman the infection must have spread to the foetus in one of four ways: first, directly from the maternal bloodstream to the foetus by traversing the placental barrier. It has often been claimed that if a woman is vaccinated late in pregnancy she may transmit a certain amount of immunity to her child and many children born to such mothers cannot be successfully vaccinated, or give an immune response when vaccination is attempted during the neonatal period (Ballantyne, 1902). If it is accepted that in vaccinia the foetus may develop active immunity *in utero*, the foetus must be invaded by the virus about the same time as the maternal viraemia or it would become immune with the mother and therefore very unlikely to suffer disease if later attacked by the virus. Much depends on whether maternal immunity to vaccinia is transferred to the foetus or is not; unfortunately published opinion is divided on this point. It cannot be assumed that once foetal infection has occurred the incubation period of the transplacental infection is the same as that which follows inoculation of the skin. Mothers with variola have been delivered of children with a typical variola rash

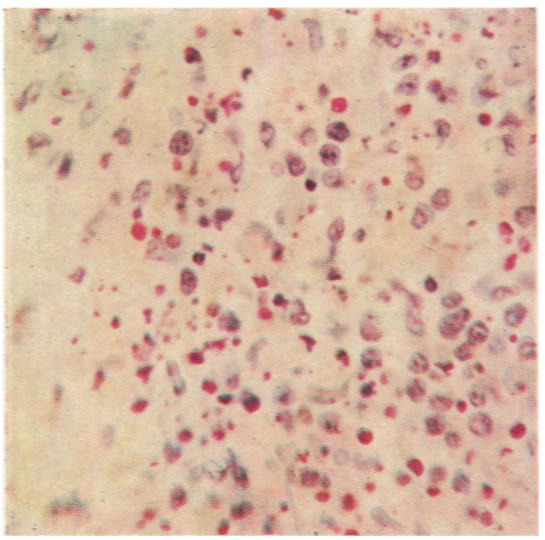

FIG. 5.—A hair follicle, to show the necrosis and the surrounding cellular reaction including many eosinophils. Haematoxylin and eosin × 150.

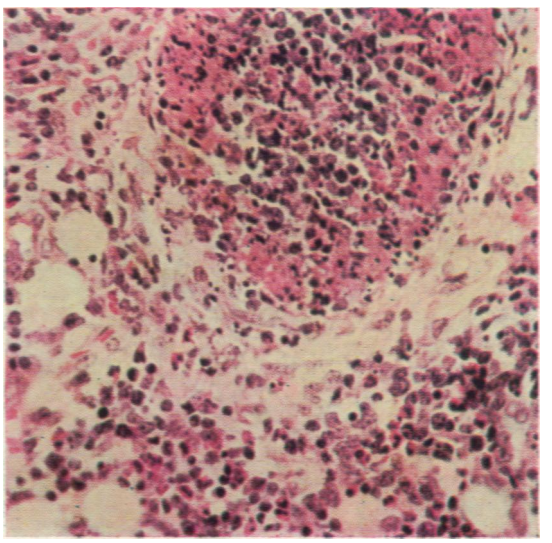

FIG. 6.—The inclusion bodies in the corium with the type of cellular reaction associated with them. An identical picture was seen in the tissue surrounding the lesion of the lung. Phloxin-tartrazine × 400.

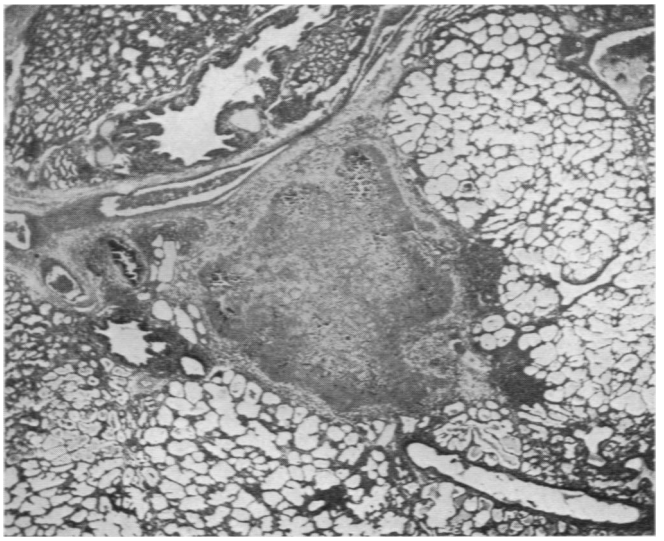

FIG. 7.—Low power view of lung lesion. Even with this stain the presence of calcium can be detected. Haematoxylin and eosin · 20.

at periods ranging from two weeks to three months after the maternal eruption and the same may well occur in vaccinia.

Second, maternal viraemia may have led to a metastatic lesion or lesions in the placenta and subsequent invasion of the foetus from this lesion. The foetal disease would then occur later than the maternal infection and it thus must be assumed that the foetus did not acquire immunity synchronously with the mother's immunity.

Third, the placenta and the membranes could develop a general infection, like the allantoic sac of an experimentally infected fertile hen's egg, bathing the foetal skin with infected amniotic fluid. There is no evidence that this did occur because unfortunately the placenta and membranes were not seen and could not be obtained for examination. Nevertheless there is indirect evidence that tends to favour this hypothesis. The skin lesions are very irregularly distributed but are most widespread on the extensor surfaces where the massage effect is greatest and the inflammatory reaction is maximal at the roots of the hair follicles in the corium, possibly indicating that the virus entered through these channels from the surface of the body by a means similar to inunction. Furthermore it seems possible that the lesion in the lung is not blood-borne but due to direct contact with the infected amniotic fluid during foetal respiratory movements. However, Professor A. W. Downie kindly drew our attention to the magnificently illustrated monograph of Ricketts and Byles (1908) in which the effect of mechanical trauma to the skin during the incubation period of smallpox has been extensively studied and depicted. These authors show that in smallpox mild irritation of the skin can determine the site of a very profuse crop of lesions or even a confluent patch. It may be that this factor determined the irregular distribution of the lesions in the present case.

The fourth hypothesis is purely conjectural and is put forward for completeness and because it might help to explain why generalized foetal vaccinia is such a rare condition though there must have been many women who were vaccinated during pregnancy. The woman was about three months pregnant when vaccinated. She was unmarried. She had already one other child to provide for. Presumably this pregnancy was unintentional and the child unwanted. Furthermore during the period of viraemia she was ill, unfit for work, and probably depressed. It is possible that she attempted abortion at this time, and by damaging her own tissues opened up blood vessels which transmitted the virus in her blood to the amniotic cavity. If this series of events occurred the condition described in our second hypothesis could occur but synchronously with the maternal viraemia and before the foetus could have acquired immunity from the mother.

The time factor is difficult to assess. The granulations of the skin had been present for a period of weeks and the time required for calcium to form in the lungs may be estimated in similar units. Inclusion bodies were not found in any tissues other than the skin and lungs. We believe that the infection of the foetus may have come from infected amniotic fluid, but in the absence of the placenta and membranes final proof of this is lacking. The rarity of the condition may be due to the sequence of events in our fourth hypothesis or it may be that abortion normally follows in almost all cases where vaccination of the pregnant woman leads to viraemia in the foetus.

Summary

A description is given of the clinical and pathological findings in a premature infant born three months after the primary vaccination of the mother. It is claimed that the child was infected with the virus of vaccinia *in utero* and was born suffering from generalized congenital vaccinia. Previous reports of a similar condition were sought and only one other example of the disease has been found.

The pathogenesis of the condition is discussed in the light of the present case and the rarity of this complication of vaccination is emphasized.

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