THE SCHÖNLEIN-HENOCH SYNDROME AND COLLAGEN DISEASE

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The clinical manifestations of the Schönlein-Henoch syndrome as described in articles by Gairdner (1948), Davis (1948) and other writers, are a typical exanthem, colic, haematuria, articular and periarticular swellings, and a liability to develop nephritis. Gairdner drew attention to the possible relationship between this syndrome, acute nephritis, rheumatic fever and polyarteritis nodosa.

It is proposed to record 35 cases occurring in children between 4 and 13 years old who have been in-patients at Alder Hey Children's Hospital, Liverpool. For convenience these 35 cases will be considered in two groups: Group A, comprising 14 cases admitted between 1944 and 1947, and Group B, comprising 21 cases admitted between 1948 and the end of 1950. Those in the second group were more extensively investigated and their progress has been closely followed.

In addition, it is proposed to describe four atypical cases which have features in common with the syndrome and also appear to be diseases of the collagen system.

Clinical Manifestations of the Typical Cases

At the time of admission to hospital the typical exanthem was present in 11 of the 14 earlier cases: in the remaining three abdominal colic was the initial symptom and the rash appeared from one to 21 days later. Of the 21 cases in Group B the rash was present at the onset in 20 and occurred subsequently in the other case. Of the total 35 cases in both groups, 19 patients had complained of a sore throat before admission to hospital and one child had had ulcerative stomatitis. Twenty-six children had abdominal colic; all had anorexia and were drowsy or listless. Blood was passed per rectum in 11 cases, and in one of these an acute abdominal condition had been diagnosed on admission and laparotomy performed. Amongst the earlier cases (Group A) only three had joint

manifestations, whereas of the 21 more recent cases (Group B) 17 had pain and swelling around joints, the ankles, knees and wrists being most commonly affected. A puffy swelling of the backs of the hands was frequently observed.

The rash in all cases was distributed over the extensor surfaces of the elbows, the dorsa of the feet and ankles and on the buttocks. Red macules appeared early varying in size and frequently tending to spread: they later became darker in colour, almost semi-necrotic, and eventually faded leaving brown staining which was visible for many days, especially on the front of the ankles. In more than half of the recent cases a small, raised, white patch was noticed on the prominent upper part of the antihelix (Fig. 1); this later became reddened and necrotic, finally leaving a brown scab. The phenomenon did not seem to be directly related to pressure of the head on the pillow.

FIG. 1.—Papule on antihelix.

Aetiological Factors

Of the 21 later cases (Group B) a careful history was taken to explore the pathogenesis.

The possibility of a food sensitivity was investigated but in no instance was there any definite indication. One child was thought by the relatives to be 'sensitive' to grapes, but she was discovered eating some after a visiting day and there were no untoward effects. Skin tests (Bencard) were carried out in five cases: one child gave a positive reaction to potato and another to tomato. The former child had several relapses of the condition which were not prevented by the exclusion of potato from her diet, and the other ate tomatoes while in hospital without, apparently, any ill-effects.

Special consideration was given to the suggestion that there might be an acquired sensitivity to sulphonamides, the subsequent exhibition of which might provoke the syndrome. Only two children had a history of having received sulphonamides shortly before admission to hospital and in one of these the drug had been given only after the rash had appeared. Sulphonamides given during the observed course of the illness did not precipitate a relapse of the syndrome nor seem to lessen the symptoms.

The relationship between the onset of the syndrome and an infection with a haemolytic streptococcus was suggestive as this organism was isolated from the throat swabs of 15 of the 21 cases in Group B; some of these organisms were typed but the findings lacked uniformity, types 6, 12 and 25 being encountered in the three cases in which this investigation was carried out. Half the cases in Gairdner's series were also associated with haemolytic streptococcal infections.

A particularly close relationship was found between throat infections and relapses of the condition. Seven children had recurrences of the rash: from three of these children, who each had two relapses, haemolytic streptococci were cultured at the time of each relapse, but this organism was not found during the symptom-free intervals. The interval between the onset of the sore throat and the appearance of the rash was noticeably shorter in the recurrences than in the original attack. This occurred in six of Gairdner's 12 cases and might be claimed as support for the theory that the condition is of an allergic nature; the alternation of symptoms, which was observed in those who had recurrences, might also support such a supposition.

Pronounced histamine sensitivity was found in some cases, a solution of histamine in as great a dilution as 0.0003 mg. ml. producing a positive skin reaction.

Treatment

Dietetic measures were directed towards the exclusion of substances to which skin tests have positive results, but without lessening the severity of the symptoms or, apparently, preventing recurrences.

When evidence of a throat infection was present, or when haemolytic streptococci were isolated from the throat swabs, courses of systemic penicillin were given. Three patients, in whom the syndrome recurred more than once and was associated with haemolytic streptococci in the throat swabs, were submitted to tonsillectomy. Two of these children had no further attacks of the syndrome after this operation.

Certain anti-histamine drugs (benadryl, antistin, anthisan, phenergan and thephorin) were used, variously, in 18 of the 21 cases in Group B without benefit.

Prognosis

Of the 21 cases which have occurred since 1948 (Group B) all are alive and appear well. Recurrences have, however, been frequent and one child has had five within two years. Albuminuria has been the commonest sequel. This has occurred in three cases since other manifestations ceased. One child had albuminuria for 18 months after the onset of the condition but subsequently her urine has remained clear: at no time has there been a rise in blood pressure or nitrogen retention. None of these children has developed clinical evidence of carditis or any change in the electrocardiogram.

Four Atypical Cases

All of the 35 cases described above conformed to a similar pattern and were of a comparatively mild nature. The Schönlein-Henoch syndrome has, however, been described as one of a 'family of diseases', another member of the family being polyarteritis nodosa. Harkavy (1950) has linked together lupus erythematosus, dermatomyositis, polyarteritis nodosa and the Schönlein-Henoch syndrome with nephritis, as presenting common features referable to disease of the collagen system. Four children, in addition to the 35 described, presented clinical manifestations of the Schönlein-Henoch syndrome but later developed graver aspects of collagen disease.

Case Reports

Case 1. Rodney McM., aged 5½ years, was admitted to Alder Hey Children's Hospital with a purpuric eruption on the face, palms of the hands and buttocks.

There was a history of a morbilliform rash two months previously and he had also had attacks of asthma and bronchitis. The onset of the exanthem was accompanied by prostration, swelling of the wrists and knees, haematuria and severe colic with blood-stained diarrhoea. The skin over the sacrum became gangrenous (Fig. 2) and albuminuria developed. The child remained very ill for 14 weeks and more than once seemed likely to die: after a blood transfusion, however, his condition slowly improved. A muscle biopsy showed diffuse inflammatory changes, frequently perivascular in distribution, with occasional areas of necrosis of the walls

FIG. 2.—Gangrenous area over sacrum.

of small vessels (Figs. 3 and 4). No nodules were found, there was no evidence of peripheral neuritis, and the optic fundi showed no changes: there was, however, considerable emaciation with persistent tachycardia and recurrent attacks of severe abdominal pain. The urine eventually cleared and the skin healed. The

FIG. 3.—Muscle biopsy (H. and E. $\times 125$) showing diffuse inflammatory infiltration.

FIG. 4.—Muscle biopsy (H. and E. $\times 600$) showing partial necrosis of vessel wall and overlying thrombus.

child was discharged after five months in hospital when his condition had considerably improved. He has been observed as an out-patient for a year and continues to make good progress: the skin now appears normal except for a scar over the sacrum.

This child presented as a severe case of the Schönlein-Henoch syndrome, but, as shown in Figs. 3 and 4, vascular involvement indicates a relationship to polyarteritis nodosa. Werlhof's purpura haemorrhagica has been excluded by a normal blood platelet count. This case resembles two of the three cases described by Sheldon (1947) in which there were purpuric patches with black haemorrhagic centres which eventually left permanent scars on the buttocks; these he called purpura necrotica.

Case 2. Jeanette D., aged 15 years, was admitted to Alder Hey Children's Hospital with a history of swelling of joints and a purple rash on the arms and legs, both of which manifestations had been present from time to time during the previous three years. At the age of 12 years she had been diagnosed as a case of erythema nodosum and her joint symptoms had been attributed to acute rheumatism. A skin biopsy, however, then showed the appearances of disseminated lupus erythematosus. Latterly she had been found to have tender nodules on the forearms and also on the chest wall. A more recent muscle biopsy showed panarteritis with thrombosis and

recanalization (Fig. 5), together with cellular infiltration of the vessel walls.

The urine was consistently normal and there was no clinical or electrocardiographic evidence of carditis.

This child showed an extensive collagen involvement and the histological evidence supports the theory that disseminated lupus erythematosus and polyarteritis nodosa may co-exist. A similar case has been described in the 'Case Records of the Massachusetts General Hospital' (Mallory, 1938) and this relationship has also been stressed by other writers, including Banks (1941), Krupp (1943) and Harkavy (1950).

Case 3. Beryl R., aged 9½ years, was admitted to Alder Hey Children's Hospital with a widespread rash over the trunk and limbs resembling papular urticaria (Fig. 6). This rash changed rapidly in configuration, being at times indistinguishable from erythema marginatum. Abdominal colic and haematuria were present from the onset and recurred eight times in 12 months. It was noticed that the haematuria was most severe when the rash was extensive and at these times the child was drowsy and irritable. The blood sedimentation rate remained consistently very high, figures of the order of 60 and 120 mm. (Westergren) in the first hour being recorded. There were no joint

FIG. 6.—Widespread eruption (Case 3).

manifestations and the heart sounds remained normal, and there was no abnormality in the electrocardiogram. A muscle biopsy did not show any abnormality of the larger vessels. It was found that there was a marked sensitivity to histamine, a positive skin test being obtained with a solution of 0.0003 mg. ml.

This was the only case in the whole of the series that showed any response to the anti-histamine drugs: it was found that phenergan, 25 mg. t.d.s., lessened her symptoms.

Two years after the onset of her illness the child is still being observed as an out-patient, and the rash still appears at intervals, although to a less marked degree; she also has a persistent albuminuria.

Although in this case the rash was not typical of the Schönlein-Henoch syndrome, its coincidence with abdominal pain and haematuria suggests a relationship with that condition. There were, moreover, many recurrences and at one and the same time she presented the urinary findings of nephritis and a rash then conforming to the marginal erythema of acute rheumatism.

FIG. 5.—Muscle biopsy (H. and E. $\times 750$) showing panarteritis with thrombosis and recanalization.

Case 4. Brian J., aged 13 years, was admitted with a rash on the front of the legs which first resembled erythema nodosum, but later faded and was replaced by a rash similar to that characterizing the Schönlein-Henoch syndrome. He also had joint pains and developed severe abdominal colic with vomiting of blood. Surgical opinion was sought and it was decided to perform a laparotomy. When the small intestine was examined petechial haemorrhages were observed in the wall of the gut and also in its mesentery; no other abnormality was found. Albuminuria was present on the day of operation and continued from that time. The blood pressure rose steadily reaching 175/150 mm. Hg. He gradually became more drowsy, convulsions supervened, and he died in uraemia six weeks after the onset of the illness.

Post-mortem examination showed marked hypertrophy of the myocardium. The macroscopic appearances of the kidney were those of polyarteritis nodosa and, histologically, were interpreted as polyarteritis nodosa with acute hypertensive changes (Fig. 7).

This patient's earlier manifestations could be identified with those of the Schönlein-Henoch syndrome but the subsequent events indicated the development of polyarteritis nodosa with renal ischaemia and hypertension. This case supports the view that the Schönlein-Henoch syndrome and polyarteritis nodosa are closely related members of the family of collagen disease.

Summary

Thirty-nine cases of collagen disease in children are reported, 35 of these being typical of the Schönlein-Henoch syndrome. Four further cases

FIG. 7—Kidney (H. and E. $\times 9$) showing patchy infarction of cortex.

are described in greater detail. The aetiology and prognosis are considered.

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