MILK ALLERGY AND HAEMETEMESIS

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Allergy to cow's milk preparations has been known and reported on for many years (Abt, 1912), although prior to 1958 it was still regarded as a rare occurrence in the United Kingdom (Davies, 1958). However, although many papers have been written on the subject, few authors apparently found frank haemetemesis as a presenting symptom. This paper presents such a case and reviews the literature on the various aspects of the subject.

CASE REPORT

C.B.K., a Chinese girl, was first seen at the age of 5 months, on 25th October 1968 with a complaint of having vomited blood clots on two occasions in the two days prior to admission. She had also vomited milk once one week previously. She was the second of two children; had a normal delivery, birth weight 5 lbs. 11 oz. She had been breast fed for one and a half months and was then fed with condensed milk.

On examination, she was pale, weight 13 lbs. 2 oz. Otherwise there were no abnormal clinical findings. Laboratory results revealed a haemoglobin of 6.9 gm.%, total white count of 12,000, platelets 270,000. Bleeding time was 3½ minutes, prothrombin time 18 seconds, compared to a control of 16 seconds. She was given a blood transfusion of 125 cc. For two days after admission, she vomited the milk feeds that were given her and 4 days after admission, she had one bout of haemetemesis. After that she had vomiting on and off but had no diarrhoea. Stools for occult blood was positive. A barium meal study showed no hiatus hernia and no other abnormality of the upper gastrointestinal tract. She was discharged on 5.11.68 with a provisional diagnosis of gastritis.

However, she was readmitted one week later, on 12th November 1968 after another bout of haemetemesis. While being examined, she vomited out dark red blood clots mixed with milk curds. She was pale. Haemoglobin 6.7 gm.%; stools were positive for occult blood. Partial thromboplastin time was 80 seconds (normal range 100 seconds or less). She continued to vomit the milk feeds on and off while in the ward, and had a few bouts of haemetemesis. Liver function tests showed alkaline phosphatase 21.2 units, thymol turbidity 2 units, serum albumen globulin ratio of 4.1 : 2.5 gm.%, serum glutamic pyruvic transaminase 185 units (normal 30-110 king's units).

She was referred to the ENT Surgeon who excluded any ENT abnormality or source of bleeding. On 28.11.68 she was referred to the surgeons who did a laparotomy and found the liver only slightly enlarged, but normal looking. Gastrostomy was done and generalised oozing of blood from the gastric mucosa was found; there was no definite bleeding point. Biopsy of the liver was normal.

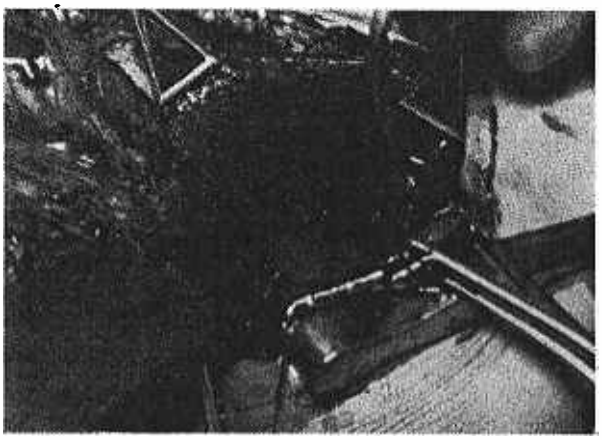

Fig. 1. Haemetemesis and gastritis.

After the operation, she continued to have haemetemesis on and off and the haemoglobin continued to be rather low, around 9 to 10 gm.%, dropping to 7.3 gm.% on one occasion requiring blood transfusion. Stools for occult blood continued to be positive. For a time she was given injection Hesna daily (a "multiple hemostatic" containing methylhesperidin, vit. C and menadiol or vit. K) and "Premarin", (an Ayerst Laboratory product, containing "conjugated oestrogenic substances" for which the indication was "capillary bleeding") with the hope that these "hemostatics" might reduce or stop the bleeding. She developed an urticarial rash and was taken off these drugs.

On 21.2.69, she was taken off milk feeds and given SOBEE instead. SOBEE, a Mead Johnson product, is a milk-free soya preparation. There was no vomiting at all and stools for occult blood became negative. Within five days,

her haemoglobin had climbed up from 11.1 gm.% to 12.3 gm.%.

On 7.3.69, she was taken off SOBEE and challenged with milk. That night, she vomitted out the milk together with some blood. She had another bout of haemetemesis on 12.3.69 while still on milk feeds. She had four times loose stools the day after being put on milk feeds and her stools were positive for occult blood. Her haemoglobin dropped from 12.3 gm.% to 10.8 gm.%.

On 13.3.69, her feeds were again changed from milk to SOBEE, and during the period she was on SOBEE (13.3.69 to 18.3.69) there was no vomiting at all; stools for occult blood were negative; haemoglobin around 11.2 gm.%.

On 19.3.69, she had her second milk challenge. That afternoon, she vomited out milk two times. The next day, she vomited out blood. Her stools for occult blood was positive. A few days later, she had another bout of haemetemesis.

From 23.3.69 to 26.4.69, she was put back on SOBEE. However, during this period, she had vomiting three times. Her stools were negative for occult blood and her haemoglobin came up from 10.2 gm.% to 12.1 gm.%. During this period, we took a sample of blood for antimilk antibodies which was found to be negative.

From 27.4.69 to 29.4.69 she was on milk feeds, and vomited two times. Stools were positive for occult blood. Blood sample for antimilk antibodies was negative and so was a stool sample.

On 13.5.69 she was again put on milk feeds. She vomited two times that day and continued to vomit daily for the next three days; on the 15th she vomited six times. However, there was no haemetemesis. Stools for occult blood was positive; her haemoglobin fell from 11.1 gm.% on 13.5.69 to 9.7 gm.% on 24.5.69. A sigmoidoscopy done during this period showed no abnormal findings. She was finally taken off milk and put back on SOBEE and slowly weaned.

DISCUSSION

Diagnosis

To aid in the diagnosis of milk allergy, Goldman *et al* (1963) postulated a concise set of criteria:—

1. The symptoms must subside after milk elimination from the diet.
2. The symptoms occur within 48 hours following a trial feeding of milk.
3. Three such challenges must be positive and similar as to onset, duration and clinical features.
4. Symptoms must subside following each challenge reaction.

The case we present fulfills most of the criteria set up above. The baby presented with haemetemesis, which recurred during the first two milk challenges. At no time during the periods she was on SOBEE (a milk-free soy-product) did she have haemetemesis. During the first two challenges, she vomited out blood within 12 hours of the introduction of a full-cream cow's milk preparation into her feeds. However, it must be pointed out that the four milk challenges did not produce exactly the same clinical features as suggested by the set of criteria by Goldman *et al.* Only the first two milk challenges produced haemetemesis—the third and fourth challenges caused only vomiting of the milk feeds; and although there was no vomiting at all while the child was on SOBEE before and after the first milk challenge, she did vomit SOBEE between the other challenges. However, it is to be noted that for a period of more than a month while she was on SOBEE, she vomited only three times, whereas during the fourth milk challenge, she vomited out her milk feeds daily for the first 4 days, with a total of eleven bouts of vomiting. Also, although there was no haemetemesis during the third and fourth milk challenges, her stools were consistently positive for occult blood, which was negative while she was on SOBEE feeds. It is also to be noted that her haemoglobin level dropped during her milk challenges. As a word of caution, it should be borne in mind that babies may go into shock while on milk challenge (Gryboski, 1967), although this did not happen in our case.

Other laboratory procedures can only be confirmatory and will be discussed below.

Incidence

As quoted by Davies (1958), Collins-Williams in 1956 found an incidence of 0.3%, while Clein (1951) found a much higher incidence of 1:15 (c. 7%). This range of 0.3% to 7% was agreed with by Gryboski (1967), who also thought males were affected more than females.

Age

Clein (1954) found 82% of cases presented before the fourth month. Our case presented

at the fifth month, after having been breast-fed for the first one and half months.

Symptoms

According to the literature, frank haemetemesis seems to be a rather uncommon presentation of milk allergy. Bachman and Dees (1957) found that skin manifestations e.g. eczema, was the commonest presentation, with gastro-intestinal symptoms (vomiting and/or diarrhoea) next, followed by respiratory symptoms (rhinitis and asthma.)

Gryboski (1967) found diarrhoea the predominant symptom in a review of 21 cases between 2 days old and 2½ years old. Gross mucus was present in 84%; vomiting as the first symptom occurred in 4 of the 21 cases (i.e. c.5%), with diarrhoea occurring later. The 4 cases studied by Silver and Douglas (1968) presented with vomiting and/or diarrhoea.

Davies (1958) presented a comparative chart of the symptoms in cases of milk allergy studied by various authors. This is reproduced below (Table I).

Kravis *et al* (1967) reported on a case of milk allergy with haemetemesis, saying that the site of bleeding may be from the mucosa of the large bowel giving rise to blood and mucus in the stools, or from the upper gastro-intestinal tract, causing haemetemesis.

Our case represented with recurrent haemetemesis and had no diarrhoea. She had an urticarial rash on one occasion while she was on a milk challenge.

Pathogenesis

As long ago as 1916, Schloss and Worthen commented on the permeability of the gastro-intestinal tract of infants to undigested protein. They conducted tests on 14 infants and concluded that in nutritional or gastrointestinal disorders, foreign protein may be absorbed in an undigested or partially digested state.

Clein (1954) stated that the symptoms of gastrointestinal milk allergy were explained by the usual pathological changes in allergy—i.e. oedema of mucous membrane, spasm of smooth muscle and increase in mucous secretion.

TABLE I

Author	Kane (1957)	Clein (1951)	Rosenblum and Rosenblum (1952)	Clein (1954)
No. of Cases	102	140	No. Unknown	206
Symptoms	%	%	%	%
Eczema	74	—	—	44
Vomiting/diarrhoea	20	—	15	—
Irritability, colic	37	29	5	31
Asthma	1	—	—	7
Recurrent rhinorrhoea	2	—	—	13
Vomiting	—	39	8.3	—
Diarrhoea	—	24	31.6	22
Mucus in stools	—	6	—	—
Blood in stools	—	5	—	—
Anorexia	—	4	—	3
Diarrhoea and colic	—	—	16	—
Diarrhoea, vomiting and colic	—	—	20	—
Pylorospasm	—	—	—	33
Cough	—	—	—	17
Constipation	—	—	—	4
Urticaria/angio-oedema	—	—	—	1
Apathy, cyanosis	—	—	—	2
"Very unhappy all the time"	—	—	—	19

Paterson and Good (1963) supported the work of other investigators by demonstrating the presence of antibodies to cow's milk proteins in the sera of most people who drink cow's milk. As stated by Gruskay and Cooke (1955), the presence of antimilk antibodies is not necessarily disease-provoking.

Gryboski (1967) stated that the possible association of enteric Staphylococcal infection with subsequent development of milk allergy provided evidence to support the theory of sensitisation following protein transfer across a damaged small bowel mucosa.

Katz *et al* (1968) said that the gut produces and secretes immunoglobulins ("coproantibodies"). These antibodies are for the protection of the mucosa and may remain largely within the gut and the intestinal secretions. The immunoglobulins in the gut differ from those in the blood where the predominant immunoglobulin is IgG, whereas in gut secretions, IgA is high.

Coproantibody is often destroyed in the stools and inability to detect it does not mean it is absent.

Milk proteins have a noxious effect on the gastrointestinal tract in certain infants which may be unrelated to immunologic mechanisms. This effect could be secondary to enzymatic insufficiency with consequent inability to degrade milk proteins, or to an abnormal permeability of the mucosal barrier. The outpouring of antibodies then is only a response to the exogenous protein. On the other hand, the antibody—antigen complex may injure the mucosa.

Investigations

Circulating serum antimilk antibodies

A lot has been written about antimilk antibodies in the serum. Silver and Douglas (1968), reporting on 4 cases of milk allergy, found a rising titre of "whole milk antibody" after the introduction of milk, varying from 1/320 to 1/640 after 3 days.

However, Gryboski (1967) found no serum precipitating antibodies to milk in her cases of milk allergy. She stated that tests for circulating (antimilk) antibodies were usually negative in cases of milk allergy. Katz *et al* (1968), while detecting antimilk antibodies in the stools, failed to detect them in the serum.

As pointed out by Gryboski (1967), antibodies to milk proteins are found in a wide variety of diseases, e.g. coeliac disease and Down's syndrome. Thus, the presence of these antibodies does not prove allergy nor their absence excludes it.

In our own case, we tried to detect the presence of antimilk antibodies in the patient's serum and stools on two occasions. The method of "cross-over electrophoresis" was used, whereby the antigen (cow's milk) and antibody (serum) were so placed on a cellulose acetate strip that in the subsequent electrophoretic run, the possible antigens in the milk were brought into contact with the antibodies in the serum, if any were present. No antibodies were able to be detected.

Antimilk antibodies in stools

Katz *et al* (1968) commented on the presence of "milk-precipitating substances" in the stools of patients with gastrointestinal milk sensitivity.

They stated that the coproantibodies were often destroyed in the stools and inability to detect them did not mean they were absent. In our case, we tried to detect antimilk antibodies in the stools but failed.

Stools for occult blood

Gryboski (1967) who reported on 21 cases of milk allergy said that diarrhoea was the predominant symptom and that all had stools which were positive for occult blood. All of them also had hypochromic, microcytic anaemia. Results of these laboratory tests were also similar in our case.

Sigmoidoscopy

Gryboski (1967) found a sigmoidoscopic appearance varying from slight injection of the mucosa to ulcerations as seen in ulcerative colitis. Histology showed aggregations of lymphocytes and plasma cells. Repeat sigmoidoscopy two days to one month after milk elimination from the diet showed no abnormality of the mucosa.

In our patient, sigmoidoscopic findings were normal even though the patient was on milk feeds. However, it is interesting to note that at laparotomy, when gastrostomy was done, generalised oozing of blood from the gastric mucosa was found, with no definite bleeding point.

Other tests

Gryboski (1967) did barium meal examinations on her cases, but no abnormality was

detected. This has also been our experience. Lactose tolerance tests were also performed to exclude alactasia being responsible for the diarrhoea. This test was normal in our case.

Skin tests

Kravis *et al* (1967) described a skin test where 0.02 mls. whole milk antigen was injected intradermally. A positive reaction gave a 10 mm. x 5 mm. area of induration and erythema, whereas a saline control was negative.

Bachman and Dees (1967) did skin tests on 72 infants using, in turn, as antigen, whole cow's milk, bovine lactalbumen and casein. They concluded that there was no correlation between a positive reaction and any allergic symptoms. Davies (1958) agreed that "skin tests are unreliable".

No skin tests, however, were done on our patient.

Family history

Bachman and Dees (1957) stated that a family history of allergy may or may not be positive in cases of milk allergy. In our patient, there was no family history of allergy manifested by urticaria, asthma or recurrent rhinitis.

MANAGEMENT

The obvious step to take in the management of cow's milk allergy, is to replace the milk with a substitute. Human milk would be ideal. Goat's milk may be tried but, according to Davies (1958) is often disappointing. Various preparations of soya bean milk have been used, as in our case, where SOBEE proved successful.

However, Davies (1958) stated that soyabean milk preparations, while containing most of the aminoacids necessary for normal growth, may be slightly deficient in methionine. In his case report, the child, who was fed on SOYOLK, took it well for a few days, then began to lose weight and became irritable, vomited and had loose stools. Glaser (1956) said that such symptoms can occur frequently for the first few days, and suggested that the preparation be tried at half-strength at the beginning. Our patient was introduced to SOBEE at half-strength initially, progressing on to full strength. However, although on the whole, she took it very well, she did have occasional bouts of vomiting.

Silver and Douglas (1968) reported the occurrence of dermatoses and stomatitis in their four cases after having been given a soyabean preparation for three weeks. They said that this occurred although the soyabean feed was supplemented with Vitamins A and D, Vitamin B Co. and Vitamin C, and said that the evidence suggested a deficiency of an essential aminoacid rather than a vitamin. However, this has not been our experience.

Prognosis

Silver and Douglas (1968) found that all their infants tolerated the re-introduction of cow's milk after three weeks of a milk-free regime, without recurrence of symptoms.

In our case, after a milk-free dietary regime for two months, we challenged the child again with milk at the age of fourteen months, and found that she took it very well without vomiting or haemetemesis. Her stools were consistently negative for occult blood and her haemoglobin level remained constant.

SUMMARY

A baby with milk allergy presenting as haemetemesis is discussed. The clinical features and laboratory investigations are compared to cases of milk allergy reported by other authors.

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