Lesson of the Week

C1 esterase inhibitor deficiency as a cause of abdominal pain

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C1 esterase inhibitor deficiency causes abdominal pain because of oedema of the gastrointestinal submucosa and may do so in the absence of the more readily recognised symptoms of oedema of the arms and legs. We report such a case in a middle aged man who had had lifelong recurrent bouts of abdominal pain, for which he had had numerous surgical operations.

Case report

A 45 year old man was seen during a family study after two of his children had been found to have hereditary angioneurotic oedema. They had both presented with recurrent swelling of the face, hands, and feet. The patient had complained of recurrent bouts of abdominal pain associated with vomiting. These simulated subacute small-bowel obstruction, for which he had had three laparotomies, an appendicectomy, a cholecystectomy, partial resection of the terminal ileum, a Noble's plication, and insertion of a Baker's tube. At present he has troublesome diarrhoea and vitamin B₁₂ deficiency.

Though the histological findings had always been non-specific, a presumptive diagnosis of subacute Crohn's disease was made, and for the past 15 years treatment with steroids (prednisone up to 40 mg/day) had been prescribed. At the age of 28 he had oedema of the scrotum and prepuce and at 35 swelling of the left hand and heaviness of the left arm. These episodes had resolved spontaneously. On two occasions a psychiatric opinion had been obtained and electroconvulsive treatment given.

Throughout his long history the erythrocyte sedimentation rate had been raised only once (25 mm/first hour). A mild eosinophilia of $0.6-1.7 \times 10^9/l$ ($600-1690/mm^3$) had occurred intermittently without evidence of parasitic infestation. Serum amylase activity had never been increased, and repeated screening for porphyrin had been negative.

Because of his daughters' diagnoses and this history, we thought that he might also have angioneurotic oedema, though in his case the primary manifestation of the condition was abdominal pain. This diagnosis proved to be correct. He was deficient in

Persistent abdominal pain may be a symptom of angioneurotic oedema even when there is no accompanying swelling of the hands and feet

C1 esterase inhibitor both by immunochemical assay (C1 inhibitor <0.07 g/l) and functionally (C1 inhibitor <100 U/ml) (reference ranges $0.15-0.35$ g/l and $800-100\,000$ U/ml respectively).

Comment

Biochemically, hereditary angioneurotic oedema is identified by reduced C1 esterase inhibitor activity.¹ Two forms have been reported,² both of which show an autosomal dominant inheritance, even though up to 25% of patients do not have a family history of symptoms. About 85% of patients have the common form (as did our patient), in which both immunochemical and functional concentrations of C1 esterase inhibitor are between 0% and 50% of normal. The remaining 15% have the variant form, in which an antigenically identical protein is produced in normal or even increased quantities but it is functionally deficient. Estimation of the C4 value may be used in screening for hereditary angioneurotic oedema, since invariably it is low during an acute attack. The definitive diagnosis rests, however, on the immunochemical and functional measurement of C1 esterase inhibitor.

In a recent series³ 75% of patients had swelling of the hands and feet, 36% facial oedema, and 52% recurrent bouts of abdominal pain; in total 93% had had recurrent abdominal pain and 88% associated nausea and vomiting. During an acute attack the abdomen is usually tender but there is no peritonism. Bowel sounds may be normal or increased, and occasionally they are high pitched. The attacks are usually self limiting, lasting between 24 and 72 hours. A radiological feature⁴⁻⁶ seen during an acute attack of abdominal pain is a "stacked coin" appearance with prominent spiculation and thumb printing suggesting mucosal oedema which reverts to normal as the attack subsides.

Though the haematocrit and erythrocyte sedimentation rates were normal in our patient, a persistent leucocytosis ($10.8-15.2 \times 10^9/l$) with an intermittent mild degree of eosinophilia was present. In the Bethesda series³ the mean time from the onset of symptoms to the diagnosis was 21 years; this case took 42 years to diagnose.

Thus C1 esterase inhibitor deficiency should be included in

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the differential diagnosis of abdominal pain. A family history of angioneurotic oedema will be a feature in 75% of cases.

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Epidemiology

Malaria prophylaxis

PUBLIC HEALTH LABORATORY SERVICE MALARIA REFERENCE LABORATORY

Prophylaxis does not provide an absolute guarantee of protection against malaria; breakthroughs can occur in patients taking antimalarial drugs. The recommended regimens for prophylaxis require antimalarial drugs taken weekly to be started one to two weeks before arrival in an endemic area; tablets taken daily should be started at least 24 hours before arrival. Both regimens must be continued for an absolute minimum of four weeks, and preferably six weeks, after leaving a malarious zone. Children of all ages, including breast fed infants, require antimalarial prophylaxis. Proguanil and chloroquine based prophylactics are suitable from birth but pyrimethamine-sulfadoxine (Fansidar) and pyrimethamine-dapsone (Maloprim) are contraindicated during the first eight weeks of life, as sulphones and sulphonamides may induce neonatal jaundice.

Malaria poses a distinct threat both to the pregnant woman and to her fetus; prophylaxis is desirable. Proguanil and chloroquine based antimalarials may be used with safety throughout pregnancy. Fansidar and Maloprim are contraindicated in pregnancy, although so far there is no recorded evidence of malformations in the human fetus in the doses used for antimalarial prophylaxis. The possibility does exist, however, and must be weighed against the threat of malaria where the prevalence of resistant strains is high. Antimalarials containing sulphones and sulphonamides should be avoided by breast feeding mothers during the first eight weeks after delivery because of a risk of brain damage to the infant.

Fansidar is contraindicated in anyone allergic to sulphonamides. Maloprim may be a useful alternative provided the subject has no cross hypersensitivity to sulphones. If an adverse reaction is noted after the first dose(s) the prophylactic drug should be changed.

Recommended drugs and dosages

Antimalarial prophylaxis should be selected on the basis of the algorithm shown in fig 1. In areas of high exposure to *Plasmodium vivax*—that is, East Africa, Brazil, Papua New Guinea, south east Asia, and so on—chloroquine in the normal dosage may be used in conjunction with either Fansidar or

*Also where Maloprim and chloroquine resistance are reported together

Weight	Age	Dose in relation to adult dose
< 5 kg	< 1 year	1/4
5-20 kg	1-5 years	1/2
21-40 kg	6-12 years	3/4
> 40 kg	> 12 years	Adult dose

FIG 1—Selection of antimalarial drugs. Maloprim=pyrimethamine-dapsone. Fansidar=pyrimethamine-sulfadoxine.

Maloprim, since these two antimalarials are not very effective against the *P. vivax* parasite. Alternatively, proguanil 200 mg daily may be recommended in chloroquine resistant areas.

In multiresistant *P. falciparum* areas combined Fansidar and chloroquine should be used as prophylaxis, but the intending traveller must be advised of the increased risk of acquiring malaria and should be especially alert for the development of a feverish illness. Protective measures can reduce the risk. Anopheles mosquitoes have nocturnal feeding habits; between dusk and dawn, therefore, is the time of greatest risk. Exposure outside can be reduced by wearing suitable clothing that adequately covers arms and legs and by using repellent creams