Case reports


Myopathy from E-aminocaproic acid: a second case

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Epsilon-aminocaproic acid (EACA) is an anti-fibrinolytic agent which inhibits the activation of plasminogen to plasmin (Alkjaersig, Fletcher & Sherry, 1959). Its main therapeutic use is in the arrest of bleeding when abnormal fibrinolytic mechanisms are present (Sweeney, 1965). Because of suggestions that fibrinolysis in the colonic mucosa might be abnormal in ulcerative colitis (Kwaan, Cocco & Mendeloff, 1964). EACA has been used to control excessive bleeding in this condition with apparent success (Nilsson, Anderson & Bjorkman, 1966; Salter & Read, 1970). There is a high incidence of side-effects from EACA, such as nausea, diarrhoea, giddiness and faintness, but few serious toxic effects have been encountered other than possible thrombosis. However, one patient who developed extensive muscle necrosis during EACA treatment for periodic oedema has been described (Korsan–Bengsten et al., 1969) and this report is of myopathy due to EACA in a patient with ulcerative colitis.

Case report

A male clerk developed frequent, watery, blood-stained diarrhoea at the age of 32, and initially improved on self-administered herbal treatment. He was first seen in relapse after 2 years’ illness when he was acutely ill, with an oral temperature of 104°F. There was oral ulceration and sigmoidoscopy showed the rectal mucosa to be thickened, granular, friable and bleeding. Barium enema was normal and initial investigations gave these results: Hb, 12-2 g/100 ml; serum sodium, 133 mEq/l; potassium, 3-9 mEq/l; chloride, 100 mEq/l; serum mucoproteins, 187 mg/100 ml. Microscopy and culture of faeces revealed no parasites or pathogenic bacteria.

Treatment with intramuscular corticotrophin gel 80 U daily, oral sulphasalazine 1 g 6-hourly, hydrocortisone enema 100 mg daily, with intravenous fluid and electrolyte replacement (1 September 1970) caused early improvement and he became afebrile within 4 days. Nevertheless, diarrhoea with copious visible bleeding persisted and after 2 weeks’ treatment the rectal mucosa still looked acutely inflamed sigmoidoscopically. EACA (as Epsilakron syrup) 6 g every 6 hr was commenced on 14 September, and a week later (21 September) azathioprine 100 mg daily was added to his treatment; subsequently both the frequency of diarrhoea and quantity of bleeding diminished. Corticotrophin was gradually withdrawn and stopped on 16 October, but he remained on
EACA, azathioprine, sulphasalazine and methyl

cellulose.

On 16 November 1970 he was seen because of pro-

gressive weakness of his legs which he first noticed

about 2 weeks earlier. Examination showed weakness

of all leg muscles, particularly the proximal groups,

and weak anterior abdominal musculature, while the

shoulder-girdle muscles were only slightly affected.

Azathioprine, EACA and sulphasalazine were

stopped, but he continued to use hydrocortisone

enema. The weakness started to improve imme-

diately. An electromyogram (EMG) of quadriceps

femoris and gastrocnemius showed a reduced in-

terference pattern and bursts of giant potentials up to

10 mV. Two weeks later (3 December) the left
deltoid was examined by EMG and showed many
polyphasic action potentials, most between 2 and

4 msec duration. The mean potential duration was

2 msecs suggesting a myopathy (Dr M. Rawson).

Serum creatine phosphokinase (SCPK) on 16

November was 1360 mU/ml (normal 50) falling
gradually to reach normal on 2 December.

As it was possible that any of the three drugs under

suspicion might be required to treat him in the future

it was decided to challenge him with them serially and

the patient consented after full explanation. Azathi-

oprine 100 mg, EACA 4 g, and sulphasalazine 2 g

were given by mouth consecutively with 2 days

between; none caused pyrexia, weakness or rise in

serum creatine phosphokinase or serum aspartate

transaminase. EACA was then given 4 g 6-hourly for

six doses without causing any abnormality.

Despite maintenance therapy with prednisolone

enema its procto-colitis relapsed in early March

1971. Systemic corticotrophin, milk-free diet,
sulphasalazine 1 g 6-hourly, and twice daily hydro-
cortisone enema produced no significant benefit, and

on 29 March 1971, azathioprine 100 mg daily

was added. No muscular weakness was noted and
twice weekly estimations of SCPK and SGPT showed

no rise. By 4 April daily faecal weights had fallen

from 300–500 g to 100–200 g with single daily

evacuations and no rectal bleeding. Sigmoidoscopic

appearances also improved. Corticotrophin was

withdrawn during May 1971, but the other drugs

were continued until November 1971 without clinical

or biochemical evidence of myopathy.

Discussion

Myopathy is not a recognized complication of

ulcerative colitis and circumstantially it seems likely

to have been a toxic effect of a drug. Proximal myo-

pathy due to corticosteroids is well recognized

(British Medical Journal, 1962) though usually in

patients on high doses. This patient was not having

ACTH at the time the myopathy developed, though

he was having hydrocortisone alcohol enema.

Corticosteroids are absorbed when administered

rectally (Nabarro et al., 1957; Sampson & Brooke,

1963; MacDougall, 1963) but the quantities are not

likely to be sufficient to produce myopathy—certainly

this complication has not been reported. Further, the

myopathy improved while he continued with the

enema, and they have been used since with no recurrence

of weakness.

Sulphasalazine, azathioprine and EACA were

suspected, but none produced detectable abnormali-

ties after brief challenge courses. However, the first

two have since been used for clinical reasons without

myopathy recurring, and by exclusion it is probable

that EACA was the provocative agent. In the only

other reported instance of EACA myopathy (Korsan-

Bengsten et al., 1969) myopathy developed after 5

weeks of commencing EACA 30 g daily, though

‘orthostatic reactions’ had been noted earlier. After

recovery EACA was given again at the same dosage

with earlier rhinitis, facial oedema and orthostatic

reactions, but muscle pains with raised SGPT and

SCPK occurred only after 7 weeks treatment. In our

patient weakness was noticed about 6 weeks after

commencing EACA, and the long time lag presumably

explains the failure of a single day’s treatment to

cause even changes in serum enzyme levels.

In the other reported case muscle biopsy showed

‘hyaline degeneration breaking down to necrosis’

similar to Zenker’s degeneration seen in typhus,
diphtheria, Weil’s disease and anaphylaxis. The

authors offer no satisfactory explanation of the

myopathy, and none is evident from our own

observations.

It is recommended that, whenever EACA is given

for more than a month, patients should be warned to

report any muscular weakness, and serial measure-

ments of SCPK should be performed.

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Eosinophilic leukaemia

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Marked leucocytosis with eosinophilia in the peripheral blood can occur due to various causes which may be either benign or malignant (Islam, 1964). It is therefore very difficult at times to establish the diagnosis of eosinophilic leukaemia.

In spite of earlier doubt about the existence of eosinophilic leukaemia as a distinct entity (Dameshek & Gunz, 1964) it is now established that it does exist. According to Chen & Smith (1960) less than thirty cases were reported by 1957. Wintrobe (1967) states that 100 cases have been described of which Bentley et al. (1961) could accept only twenty as true cases of eosinophilic leukaemia. These authors also reported a case of their own with their review. Evidently true cases of eosinophilic leukaemia are extremely rare.

Case report

F.A. 11 years, a school student from Dacca came to one of us (N.I.) on 2 November 1968 with a history of cough with scanty expectoration, fever (100°F) and vague abdominal discomfort for the previous 3 weeks.

On examination there was no abnormality except a few scattered rales on both sides of the chest. A chest X-ray was not abnormal while the blood count showed a leucocyte count of 100,000/mm³ with 80% eosinophils. A tentative diagnosis of tropical eosinophilia was made. Diethylcarbamazin 400 mg a day for 2 weeks was advised. Three weeks later on re-examination the child showed no sign of improvement but was anaemic and presumably had lost some weight. Axillary lymph nodes were enlarged and there was sternal tenderness. Liver was 25 cm and spleen 5 cm below the costal margins. A week later he was admitted under one of us (N.I.) in the Institute of Postgraduate Medicine, Dacca (4 December 1968) when an infiltrate in the right fundus was discovered. His total leucocyte count was found to be 190,000/mm³ with 96% eosinophils. Filarial complement fixation test (FCFT) was negative. A diagnosis of eosinophilic leukaemia was made. A lymph node was removed and sent to Professor C. V. Harrison of the Royal Postgraduate Medical School, London. Meanwhile therapy was started with prednisone and 6-mercaptopurine which was continued for about 4 weeks followed by Myleran and parenteral hydrocortisone. Microscopically the lymph node was found to retain its normal architectural pattern. Scattered through the node there were numerous eosinophil granulocytes. The majority of these were fully differentiated leucocytes and the rest were eosinophil myelocytes which Professor Harrison thought was consistent with the clinical diagnosis of eosinophilic leukaemia.

On request from his relations the boy was then sent to the Royal Postgraduate Medical School where he was admitted on 5 February 1969.

Investigations

Peripheral blood. WBC, 21,000/mm³; neutrophils, 12%; eosinophils, 72%; lymphocytes, 15%; monocytes, 1%; Hb, 7 g/100 ml; reticulocytes, 1%; PCV, 23%; MCHC, 30%; platelets, 63,000/mm³.
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