Meningeal leukaemia in lymphoid blast crisis of chronic myeloid leukaemia

Recent reports have drawn attention to a subgroup of patients with blast crisis of chronic myeloid leukaemia (CML) in which the blast cells have the features of lymphoblasts. Such cases often have atypical clinical features: they may first present in blast crisis, they often respond to the type of treatment used for acute lymphoblastic leukaemia (ALL), and it is becoming apparent that they have a much higher incidence of meningeal leukaemia. We report two patients who presented with acute leukaemia in whom CML presenting in lymphoid blast crisis was diagnosed on the characteristics of the blast cells (see table), and who subsequently developed meningeal leukaemia while in haematological remission.

Case reports

Case 1—Initial complete remission was achieved in a woman of 33 with chemotherapy (including vincristine and prednisolone) and maintenance treatment given. Nine months later she presented with headaches, neck stiffness, and mild papilloedema without other neurological signs. Marrow examination showed continuing remission. The cerebrospinal fluid (CSF) contained many blast cells (white cell count 3.33 x 10⁶/l). Treatment with dexamethasone and intrathecal methotrexate (12.5 mg twice weekly for four weeks) gave rapid symptomatic relief, and the CSF became clear of blast cells. Further intrathecal treatment was given at increasing intervals for two months. The symptoms did not recur, and monthly CSF examinations showed only a few blasts on one occasion. She died 18 months after diagnosis following bone marrow relapse.

Case 2—Initial complete remission was induced in a woman of 52 with vincristine and prednisolone and maintenance treatment given. Six months later she presented with headaches, left brachiofacial paraesthesiae, and mild papilloedema. Marrow examination showed continuing complete remission. CSF examination showed many blast cells (white cell count 0.69 x 10³/l) and she was treated with eight injections of intrathecal methotrexate (12.5 mg twice weekly). Her neurological symptoms cleared rapidly and the CSF was clear after four weeks. The CSF has remained clear, and she continues in haematological remission of blast crisis 10 months after diagnosis.

Comment

Lymphoid blast crisis was diagnosed on the basis of the Ph¹ chromosome, and in case 2 myeloblastic proliferation was also present. Such lymphoid blast crisis may also occur after a typical chronic phase of CML, and may precede, follow, or coexist with myeloid blast crisis, and we feel should not be classified as ALL incidentally associated with the Ph¹ chromosome.

Meningeal leukaemia in CML blast crisis is rare. It occurred only in seven of 101 patients and in nearly half of those achieving remission, and the meninges were often the site of first relapse. Some of these patients responded well to vincristine and prednisolone and may have had lymphoid blast crisis. In another study, four patients developed meningeal leukaemia, including two of the six lymphoid cases. Another patient with lymphoid disease had prophylactic craniospinal irradiation and survived two years without meningeal involvement. Atkinson et al reported two patients who developed meningeal leukaemia, both having the lymphoid type of blast crisis. At St Bartholomew’s Hospital we find that meningeal leukaemia complicating typical myeloid blast crisis is extremely rare.

The high incidence of meningeal leukaemia in patients with lymphoid blast crisis is attributable to their better response to treatment and longer survival. Meningeal leukaemia occurring during haematological remission was a major clinical problem in our patients. Both responded well to intrathecal treatment, but these and other

References


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patients recorded suggest the need for prophylactic treatment. We feel that once haematological remission has been achieved in patients with lymphoid blast crisis they should receive prophylactic irradiation and intrathecal chemotherapy, as the chances of developing meningeal leukaemia are high.

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Prolonged defibrination syndrome after bite by the carpet viper Echis carinatus

Snake bite is probably the most common cause of defibrination syndromes in the world. Although snake bite defibrination is a remarkably benign in itself and not a primary cause of spontaneous bleeding,1 observing non-clotting blood is a vital bedside test that should alert doctors to the possibility of haemorrhage. The following case emphasises how important it is to monitor clot-quality in snake bite patients.

Case report

For venom research purposes I was “milking” Echis carinatus vipers on 25 February, 1975. The technique used is to grasp the viper’s neck by forceps and then grasp the triangular head by a second forceps (the first forceps being released); the viper’s neck is then held by the forefinger and thumb immediately behind the jaws—so close behind the jaws that this dangerously agile creature cannot turn its head and bite the milker. I had just released the second forceps but must have had my forefinger a trace too far back because I felt a painful prick at the top of my finger nail. The specimen was an adult E carinatus, 48 cm long, from Northern Nigeria. I rapidly reapplied the head forceps, adjusted my grip, and completed milking the snake, which yielded venom weighing 18.5 mg after freeze-drying.

Throbbing pain in the finger increased during the next hour and extended to the axilla. Swelling remained confined to the finger and had completely resolved without necrosis five days after the bite. Salivary sput was blood-stained five hours after the bite although hard coughing produced spit that was not bloodstained. On 26 February a discoid ecchymosis, 1 cm diameter, developed spontaneously over the right arm. No further haemorrhagic or other systemic signs were observed. Antivenom was not administered because poisoning, as judged by local effects, appeared mild and because I had previously had a severe anaphylactic reaction.2 I was surprised when a capillary clot-quality test four hours after the bite showed that my blood failed to clot, and even more surprised during the next four days that my blood continued to show a grade 4 “micoinc.”3 From 2 March onwards my blood was therefore more extensively studied by methods previously outlined.4 The platelet count returned to normal 10 days after the bite, but it was 20 days later before clot-quality and concentrations of plasma fibrinogen and serum fibrin/fibrinogen degradation products returned to normal (see figure). At that time the results of serum urea and liver function tests (serum bilirubin, alkaline phosphatase, alanine aminotransferase) were normal.

Comment

So far as I am aware the longest duration of defibrination after snake bite previously recorded was 26 days after bites by the Malayan pit viper, Agkistrodon rhodostoma1; in such cases, local poisoning features, especially swelling, were pronounced. In my case local poisoning features were deceptively mild. In a study of E carinatus bites in Nigeria, Warrell noted that local swelling could not be used as a clinical indicator of systemic poisoning; maximum natural duration of incouagulable blood observed was 10 days.5 What is the mechanism of this prolonged and sometimes recurrent defibrination? I assume there is a persisting depot of procoagulant toxin of which minute concentrations can cause total defibrination (experimentally, defibrination can last five to six days after subcutaneous injection of only 0.01 mg E carinatus venom per kg in rats6); and the toxin must be of relatively low antigenicity to man.

Since bites by E carinatus are so common in many rural areas of Africa and Asia, there must be countless folk pursuing normal activities unaware they are “defibrinated.” It is therefore fortunate that snake bite defibrination by itself is a relatively benign state. Defective clot-quality, however, may herald serious and possibly lethal haemorrhage—and haemorrhage that may be delayed until several days after the bite.1 Therefore, victims of snake bite (in the Western world if only for medicolegal reasons) should be competently observed until clot-quality remains consistently normal.

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