Extramedullary haemopoiesis in the central nervous system: an unusual cause of epilepsy

Sir: Myelofibrosis is characterised by progressive splenomegaly, fibrosis of the bone marrow, a leucoerythroblastic peripheral blood picture and extra medullary haemopoiesis.1 Extramedullary haemopoiesis predominantly affects the reticuloendothelial organs such as the spleen, liver and lymph nodes and, less frequently, the kidneys, skin, heart, pleura and mesentery.2 3 Only very rarely is the central nervous system involved.4 We describe a case of idiopathic myelofibrosis, associated with epilepsy, in which necropsy revealed multiple "tumours" of extramedullary haemopoietic tissue in the cranial dura mater, together with microscopic foci in the brain and leptomeninges.

A 65 year old man with idiopathic myelofibrosis had been maintained on busulphan with occasional transfusions of whole blood. Two years following diagnosis, he was admitted to hospital for elective splenectomy, with symptoms attributable to its massive size. The spleen, which weighed 3·8 kg, was removed and subsequent microscopic examination confirmed extensive extramedullary haemopoiesis. The procedure was uneventful and the patient made a good recovery.

Seven months later, however, purplish umbilicated nodules, ranging in size from 0·5 to 2 cm maximum dimension, appeared in the skin of the upper and lower limbs and abdomen. Biopsy of some of these lesions showed extramedullary haemopoiesis in the dermis and subcutaneous fat. Over the next few weeks more skin nodules appeared and, at the same time, the patient's haematological status deteriorated. Anaemia became more severe, the interval between transfusions became shorter and he complained of increasing tiredness and lethargy. Four weeks following the first appearance of the skin lesions, the patient had an epileptiform seizure with loss of consciousness, cyanosis, urinary incontinence and jerking movements of both upper limbs. The patient recovered spontaneously, but two further similar episodes occurred during the next few hours until he was stabilised on anti-convulsant therapy.

The patient had no previous history of epilepsy and all investigations, including CT scan, failed to elucidate the cause of his seizures. Twelve days later, however, his seizures recurred. On this occasion, there was loss of consciousness accompanied by twitching of the facial muscles and all four limbs. The seizures were continuous with increasing periods of apnoea and finally, respiratory arrest and death.

At necropsy, the sclerae were mildly icteric and multiple, well-circumscribed, purplish nodules, up to 3 cm maximum dimension were present in the skin. The bone marrow appeared pale. The liver was enlarged, weighing 1900 g, and there was marked para-aortic lymph node enlargement. Small discrete pale nodules were present in the kidneys, mesentery, pleura, heart and oropharynx. Microscopy of the liver, lymph nodes and the nodular lesions confirmed extramedullary haemopoiesis. The inner aspect of the cranial dura mater contained several nodules of fleshy reddish-brown tissue, the largest 3 cm maximum dimension (fig 1). The larger nodules had indented the underlying cortex. Microscopic examination showed these nodules to consist of extramedullary haemopoietic tissue (fig 2). Apart from the cortical indentations, the brain and leptomeninges appeared normal to the naked eye. Microscopic deposits at extramedullary haemopoiesis however, were identified in the leptomeninges of the mid-brain and medulla, as well as the choroid plexus of the fourth ventricle. Tiny focal deposits were also noted in the occipital cortex. There was no evidence of blast transformation, a recognised late complication of myelofibrosis.5 6

Extramedullary haemopoietic tumours of the spinal and cranial dura mater are rare. Those in the spine may result in symptoms attributable to cord compression and, if recognised, may be treated successfully by radiation therapy.7 Deposits in the cranial

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Fig 1 Inner surface of cranial dura mater showing tumour-like nodules of extramedullary haemopoiesis.

Fig 2 Microscopy of dural nodule showing extramedullary haemopoietic tissue (× 200).
dura mater occur even less commonly and when described, have usually been reported as incidental findings at necropsy.  

Ligumski et al reviewed a series of seven post-mortem examinations of patients in whom deposits of extradural haemopoiesis were present in the central nervous system, and who had developed neurological manifestations prior to death. Four of these showed tumour masses in the dura mater which varied in size up to 5 cm in diameter, two showed involvement of the leptomeninges only and the remaining case showed a single focus in the right frontoparietal lobe. The clinical manifestations in these patients were diverse and included headaches, disorientation, episodes of unconsciousness and coma. Lund et al have reported the CT findings in a case of sym- ptomatic intracranial haemopoiesis occurring secondary to myelofibrosis. CT was performed in our patient 2 weeks prior to death, but no dural tumours were seen. Presumably the deposits of haemopoietic tissue present at that time were too tiny to be seen, but subsequently, like the nodules in the skin, grew very rapidly, reflecting the accelerated deterioration of the patient’s disease.

The reasons for the exacerbation of his myelofibrosis, with the development of widespread foci of extradural haemopoiesis in many unusual sites, are not clear. Splenectomy may be implicated, although most studies have shown splenectomy to result in a modest improvement in haematological status, complications being related mostly to the immediate post-operative period. Whatever the reason, this patient showed sudden rapid deterioration of his bone marrow disease, with the subsequent deposition of extradural haemopoietic tissue in the brain and cranial dura mater, resulting in seizures, status epilepticus and death.

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C ANDERSON  
C DUGGAN  
WF KEALY  
Departments of Histopathology and Haematology, Cork Regional Hospital, Cork, Ireland

References


Neuralgic amyotrophy due to parvovirus infection

Sir: Neuralgic amyotrophy is commonly associated with unspecified viral illnesses. We describe here an association with parvovirus infection, the first such case reported.

A 26-year old previously fit policeman presented in the winter months five days after the onset of a febrile illness. It was characterised by myalgia, arthralgia, sore throat and mild headache. A fever of 38.5°C had been recorded once. On the fifth day of illness he noticed a fine non-titchy rash on his body. On the same day severe pains in the arms and shoulder girdle developed suddenly. The pain was present at rest and worse on movement. Paracetamol had no effect.

Examination disclosed no fever or abnormalities in the respiratory or cardiovascular systems or abdomen. The fauces were slightly red and there was palpable cervical lymphadenopathy. Over the face and trunk there was a fine maculo-papular rash which extended to the shoulders, upper arms and upper thighs but spared the distal extremities. In places the rash coalesced. There was visible fasciulation of the right deltoid muscle and movement at both shoulders was limited by pain. Over the next two days the rash faded and he was left pain free but weak. Neurological examination on the right revealed very severe weakness of the supra and infraspinatus and deltoid muscles. On the left there was severe weakness of the left wrist, fingers and thumb extension. No upper limb reflexes were elicitable. There were two areas of sensory deficit coincident with the distribution of the axillary nerve on the right and radial nerve on the left. A clinical diagnosis of neuralgic amyotrophy was made. An EMG showed severe but patchy denervation predominantly in the C5 and C6 innervated muscles on the right and forearm extensor on the left. The left radial sensory action potential was absent. Con- valescent serology revealed recent infection with parvovirus, the IgM (by RIA) being 46 units eleven days after the onset of the febrile illness then falling, and the IgG (also by RIA) rising to more than 100 units twenty nine days after onset.

This patient presents a typical picture of neuralgic amyotrophy, otherwise known as brachial neuritis. The EMG study is consistent with this diagnosis. Neuralgic amyotrophy is an axonal disorder of unknown aetiology. It may follow trauma, vigorous exercise, heroin abuse, immunisation and viral infection, usually unspecified. There have been 15 reports of it occurring after Epstein-Barr virus infection. It has also been reported after herpes zoster infection. This is the first report of neuralgic amyotrophy occurring after parvovirus infection.

Erythema infectiosum or fifth disease, recognised for decades, has recently been linked to a human parvovirus. Our patient manifested the typical clinical features of fever, rash, myalgia and arthralgia. Asympto- matic infection occurs and 61% of UK blood donors have antibody to the virus. Complications reported are aplastic crises in those with haematological abnormalities such as sickle cell disease or hereditary spherocytosis and possibly syphovitis and
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C Anderson, C Duggan and W F Kealy

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