Idiopathic hypereosinophilic syndrome presenting as childhood hemiplegia

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Summary: A case of childhood hemiplegia due to idiopathic hypereosinophilic syndrome is reported. There was no cardiac lesion. The neurological complications associated with hypereosinophilic syndrome and the pathophysiological mechanism of neurotoxicity of human eosinophils are discussed. It is likely that the neurological deficit was due to eosinophilic neurotoxicity.

Introduction

The idiopathic hypereosinophilic syndrome (HES) represents a heterogeneous group of disorders with the common features of prolonged eosinophilia of an undetectable cause and organ system dysfunction. Diagnostic criteria have been established for the idiopathic hypereosinophilic syndrome. They include persistent eosinophilia of 1,500 eosinophils/mm³ for at least 6 months or death before 6 months with signs and symptoms of HES, lack of evidence for other recognized causes of eosinophilia despite careful evaluation, and signs and symptoms of organ dysfunction either directly related to eosinophilia or unexplained in the given clinical setting.^{1,2} Neurological manifestations of HES include: (a) diffuse central nervous system abnormality characterized by altered behaviour and cognitive dysfunction, spasticity and, occasionally, ataxia; (b) peripheral neuropathy; and (c) focal central nervous system deficits from cardiac emboli or haematological disturbances.^{3–5} The neurological symptoms and signs can precede the first symptoms of cardiac involvement.³ This paper presents a child with idiopathic HES in whom the initial presentation was hemiplegia.

Case report

An 8 year female child was admitted with sudden onset of weakness of the left half of the body. There was no history of seizures, altered sensorium, headache or vomiting. She had a low grade fever one week before admission. There was no history

suggestive of bronchial asthma, nasal allergy, skin rash or worm infestation. She was not from an endemic area for filariasis.

On examination, she was fully alert and well orientated. Speech and ocular fundi were normal. There was a left upper motor facial nerve palsy and hemiparesis, power was graded at 2–3/5. The tendon reflexes were brisk on the left side with an extensor plantar response. Sensory and cerebellar systems were normal. She had mild hepatosplenomegaly. Lungs were clinically normal. There were no cardiac murmurs.

Investigations showed a total white cell count of 20,800/mm³ with 63% eosinophils. The absolute eosinophil count was 13,200/mm³. The erythrocyte sediment rate was 150 mm/hour. The patient was started on steroid therapy and was referred to this Institute for further management, when the absolute eosinophil count was 1,500/mm³. Bone marrow examination revealed a normal erythroid–myeloid ratio, and 10% eosinophilia without premature cells. Repeated examinations of stool were negative for any ova or cyst. Blood smears were negative for haemoparasites. Casoni and Mantoux tests were negative. Sputum was negative for acid-fast bacilli by smear and culture. Biochemical and cytological analysis of cerebrospinal fluid was normal without any eosinophilia. No micro-organisms, including *Toxocara canis* and *Angiostrongylus cantonensis*, could be isolated from it. Chest X-ray showed evidence of miliary mottling and ultrasonic examination of the abdomen confirmed hepatosplenomegaly. The electrocardiogram and two-dimensional echocardiographic examinations were essentially normal. A computed tomography scan of the brain showed hypodense lesions bilaterally in the parietal regions (Figure 1). There was no significant enhancement on contrast.

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Figure 1 Computed tomographic scan of the brain showing a definite low attenuation area in the right parietal region with ill-defined low attenuated areas in both parietal lobes.

The child was restarted on prednisolone and the absolute eosinophil count was monitored during follow-up. The patient improved in the next 3 months and recovered completely from the hemiparesis. At 4 weeks, the absolute eosinophil count was $1,800/\text{mm}^3$ and it further fell to $200/\text{mm}^3$ at 6 weeks and to $100/\text{mm}^3$ at 3 months. Attempts to withdraw steroids completely have resulted in increasing eosinophil counts within a few weeks, necessitating a continuous maintenance dose of steroids. Repeat chest X-ray showed clearance of the miliary mottling and ultrasound examination of abdomen showed regression of hepatosplenomegaly. The patient is under regular follow-up and there is no evidence of other organ involvement.

Discussion

This patient had clinical and laboratory features which fulfilled the diagnostic criteria of idiopathic HES. She presented with hemiparesis accompanied by hypereosinophilia, hepatosplenomegaly and miliary mottling of the lungs. There was no evidence of worm infestation and the clinical presentation is unlike that of an unusual infection like *Angiostrongylus cantonensis*, since the patient had no meningitic illness or cerebrospinal fluid abnormalities.^{6,7} Moreover, *A. cantonensis* infection is

rare in this country, only two cases having been reported so far.⁸ The low bone marrow eosinophilia seen in this patient could be related to the steroids she received prior to admission, as the peripheral blood at the time of bone marrow examination also showed a lower eosinophil count.

Neurological complications in association with idiopathic HES have been described in three children,⁹⁻¹¹ all of whom had an associated endocarditis. The neurological manifestations can be due to a thromboembolic phenomenon or to a tissue-damaging potential of the eosinophils. The ability of the eosinophils or its contents to cause tissue damage was noted as early as in 1933 by Gordon.¹¹ A neurotoxic fraction has been isolated from human eosinophils but not from human neutrophils.¹² Intracerebral and intrathecal administration of eosinophils or eosinophil-derived neurotoxin causes weakness and incoordination in experimental animals.¹¹⁻¹³ The pathological findings disclosed a loss of Purkinje cells, severe axonal damage and vacuolization of the white matter of the cerebellum, brainstem and spinal cord. A recent study by Sunohara *et al.*¹⁴ supports the possibility that a peripheral neuropathy can be caused by agents derived from the eosinophils. It is possible that the eosinophilic major basic protein, by its endothelial damaging effect, may also contribute to tissue damage.¹⁵ Eosinophilic cationic protein has been reported to have a profound effect on the coagulation system *in vitro*.¹⁶ This protein may be partially responsible for the thromboembolic phenomenon. In this patient, there was no evidence of cardiac involvement, either clinically or on echocardiographic evaluation. It is likely that in this patient, the neurological deficit is due to agents derived from eosinophils.

The prognosis in idiopathic HES depends upon the degree of involvement of vital organs. Since the ultimate prognosis is dictated by the extent of cardiac involvement, it is imperative to start aggressive therapy in patients with cardiac involvement before congestive heart failure develops.^{1,2,17} Initially, therapy is started with prednisolone, which is tapered to the lowest possible dose if the disease stabilizes or improves. If progression occurs despite steroid therapy, the antimetabolite hydroxyurea may be useful. Leukapheresis may rarely be required, if eosinophilic counts are extremely high.^{1,2,17}

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