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Benign childhood occipital seizures

Benign childhood epilepsy with centrotemporal spikes or rolandic epilepsy is well recognised,^{1–3} but benign childhood occipital seizures (BCOS) are not widely known.^{1–7}

BCOS have a prevalence of 20–25% among benign childhood partial seizures,⁶ with two clinical forms: early onset BCOS described by Panayiotopoulos^{4,6} and late onset BCOS of Gastaut.⁵ Idiopathic photosensitive occipital seizures are also well documented.^{8–10}

Early onset benign childhood occipital seizures

Seizures consist of autonomic and behavioural disturbances with vomiting and deviation of the eyes lasting from minutes to hours. They are mainly nocturnal and often progress to convulsions. Consciousness is usually impaired from onset or during the ictus. By definition, seizures lasting for more than half an hour are status epilepticus. In one third of these children, the phase of deviation of the eyes with vomiting and impairment of consciousness is prolonged for more than 30 minutes (partial status epilepticus) and usually ends with generalised convulsions. A typical case is of a child who wakes up from sleep agitated, vomiting, eyes deviated to one side, and who may or may not be able to communicate for minutes to hours before hemiconvulsions or generalised convulsions begin. Onset is between 1–12 years, peak is at 5 years, and remission occurs within 1–2 years from onset. In one third of the patients, seizures or even partial status epilepticus are single events in the child's life. The mean total of seizures is three and the maximum is 15.⁷ Early onset BCOS are entirely benign. Only four out of 113 children with early onset BCOS developed rolandic seizures, and only one continued with infrequent generalised convulsions.⁷ A grave neurological condition may be suspected during the prolonged ictus but the normal state after ictal should be reassuring.

The electroencephalogram manifestations are severe with long runs of high amplitude occipital sharp and slow waves. They often appear when the eyes are closed because they are activated by the elimination of fixation and central vision (fixation-off sensitivity).^{4,6,7} Spikes in the centrotemporal or other locations occur in 10–30% of patients.^{6,7} There is no photosensitivity. Occipital spikes should raise the possibility of BCOS, but they may also occur in children who do not suffer from seizures and in those with severe symptomatic epilepsies.⁶ Furthermore, 10% of children with early onset BCOS may have a normal interictal electroencephalogram.^{6,7}

Late onset benign childhood occipital seizures

Seizures manifest with visual hallucinations and/or blindness, they are frequent, mainly diurnal lasting from seconds to less than three minutes. They may progress to other seizure manifestations, mainly hemiconvulsions. Loss of consciousness may occur with or without convulsions. A post-ictal headache occurs in 30% of patients. Mean age at onset is 7–8 years, and prognosis is usually good with remission often occurring within two to three years.

The electroencephalogram is identical to that of the early onset BCOS with occipital paroxysms when the eyes are closed.^{1–7}

The differential diagnosis of late onset BCOS from basilar migraine or migraine with aura has been recently detailed.¹¹ The main cause of misdiagnosis is that visual hallucinations are often not evaluated quantitatively and qualitatively.¹¹ Instead, they are erroneously abbreviated in terms such as fortification spectra, teichopsia, scintillating scotomata, phosphenes, and their variations, whose meaning often misrepresents the actual descriptions of the patients.

In epileptic seizures, elementary visual hallucinations are frequent, nearly daily, and short—they usually last from a

few seconds to less than three minutes. They consist of predominantly multicoloured circular patterns, "hundreds of brilliant small balls of many colours". Onset is always on the same side. These visual fits may progress to other motor partial seizures, loss of consciousness, and convulsions. Postictal headache is rarely throbbing and severe. Interictal electroencephalogram occipital spikes usually reveals their epileptic nature.

In migraine with aura, visual hallucinations are prolonged, developing over more than three minutes and lasting for 20–30 minutes. They are not as frequent as those in BCOS. They are characterised by predominantly black and white linear and zigzag patterns. Colours may be described, but they are usually not predominant and occur in the periphery of the visual hallucinations along with the zigzag bright streaks or flashes of light. Side alteration between attacks is frequent. Photophobia and irritation are common. Throbbing headache and vomiting follow.

In basilar migraine, bilateral visual hallucinations similar to those of migraine with aura or blindness are associated with brain stem symptoms of vertigo, ataxia, tinnitus, and peripheral dysaesthesias. These are followed by severe, throbbing, posterior, bilateral headache occurs. Impairment of consciousness may occur in a quarter of the cases, usually between the aura and the headache. It is usually brief, from one to 10 minutes, with features distinguished from epileptic seizures. It is slow in onset, never abrupt, and never causes the patient to fall or to be injured. Prolonged and severe impairment of consciousness are rare. In between these attacks classical migrainous episodes with aura may occur. The interictal electroencephalogram is usually normal, but slow wave abnormalities are seen during the attacks.

Idiopathic photosensitive occipital seizures

Reflex epilepsies are classified as "epilepsies characterised by seizures with specific modes of precipitation".^{1,10} Idiopathic occipital seizures induced by television, video games, and intermittent photic stimulation are well documented.^{8–10} Onset is between 5–17 years.⁹ Seizures are photically triggered and manifest with multicoloured circular visual hallucinations often associated with blindness. Tonic deviation of the eyes, epigastric discomfort and vomiting, headache, and generalised convulsions may follow.⁹ Duration varies from two to five minutes or up to two hours. Prognosis is uncertain; some children may have only one or two seizures, but others may not remit.⁹ An interictal electroencephalogram shows spontaneous and photically induced occipital spikes. Centrottemporal spikes may coexist. Ictal electroencephalograms document the occipital origin and spreading of discharges to the temporal regions.⁹

Unified concept of benign childhood partial seizures

Benign childhood partial epilepsies, classified among the "age and localisation related idiopathic epilepsies"^{1–3} may be unified as they share common clinical and electroencephalographic characteristics and one may evolve into another.^{2,3,7} Seizures are infrequent or solitary, usually nocturnal, and decrease within one to three years from onset. Ictal hypersalivation, vomiting, headache, pallor, or sweating, unusual in other epileptic syndromes, are frequent and may occasionally appear in isolation. Despite normal development, normal brain imaging, and rarity of seizures, the abnormalities on the electroencephalogram are severe and exaggerated by drowsiness and sleep. Similar features on the electroencephalogram, resolving with age, are found in 1–2% of asymptomatic children of school age.

Epilepsy or seizures?

The term epilepsy, even in its strict definition of at least two unprovoked seizures, is not appropriate for 30% of the children with early onset BCOS who have only one fit.^{6,7} I consider that the other 70% of these children should not be discriminated and labelled with "epilepsy" just because they have two or more seizures. Preferable terms are benign childhood partial seizures or benign childhood seizure susceptibility syndromes,² denoting an idiopathic liability to seizures and/or electroencephalography manifestations which are age specific. The risk of recurrent seizures in adult life is less (1–2%) than in febrile convulsions (4%).²

Treatment

The conclusion from a recent study on early onset BCOS is that "treatment may not be warranted".⁷ This is certainly the case for the 30% who have only one seizure in their life. The remaining 70%, with an average of three seizures, also may not need medication.¹² If treatment is considered necessary, carbamazepine, sodium valproate, and phenobarbital are equally effective.⁷ Carbamazepine is preferred because of fewer side effects. It is important to remember that remission occurs within one to two years after the first seizure, and antiepileptic medication should be withdrawn after this period.

When early onset, BCOS presents with partial status epilepticus which may be prolonged for hours and terminate with generalised convulsions.^{6,7} This needs urgent treatment with intravenous diazepam. Rectal diazepam should be prescribed for recurrent partial status epilepticus as for febrile convulsions.

In late onset BCOS, seizures may be very frequent, often daily. They usually respond well to carbamazepine which may be needed for two to four years.¹¹

In photosensitive occipital seizures, avoidance of precipitating factors may be sufficient,^{8–10} but if seizures persist, long term medication with sodium valproate may be necessary.^{9,10}

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Gastrointestinal problems in the immunosuppressed patient

The gastrointestinal tract is a major component of the human immune system with a total lymphoid mass which is comparable with bone marrow.¹ The Peyer's patches are the principal sites of interaction among luminal antigens and lymphocytes, while the scattered lymphocytes in the lamina propria and epithelium are the effector cells that mediate immune response.² The gut is also a site of synthesis and release of a specialised form of immunoglobulin A (secretory IgA) which is resistant to digestion. These immunological mechanisms are important because the gut has a huge surface area which interacts with the numerous potentially noxious agents including micro-organisms and dietary antigens.³ The intestinal tract is also one of the most metabolically active tissues in the body, with mucosal renewal taking place every three to five days, it is not surprising therefore that the gut is often the target organ for pathological processes in the immunosuppressed patients.^{4,5} The deleterious effects of immunosuppression on the integral functioning of the gut are assuming greater importance now that the use of potent long term immunosuppression has become widespread, for example in autoimmune diseases and organ transplantation.

Pathophysiology of immunosuppression on gastrointestinal function

The effects of immunosuppression on the gastrointestinal tract are multiple and include loss of gastric acidity, impaired immune response, reduced mucosal integrity, and compromised mucosal regeneration.

THE SUPPRESSION OF GASTRIC ACID SECRETION

This may be induced by treatment with H₂ blockers or be secondary to malnutrition or immaturity (as in neonates), and the number of viable organisms surviving passage through the stomach can therefore increase by a 1000-fold causing gastroenteritis.

THE IMMUNE RESPONSE

The immune response may be globally attenuated by drugs such as steroids (reduction in chemotaxis and kinin production), or more specifically by cyclosporin A and tacrolimus, which inhibit T lymphocyte proliferation by inhibiting expression of interleukin 2.⁶ Such immunosuppression may cause persistence of normally mild infections such as cytomegalovirus or cryptosporidium, and permit an increase in commensal organisms. Epstein-Barr virus which infects B lymphocytes can induce B cell proliferation and ultimately B cell lymphoma in the presence of altered immune response.⁷ In transplantation, intestinal graft-versus-host disease (GVHD) is a risk when the mass of donor lymphocytes received is comparable with that of the recipient's, as is the case in allogenic bone marrow transplantation or even small bowel transplantation. This risk is increased when the immune system is further suppressed with potent treatments such as OKT3 and antithymocyte globulin.

MUCOSAL INJURY

Mucosal injury is well documented in patients with chronic intestinal inflammatory states. Loss of intestinal integrity is a recognised sign of rejection in small bowel transplantation.⁸ Mucosal damage (mucositis) frequently occurs after tumour chemotherapy and after conditioning

treatment before allogenic bone marrow transplantation in adults, but probably occurs less commonly in children.⁴ Radiation has been shown to cause inflammatory changes in the lamina propria in human adults.⁹ A protein losing enteropathy was reported to occur in up to 90% of paediatric bone marrow transplants,⁴ and this is associated with hypoalbuminaemia which may contribute to impaired regeneration of the villi.

Aetiologies of intestinal dysfunction

INFECTIONS

The gastrointestinal tract is a portal of entry for numerous pathogens, and infections are a major cause of morbidity and mortality in immunosuppressed patients. Common viral agents include rotavirus, cytomegalovirus, adenovirus, and coxsackie A virus,^{4,5} all of which may cause devastating diarrhoea in these patients. Bacterial infections include *Campylobacter jejuni* and salmonella,^{3,5} which are normally sensitive to gastric acid, and so are a particular risk in patients receiving H₂ blockers.¹⁰ *Clostridium difficile* infection, which is associated with the use of broad spectrum antibiotics as is common in immunosuppressed patients, may sometimes lead to pseudomembranous colitis. Fungal infections are extremely common ranging from superficial candidiasis to severe systemic infections with candida or aspergillosis involving the intestine and closely related organs such as the liver and spleen.¹¹ Infection by protozoa may also be a problem, and *Pneumocystis carinii* and cryptosporidium are the most frequently identified commensal organisms.⁵ *Strongyloides stercoralis* is a nematode which may cause a fulminating infection in immunosuppressed patients from the tropical countries.¹¹

DRUG TOXICITY

Immunosuppressive drugs can cause a variety of gastrointestinal lesions including mucosal erosions, bleeding, and viscous perforation (for example, steroids); hepatitis, cholestasis, and pancreatitis (for example, azathioprine); impaired enterocyte function causing malabsorption (for example, mycophenolate and tacrolimus).¹² Cytotoxic drugs (for example, cyclophosphamide and busulphan), and irradiation used as primary or adjunctive treatments with immunosuppressive agents cause an enteritis associated with gut mucosal ulceration and bleeding. Idarubicin has been associated with more diarrhoea than cyclophosphamide after allogenic bone marrow transplantation, necessitating support with parenteral nutrition.⁴ The use of isolated parenteral nutrition itself, however, may worsen gastrointestinal function because enteral feeding is an important stimulus to pancreatic function, villus growth, and mucosal integrity.^{13,14}

IMMUNOLOGICAL REACTIONS

GVHD may cause inflammation in the gut stroma and degeneration and necrosis of crypt cells in which apoptotic bodies are characteristically seen. A severe form of diarrhoea, often containing blood and albumin, may ensue.¹⁵ Acute GVHD is a systemic disorder typically involving skin and liver in addition to the gastrointestinal tract; other organs such as the lungs and pancreas may also be involved. It usually occurs seven to 50 days after bone marrow transplantation (and occasionally after liver or small bowel transplantation). The damage GVHD causes to the liver is focused in the portal tracts with loss of bile