occurs. It occurs in approximately one fifth of children with influenza encephalopathy. Influenza A is the most common cause of acute necrotizing encephalopathy. It can also occur in other viral infection like human herpes virus 6 and 7, rubella, measles, varicella, herpes simplex. Acute necrotising encephalopathy causes death or severe neurodisability in about 70% of affected children. An increase in CSF protein of variable degree has been noted in many patients with acute necrotizing encephalopathy yet a CSF pleocytosis is usually not present.

The pathogenesis of ANE is unknown. Isolation of virus from cerebrospinal fluid has been rare. There is no direct brain invasion by virus. Necropsy findings in fatal cases of ANE reveal diffuse cerebral edema and perivascular hemorrhage in the bilateral thalami and putamina. Congestion of arteries, veins and capillaries; acute swelling of oligodendrocytes; progressive rarefaction of tissue; and necrosis of neurons and glial cells are present suggesting a break down of the blood-brain barrier. Cytokines are considered to play an important role in the pathogenesis of influenza encephalopathy. Hypercytokinaemia causes vascular inflammation and endothelial apoptosis; lack of integrity of the cerebrovascular vessels allows seepage of plasma into the brain parenchyma; seepage of plasma causes cerebral oedema and triggers brain apoptosis.

A severely elevated transaminase level, thrombocytopenia, and hematuria or proteinuria are associated with an unfavorable outcome in influenza-associated encephalopathy which in turn results from hypercytokiniaemia induced by this disease. Our patient had mildly elevated transaminase levels along with thrombocytopenia and raised prothrombin time. Patient is usually treated with supportive care, antiviral therapy, methylprednisolone pulse therapy and immunoglobulins.

In summary we describe a patient who displayed the classical clinical features of ANE in association with a documented influenza A infection. Physicians should be aware of this unusual presentation of influenza encephalopathy especially during the flu season.

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References


Gronblad Strandberg Syndrome with Vertibrobasilar Dolichoectasia

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Abstract

The constellation of pseudoxanthoma elasticum, ocular involvement and vascular disturbances is termed Gronblad Strandberg syndrome. Pseudoxanthoma elasticum is a genetic disorder characterized by progressive calcification and fragmentation of elastic fibres in the skin, retina and the cardiovascular system. Typically the cutaneous lesions begin in childhood, but because of their asymptomatic nature they are not noted until adolescence. In some individuals, skin lesions do not develop until later in life. If recognized early, the occurrence of retinal and gastrointestinal hemorrhage and cardiovascular complications can be minimized.

Introduction

Dolichoectatic vessels mostly have an arteriosclerotic aetiology. These tortuous, elongated dilatations devoid of a true aneurysmal neck typically exert mass effects on adjacent parenchyma. However, a congenital predisposition associated with various vascular abnormalities, including pseudoxanthoma elasticum has been described. In these, abnormality of the internal elastic lamina may be congenital.

In this case report we present a 65 yr old male who presented with lateral medullary syndrome with characteristic skin findings, who was found to have dolichoectasia of the vertebrobasilar system. Although dolichoectasia is described in Pseudoxanthoma Elasticum, it is a rare finding and is hence presented.

Case History

A 65 year old male was admitted to our institution with a history of difficulty in walking, difficulty in swallowing, hiccoughs, pooling of secretions in the mouth and urinary incontinence of 4 days duration. He also complained of diminished sensation on the left side of the face and difficulty in walking.

He was recently detected to be hypertensive. He gave a past history of having had a cerebrovascular accident with right...
hemiparesis 8 years ago. There was no history of convulsions or loss of consciousness. He was a chronic smoker and occasionally consumed alcohol.

Clinical examination revealed- a moderately built and nourished man who was conscious and well oriented. His pulse rate was 88/min and blood pressure was 190/110mm in the right upper limb in the supine position. General examination was unremarkable. Head to foot examination revealed skin changes. His skin showed certain peculiarities in the form of loose skin over his neck and both upper limbs which hung in folds (Fig. 1). There were several serpiginous lesions over his axilla, upper limbs and chest (Fig. 2).

CNS examination revealed ptosis, miosis and enophthalmos of the right eye. Examination of his fundus showed greyish curvilinear bands radiating from the optic disc, suggestive of angioid streaks (Fig. 3). Cranial nerve examination revealed palatal palsy on the left with deviation of the uvula to the right and decreased gag reflex on the left suggestive of left 9th and 10th cranial nerve palsy. Examination also revealed decreased pain and temperature on the left side of the face suggestive of a left 5th cranial nerve involvement. Motor system examination revealed increased tone in the right upper limb and lower limb with a grade 3/5 power in both limbs and right plantar was extensor.

Left cerebellar signs were positive, with a positive finger nose test, positive heel knee test and patient was unable to walk in tandem.

A provisional diagnosis of Left lateral medullary syndrome/systemic hypertension/ old CVA with Rt hemiplegia/ Pseudoxanthoma elasticum was made.

Routine investigations were essentially normal. Sickling test was negative, and serum levels of calcium and phosphorus were normal. Serum alkaline phosphatase was normal. His CT head revealed left frontoparietal infarct. Contrast enhanced CT showed dolichoectasia of the basilar artery (Fig. 4).

We proceeded to do an MR Angiogram which revealed occlusion of bilateral carotids, dolichoectasia of the left basilar and vertebral arteries. Filling of the circle of Willis and its branches from the basilar artery through the right posterior communicating artery.

Skin biopsy showed thickened and hyperkeratotic dermis with the deposition of calcium within the deeper layers of the dermis. The elastic bundles were disrupted and clumped on Van Geisen staining (Fig. 5). Von Kossa staining for calcium revealed deposition of calcium within the deeper layers of the dermis (Fig. 6), thus confirming our diagnosis.

Discussion

Pseudoxanthoma elasticum(PXE) is a rare disorder in which aberrant calcification of elastic fibres leads to characteristic cutaneous, ocular, and vascular manifestations which constitute Gronblad Strandberg syndrome. Prevalence is approximately 1 case per 100,000 persons, with a female preponderance of 2.3: 1.

Historically, at least five genetic groups have been described. With molecular testing it is now apparent that most cases are autosomal recessive and no confirmed autosomal dominant form has yet been shown.

Cutaneous manifestations start in early childhood or adolescence and occasionally in late adulthood. Small yellow papules are seen in a linear or reticular pattern and may coalesce to form plaques. These are mainly seen in the lateral part of the neck, axilla, antecubital fossa, popliteal fossa, inguinal and periumbilical region. As the disease progresses the skin of the neck and axilla becomes soft, lax and hangs down in folds producing the typical plucked chicken appearance. Horizontal and oblique creases over the chin before the age of 30 are highly specific for Gronblad Strandberg syndrome. Characteristic eye manifestations are angioid streaks of the retina, which are greyish curvilinear bands radiating from the optic disc. These result from calcification of the elastic fibres of the brusch membrane of the retina, with cracking and fissuring. These are seen many years after the onset of cutaneous lesions.

In the fully developed skin lesions, the elastic fibres in the mid dermis are clumped, degenerated, fragmented and swollen and the abnormal fibres stain positively for calcium. The collagen fibres are abnormally split into small fibres.

Vascular manifestations are usually the last to be recognized in Gronblad Strandberg syndrome. Calcification of the elastic intima and media of the blood vessels lead to a variety of findings. Peripheral pulses are often diminished. Renal artery involvement leads to hypertension. Coronary artery disease causes angina pectoris and myocardial infarction. Cerebrovascular accidents may occur rarely. Gastrointestinal hemorrhages which are usually gastric in origin, are seen because of the calcified submucosal vessels.

Gronblad Strandberg syndrome is caused by mutations in the ATP binding cassette transporter gene MRP6/ABCC6 which
has been mapped to chromosome 16p13.1. Genetic studies have identified 90 different mutations, mainly missense and nonsense. The ABCC6 gene encodes for the cellular transport protein, giving rise to the concept of PXE as a systemic metabolic disorder rather than a purely structural disorder of connective tissue.

Although incurable, severity of the disease can be minimized. Ingestion of calcium should not exceed the recommended daily allowance particularly during childhood and adolescence. Avoidance of head trauma and heavy straining to prevent retinal hemorrhage is essential. Smoking should be strictly discouraged. Use of oral contraceptives and pregnancy should be avoided. Plastic surgery may be helpful in improving cosmetic appearance.

Intracranial dolichoectasia the second interesting finding in our case is characterized by enlargement, tortuosity or elongation of the major arteries at the base of the brain. It usually involves the distal vertebral, basilar, or distal internal carotid artery. Verteobasilar dolichoectasia(VBDE) is a relatively rare condition. Patients with PXE mostly present with cranial nerve compression or ischemic stroke / TIA.

VBDE is associated with Ehlers Danlos syndrome, Marfan’s syndrome, PXE, Afia 1 antitrypsin deficiency. Factors for its development are unclear. Degeneration of the vascular wall due to atherosclerosis alone or in association with arterial hypertension is suggested as a pathogenic factor.

This case report is mainly meant for enlightening the readers regarding the presence of intracranial dolichoectasia in patients with the rare disorder of pseudoxanthoma elasticum and the importance of recognizing this disorder early to minimize complications.

References

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Drug induced oesophageal disease (DIOD) was first reported in 1970. More than 100 drugs have been implicated in the causation of oesophageal disease and more than 1000 cases of drug induced oesophageal injury have been reported. Common medicines include tetracycline, doxycycline, minocycline, acetylsalicylic acid, potassium chloride, ferrous sulphate, quinidine, alpenolol, alendronic acid, vitamin C, penicillins, clindamycin and non-steroidal anti-inflammatory drugs. Chemical content, drug formulation and patient factors are specific for the drug induced oesophageal lesions. The possibility of drug induced oesophageal damage should be suspected in a patient who complains of dysphagia, odynophagia and retrosternal chest pain. The oesophageal injury ranges from mild inflammation to acute ulceration, haemorrhage, perforation or oesophageal stricture.

Gastrointestinal endoscopy will confirm the diagnosis in appropriate cases and also helps to rule out sinister oesophageal disease. It is not necessary in the acute setting if the history is specific and discontinuation of the offending drug has already started to relieve the symptoms. Acid reduction is commonly advised, but its role is not evidence based. Giving appropriate instructions to the patient can many times prevent such oesophageal injuries. We report a doxycycline induced acute ulcerative oesophagitis in a young healthy college student without prior history of oesophageal disease.

Case Report

A 22-year-old female college student went to a local polyclinic to seek advice for acne. The acne distribution was facial and had not responded to topical over the counter preparations. She was prescribed doxycycline capsules for six weeks. She did not have any past history of oesophageal disease. There was also no history of smoking or alcohol intake. She did not have any known drug allergies and was fit and healthy. After two days of doxycycline ingestion, she developed retrosternal chest pain and odynophagia. She stopped consuming the drug after three days. The odynophagia continued and on the fourth day she presented to the emergency department.

She had no history of fever, headache, myalgia and symptoms of upper respiratory tract infection. She had no other skin lesions, history of caustic ingestion or irradiation. She did not have a history of diabetes. She was afebrile and hemodynamically stable. Her general and systemic examination was unremarkable apart from mild dehydration. She was admitted for her complaints of odynophagia.

She received intravenous fluids and underwent an upper gastrointestinal endoscopy the next morning. The gastrointestinal endoscopy revealed a kissing oesophageal ulcer at the level of the aortic arch (Fig. 1). The rest of the oesophagus and stomach was unremarkable. She was prescribed a course of proton pump inhibitors. The symptoms improved over the next day and she was started on clear feeds. This was progressed to a normal diet the following day. Her symptoms gradually improved and she was discharged home on the third day. The histology of the ulcer revealed acute erosive oesophagitis (Fig. 2). The histology was negative for cytomegalovirus and there was no evidence of malignancy. Naranjo score of seven confirmed this case to be a probable adverse drug reaction rather than due to other factors.

Discussion

Drug induced oesophageal disease is a common condition...