An unusual electrocardiographic abnormality

Q1: What is shown in fig 1 (see p 539), and what is its significance?

Figure 1 shows a prolonged QT interval (corrected QT 520 milliseconds) and macroscopic T wave alternans. T wave alternans is defined as a beat to beat variation in the amplitude or polarity of the T wave. Macroscopic T wave alternans is a predictor of malignant ventricular arrhythmias.1 Microvolt T wave alternans is a validated predictor of mortality and morbidity in a variety of patient groups.2 This ECG anomaly is seen with both transient physiological stress (for example, exercise), and with pathological stress such as electrolyte abnormalities and myocardial ischaemia. Indeed, revascularisation in ischaemia has even been shown to reduce the incidence of T wave alternans.3 It has also been documented in association with the long QT and Brugada syndromes.4 T wave alternans on a millivolt scale visible to the unaided eye suggests an abnormal T wave (macroscopic T wave alternans). REGARDLESS of amplitude, T wave alternans should be regarded as a warning of malignant arrhythmias.

Q2: What is the arrhythmia in fig 2 (see p 539)?

The upper trace in fig 2 is lead II from a conventional electrocardiographic recording. It shows macroscopic T wave alternans in the first four beats degenerating into torsades de pointes (polymorphic ventricular tachycardia). REGARDLESS of amplitude, T wave alternans should be regarded as a warning of malignant arrhythmias.

Q3: What was the procedure used to treat the patient in fig 3 (see p 539)?

Figure 3 shows a ventricular paced rhythm. Torsades de pointes in this patient was treated by temporary pacing wire. The patient was given verapamil to ensure his own rhythm was slower than that delivered by the temporary pacing wire. In addition, the patient received intravenous magnesium sulphate to correct the hypomagnesaemia.

Discussion

T wave alternans is uncommon and often overlooked except when it is of a large (millivolt) amplitude such as in this case. Its mechanism demonstrates modern electrophysiological understanding of the basis of arrhythmia generation. Many arrhythmias occur as a result of re-entry circuits. A re-entry circuit occurs when a depolarising wave travels in a circle from myocyte to myocyte. Each myocyte becomes refractory for a short time to further depolarisation as the ion channels in the cell membrane are reset. By the time the wave has come full circle, however, the first myocyte is no longer refractory and is able allow the circuit movement to continue round the circuit indefinitely. Such circuits depend on heterogeneity of repolarisation. Normally the myocardium repolarises rapidly and synchronously which is represented on the ECG by the narrow QRS complex. The myocardium is then refractory until ventricular repolarisation is completed. Repolarisation is slower and more heterogeneous than depolarisation and hence the T wave appears as broad deflection on the ECG. The more heterogeneous the repolarisation, the greater the chance that part of the myocardium will no longer be refractory should an ectopic impulse arise and hence allow a re-entry circuit to be established. Heterogeneity of repolarisation is formally known as transmural dispersion of repolarisation (TDR). Increased TDR occurs with electrolyte abnormalities (for example, hypokalaemia, hypomagnesaemia), with intrinsic abnormalities of the ion channels due to genetic mutations (the congenital long QT syndromes), and as an effect of drug therapy (antiarrhythmics, β-agonists, erythromycin, etc.).

Increased TDR manifests on the surface electrocardiogram as alteration in the timing and amplitude of the T wave. This is the mechanism of both T wave alternans and the better known prolonged QT interval. Interestingly, while T wave alternans is always associated with increased TDR, long QT intervals may be found with a normal distribution of repolarisation. A long QT interval may occur when the whole myocardium repolarises late but synchronously (small TDR) or when just part of the myocardium lags behind repolarisation of the rest (large TDR). Drugs such as amiodarone prolong the action potential, and hence the QT interval, yet decrease the TDR. This patient had two separate factors operating to increase the TDR. Firstly, he had a low serum magnesium concentration which like abnormalities in potassium and calcium is known to alter the dynamics of repolarisation of the myocardium. Secondly, he was on nes- bised β-agonists (salbutamol), and given 1:1000 adrenaline during the cardiac arrest. The dispersion in the rate of repolarisation is therefore increased. Just as the T waves represent myocardial repolarisation, T wave alternans is the correlate of increased variation in the rate of repolarisation.7 Sometimes the myocytes repolarise synchronously and sometimes less so; sometimes the wave of repolarisation is in one direction, and sometimes the other. It is an early warning sign of re-entry circuits and ventricular arrhythmias and in particular torsades de pointes. Although T wave alternans is a rare electrocardiographic sign, when present it should be treated with suitable respect.

Final diagnosis

Macroscopic T wave alternans and recurrent torsades de pointes.

References


A diagnostic conundrum

Q1: What is the diagnosis in this case?

The diagnosis is Whipple’s disease. This is a rare multisystem disorder characterised by weight loss, diarrhoea, abdominal pain, arthralgia and lymphadenopathy, though presentation may be very variable. It is caused by a Gram positive, PAS positive bacillus called Tropheryma whippelii which was identified in 1992. It has been reported in all age groups, though it is commonest in middle aged white males. Whipple’s disease commonly involves the gastrointestinal tract causing a dilated thickened intestine with villous atrophy and malabsorption, resulting in anorexia, weight loss, abdominal pain, anaemia, hypoaalbuminaemia and rarely, clotting disorders. The heart and its layers can be affected. Pohlarythralgia is common though transient and episodic. Generalised hyperpigmentation can be found in up to 50% of patients. One of the striking features is mesenteric, abdominal, retroperitoneal, mediastinal, and peripheral lymphadenopathy which can often be mistaken for lymphoma, sarcoidosis, or other granulomatous disorders. Ten percent of patients have neurological involvement at some stage of their illness. Dementia, ophthalmoplegia, and facial myoclonus are the commonest features.

Q2: What is the pathognomonic central nervous system manifestation?

The answer is facial and ocular myoclonus. This includes oculomotor and oculofacial-skeletal myorhythmia. The former is characterised by a slow, smooth involuntary movement of the eyes whereas the latter is associated with synchronous contractions of the jaw and the latter is associated with contractions of other body parts.

These are rare findings present in 20% of patients with central nervous system disease and are as diagnostic as a positive biopsy or a positive polymerase chain reaction assay of the bacterial RNA.

Q3: What is the diagnostic test?

The diagnosis of Whipple’s disease requires a high index of clinical suspicion. Routine blood tests are non-specific as are tests of malabsorption. Histopathological examination of biopsies of the organs involved reveal PAS positive macrophages containing clumps of T. whippelii. In about 30% of cases this is negative. The current diagnostic test is polymerase chain reaction of bacterial 16S ribosomal RNA from tissue biopsies, cerebrospinal fluid, blood, etc.

Q4: How does one treat this condition?

Current treatment is long term co-trimoxazole (trimethoprim-sulphamethoxazole). Initial treatment in those with neurological involvement is an intravenous combination of cephalosporins and aminoglycosides, followed by oral co-trimoxazole. Locomotor and gastrointestinal symptoms may show improvement in days whereas histological remission may take 1–2 years. Relapse rates can be up to 35%.

Final diagnosis

Whipple’s disease.
Progressive furrowing of skin with digital clubbing

Q1: What is the diagnosis?

The diagnosis is primary hypertrophic osteoarthropathy or pachydermoperiostosis or Touraine-Solente-Gole syndrome. The presence of characteristic facial features with cutis verticis gyrata and advanced clubbing of the digits in the absence of any systemic features suggest the diagnosis. Radiological evidence of periostitis of the involved bones helps in confirmation of the diagnosis.

Q2: What are the radiological findings shown?

The radiograph of wrist (see p 541) shows periostitis, polychondritis, as shaggy new bone formation around the styloid process of radius. Cortical sclerosis and periosteal thickening are seen along lower ends of the shafts of radius, ulna and metacarapals, proximal and middle phalanges of both hands.

Q3: Which other conditions are to be differentiated clinically from this entity?

This condition has to be differentiated from the secondary form of hypertrophic osteoarthropathy, which occurs in relation to bronchial carcinoma, rarely of other primary malignancies, suppurative lung diseases, and congenital heart diseases. Here, facial features are minimal or absent and the osteoarthropathy and digital clubbing are painful. 1 Associated systemic features are present.

In acromegaly, patients present with similar facial features and cutis verticis gyrata, but in addition, there is proptosis, altered body proportions, change in voice, and visual field defects. 1 Hands and feet are spade shaped but clubbing is absent.

In thyroid acropathy, a rare feature of Graves’ disease, facial feature include exophthalmos along with symptoms and signs of hyperthyroidism. 2 Pretibial myxoedema is usually associated. Enlargement of distal extremities is confined to hands and feet.

In scleromyxoedema, facial features are identical but widening of distal extremities and digital clubbing are absent. 1

Discussion

Primary hypertrophic osteoarthropathy is a rare, autosomal dominantly inherited disorder with variable penetrance. It affects males predominately with a sex ratio of 9:1, and in about one third cases, family history is positive. 1

Learning points

- Hypertrophic osteoarthropathy secondary to internal malignant or other systemic illnesses are uncommon primary disease.
- Secondary hypertrophic osteoarthropathy is usually associated with tenderness of the involved joints and tender digital clubbing.
- Radiologically, in primary hypertrophic osteoarthropathy, the periosteal new bone formation is coarser than secondary form and extends distally to involve the epiphysis.

Primary hypertrophic osteoarthropathy starts insidiously in childhood or commonly during puberty and is characterised by remarkable cutaneous features, clubbing, and periostitis. Pathogenesis involves abnormalities in collagen synthesis. Fibroblasts from the affected skin are hyperactive with increased synthesis of collagen. Molecular studies reveal evidence of upregulated collagen transcrption. 2

The skin becomes thick and coarse with prominence of the usual lines of facial expression. Thickness of the eyelids gives rise to the apparence of palatal prothesis. Seborrhoa, acne, and folliculitis are common. Overgrowth of scap tissue in relation to underlying skull bone gives rise to cutis verticis gyrata. Bilateral, symmetrical, distal long bone involvements are seen, initially involving the distal diaphysis of tibia, fibula, radius, ulna, metatarsals, metacarpals, and phalanges. 1 In advanced disease, proximal long bones and flat bones of the pelvic and shoulder girdles, hands and feet are spade shaped but clubbing is absent.

In thyroid acropathy, a rare feature of Graves’ disease, facial feature include exophthalmos along with symptoms and signs of hyperthyroidism. 2 Pretibial myxoedema is usually associated. Enlargement of distal extremities is confined to hands and feet.

References


Learning points

- Patients with acute angle closure glaucoma may present with systemic symptoms and reduced vision.
- They should be referred urgently to an ophthalmologist to prevent occult morbidity and blindness.
- An acute attack may spontaneously resolve by causing ciliary body shut-down and iris atrophy and thus bringing intraocular pressure back to normal.

Final diagnosis

Idiopathic bilateral simultaneous acute angle closure glaucoma.

References


An odd case of multiple "cannonball metastases"

Q1: What abnormalities are seen on the radiograph?

The chest radiograph (see p 542) shows evidence of a raised left hemidiaphragm and small left pleural effusion. Two pulmonary nodules, which have no visible calcification or cavitation but well defined margins, are noted overlying the left midzone. One lesion lies adjacent to and above the aortic knuckle, the other one adjacent to the left heart border. A subsequent contrast enhanced spiral computed tomogram of her chest showed two small focal nodules in the right lobe, two moderate sized in the left upper lobe, and one large mass measuring approximately 6 × 9 × 11 cm replacing most of the left lower lobe, also a small left pleural effusion; there was no lymphadenopathy.

Q2: What is the differential diagnosis?

The differential diagnosis of multiple lung masses is quite complex, with metastatic disease being the most common cause. Other possibilities include an inflammatory process such as fungus, tuberculosis, nocardiosis, or septic emboli. In asymptomatic patients further considerations include the presence of arteriovenous malformations, rheumatoid nodules, or amyloidosis. Less common pulmonary lesions also include fibromas, chondromas, lipomas, hamartomas, and leiomyomas.

The radiological appearances as well as clinical features help to narrow the differential diagnosis down. On inspection of the radiograph one should note size, distribution, presence of cavitation, and that of calcification. Malignant tumours that commonly metastasise to the lung include breast, thyroid, gastrointestinal tract and renal cell carcinomas, also head and neck tumours and soft tissue sarcomas. Metastases are present in variable numbers and are usually well defined and peripheral in distribution. Cavitation is occasionally seen with squamous cell carcinomas and calcification is unusual except for chondrosarcoma and osteosarcoma metastasis. The main distinguishing features from benign lesions are the rate of growth and the presence of systemic symptoms. Hamartomas and carcinoid tumours have almost identical appearance on radiography, however most carcinoids are solitary with hamartomas being peripheral and often calcified and carcinoid being peripherial. Other conditions that cause multiple lung lesions are lymphoid hyperplasia and Kaposi's sarcoma. Finally infectious diseases including fungus granulomas, abscesses and hydatid disease and also connective tissue disorders should be considered. Fungus granulomas and hydatid disease may well be asymptomatic, while multiple abscesses will manifest with fever and symptoms proportional to their source. Rheumatoid nodules are usually small and rarely cavitate. Larger lesions are seen in Wegener's granulomatosis, but these are characteristically cavitating and often associated with haemoptysis and other symptoms of systemic vasculitis.

Q3: What important piece of information from the patient's past medical history is missing and would highlight a possible diagnosis?

The patient had had a total abdominal hysterectomy with a wedge resection for a 2 cm diameter encapsulated tumour at the age of 69 years. This condition is rather peculiar because of two contradictory findings: the tumour's clinical features help to narrow the differential diagnosis down. On inspection of the radiograph one should note size, distribution, presence of cavitation, and that of calcification. Malignant tumours that commonly metastasise to the lung include breast, thyroid, gastrointestinal tract and renal cell carcinomas, also head and neck tumours and soft tissue sarcomas. Metastases are present in variable numbers and are usually well defined and peripheral in distribution. Cavitation is occasionally seen with squamous cell carcinomas and calcification is unusual except for chondrosarcoma and osteosarcoma metastasis. The main distinguishing features from benign lesions are the rate of growth and the presence of systemic symptoms. Hamartomas and carcinoid tumours have almost identical appearance on radiography, however most carcinoids are solitary with hamartomas being peripheral and often calcified and carcinoid being peripherial. Other conditions that cause multiple lung lesions are lymphoid hyperplasia and Kaposi's sarcoma. Finally infectious diseases including fungus granulomas, abscesses and hydatid disease and also connective tissue disorders should be considered. Fungus granulomas and hydatid disease may well be asymptomatic, while multiple abscesses will manifest with fever and symptoms proportional to their source. Rheumatoid nodules are usually small and rarely cavitate. Larger lesions are seen in Wegener's granulomatosis, but these are characteristically cavitating and often associated with haemoptysis and other symptoms of systemic vasculitis.

Q4: What is the most likely diagnosis?

Spindle cell proliferation consistent with pulmonary leiomyomata secondary to a benign metastasising uterine leiomyoma.

References

on exertion, and never having smoked, make a malignant tumour unlikely.

Q4: How would you manage this patient?

The most appropriate management is surgical excision, in view of the symptoms of progressive weight loss, and to prevent complete obstruction of the bronchus.

Discussion

In our patient, a surgical opinion was sought, and a right upper lobectomy with sleeve resection of the right main stem bronchus and carina, with carinal reconstruction by trancheobronchial anastomosis was performed. Light microscopy disclosed a tumour composed of polygonal cells with clear and abundant cytoplasm contained abundant periodic acid-Schiff positive material which was digested by diastase, indicative of glycogen granules. An extensive immuno-histochemical panel was applied to the tumour, which revealed positivity to HMB-45 (a marker of melanocytic lineage). Histology was consistent with a nodular clear cell carcinoma on the basis of electron microscopy and immunohistochemistry.

The differential diagnosis of the case of a patient who died from metastatic carcinoma should further be excluded by ultrasonography or abdominal computed tomography. Although slow growth is a characteristic feature of BCCT of the lung, a case report described a tumour that doubled its diameter within 21 months. Furthermore, while BCCT of the lung has traditionally been considered benign, a 1988 report described the case of a patient who died from metastatic BCCT of the lung. This fatal case indicates that benign behaviour of this tumour is not invariably.

Final diagnosis

Benign clear cell tumour (“sugar tumour”).

References

Severe haemolysis with an important fall in haemoglobin level and deep jaundice, as in our patient, has rarely been described. In a previous study, seven patients with primary Epstein-Barr virus infection had peak bilirubin levels of 10.2–23 mg/dl (174–393 µmol/l). In five of these seven cases, however, there was evidence for both hepatocellular dysfunction and an ongoing haemolytic process either due to anti-i cold agglutinins or due to positive anterythrocyte antibodies.

Deep jaundice with signs of haemolysis always raises the possibility of Wilson’s disease. In our patient serum ceruloplasmin and copper were normal and no increased urinary copper or the presence of Kayser-Fleischer ring could be documented. Although these findings do not absolutely exclude Wilson’s disease, the fact that the patient is healthy now, more than six months after the episode of jaundice, clearly demonstrates that she cannot have any chronic metabolic disease.

In conclusion, classical Epstein-Barr virus infection is usually a benign and self limiting disease. Despite this fact, close follow up of cases in order to prevent and identify possible complications is necessary. The present case should raise clinicians’ indices of suspicion for the described unusual complications of the well known syndrome of infectious mononucleosis. A cholestatic form of Epstein-Barr virus induced hepatitis may be present in several cases, while a deepening jaundice may be the result of haemolysis due to cold haemagglutinins.

Final diagnosis
Epstein-Barr virus infection.

References
Deep jaundice in an adolescent

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