Self-assessment questions

A patient with recurrent acute abdominal pain

Mansoor Ahmad, Faiaz M Rasul

A 48-year-old Jewish woman presented to the emergency room complaining of sharp epigastric abdominal pain of acute onset. The pain was non-radiating and severe in intensity and had started 6 hours prior to presentation. It was associated with nausea and vomiting. The vomitus consisted of food particles. She denied complaints of diarrhoea, constipation, melaena, haematemesis or weight loss. The physical examination revealed a blood pressure of 110/64 mmHg, pulse rate 60 beats/min, temperature 38.2°C, and a respiratory rate of 16 breaths/min. She weighed 48 kg. She was anicteric and had no cervical lymphadenopathy. The abdomen was soft and diffusely tender. Rigidity, rebound tenderness, hepatosplenomegaly or masses were absent. Rectal examination showed guaiac-negative brown stool. The remainder of the examination was unremarkable. The patient was not taking any medications and denied use of alcohol, tobacco or intravenous drugs. Her diet consisted mainly of low fat vegetarian food products. Her family history was unremarkable.

A review of patient's medical records showed documentation of similar episodes on at least six occasions over the previous 18 months. During the attacks, the pain lasted 48 to 72 hours and was associated with a low-grade fever (37–38.5°C). Medical history was significant for long-standing back pain and degenerative joint disease involving the knees (for at least 15 years). There was a history of self-limited episode of viral meningitis 1 year prior to presentation. She had undergone tubal ligation 10 years prior to the onset of abdominal pain, followed by a laparotomy 6 years later for evaluation of pelvic pain. Adhesions were discovered during the laparotomy. The investigative work-up failed to reveal a definite diagnosis. On numerous occasions, laboratory data including complete blood count, erythrocyte sedimentation rate, and routine blood chemistry were within normal limits, except for minimal elevation of white blood cell count on two occasions. Anti-nuclear antibody assay was negative. Abdominal ultrasound and a HIDA scan did not reveal any abnormalities. Abdominal X-ray, upper gastrointestinal barium study, and a colonoscopy were normal. Computed tomography of the abdomen and pelvis was unremarkable.

The patient was admitted to the hospital for observation, as diagnostic studies were unrevealing. She became asymptomatic within 24 hours and was discharged home.

Questions

- 1 What is the diagnosis ?
- 2 Describe the pathogenesis of this clinical condition ?
- 3 How was the diagnosis made ?
- 4 Describe the most recent development in the diagnosis of this condition ?
- 5 What is the treatment ?

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Answers

QUESTION 1

The patient has familial Mediterranean fever (FMF).

QUESTION 2

Several theories have been proposed to explain the recurrent inflammation of the serosa in FMF.¹ The most favored hypothesis suggest a deficiency of C5a and IL-8 inhibitors (chemotactic factor inactivating enzymes). The result is an ineffective breakdown of C5a and IL-8, which are released in response to subclinical injuries. This facilitates neutrophilic infiltration. The neutrophils release a variety of chemicals, including a C5a-generating enzyme, thus completing a vicious circle.^{1, 2}

QUESTION 3

FMF was a diagnosis of exclusion until recently, sometimes requiring exploratory laparotomy to rule out appendicitis.¹ The diagnosis of FMF, especially during the initial attacks, requires a high index of suspicion and is based on positive family history. In some cases, therapeutic trial with colchicine may be attempted.¹ However, when additional attacks precipitate and subside, diagnosis may be established according to the presence of clinical features (box), even in the absence of family history.¹

QUESTION 4

The gene responsible for FMF, designated *MEFV*, is located close to the α -globin gene on chromosome 16, and was recently identified after years of cloning.^{3, 4} The gene is approximately 10 kb and encodes a 781-amino-acid protein called 'pyrin' or 'marenostrin'. This protein is a transcription factor and regulates the expression of target genes, some of which may be involved in the suppression of inflammation.^{3, 4} A polymerase chain reaction (PCR) can now be employed to establish the diagnosis of FMF in suspected patients.

QUESTION 5

Colchicine is known to suppress neutrophil chemotaxis.⁵ In prospective randomised double-blind studies, the chronic administration of colchicine at doses of 1–2 mg and rarely, 3 mg/day significantly reduced the frequency of the inflammatory attacks.⁵ Colchicine may result in diarrhoea and flatulence in some patients. The dosage of colchicine administered (1–2 mg/day) is inadequate to inhibit microtubule function. However, this dose may be sufficient to retard the migration of the neutrophils by an unknown mechanism.⁵

Discussion

FMF is an inherited condition prevalent among Arabs, Turks, Armenians, and Sephardic Jews.¹ It is transmitted as an autosomal recessive trait. Up to 50% of patients do not give a positive family history. By age 20, as many as 90% of patients have had their first attack.¹ FMF is characterised by sporadic, self-limited febrile attacks with acute localised inflammation, usually involving the peritoneum, pleura, and joint spaces (box). Less commonly, the pericardial space and the tunica vaginalis of the testis may be involved. Peritonitis due to FMF may present as an acute abdomen, and exploratory laparotomy shows an inflamed peritoneum with a neutrophilic exudate.¹ Recurrent abdominal pain is reported by more than 95% of patients, pain is accompanied by signs of peritonitis in most patients and often a diagnosis of appendicitis or acute abdomen is made. Chest pain, usually of a sharp stabbing type suggestive of pleuritic pain, is also reported by 75% of patients. Mono- or oligo-arthritis and sometimes migrating polyarthritis is reported by 70% of patients. Up to 25% of patients show skin lesions similar to those of erysipelas on the lower extremities. The localised erysipelas-like rash may be painful, and resolves in a few days. Meningitis may be noted in up to 1% of patients. In the preceding hours, some patients may experience a prodrome including chills. Fever is usually 38 to 40°C. In general, an attack may last from 12 to 72 hours. However, attacks involving the joints tend to last somewhat longer. The interval between attacks ranges from days to months.

Clinical features of FMF

- fever (38–40°C)*
 - abdominal pain (most common symptom)*
 - chest pain
 - joint pain (migratory polyarthritis or mono/oligo-arthritis)*
 - transient erysipelas-like rash (usually below the knee)
 - meningitis*
 - orchitis (rare episodes in childhood)
 - pericarditis
 - amyloidosis
- *features noted in our patient.

Approximately 25% of patients with FMF develop renal amyloidosis.¹ The accumulation of amyloid fibrillar protein AA (presumably due to recurrent inflammation) causes nephropathy, leading to proteinuria and nephrotic syndrome. The amyloidosis usually progresses to renal failure in 3–7 years, and almost all deaths attributable to FMF result from this complication. Otherwise, patients with FMF have a normal life expectancy. However, the quality of life may be impaired by the frequent and incapacitating episodes of inflammation. Prophylactic colchicine therapy appears to prevent amyloidosis.¹

The laboratory findings are nonspecific and include an elevated peripheral white blood cell count, an accelerated erythrocyte sedimentation rate, and elevated acute-phase reactants, including C-reactive protein, fibrinogen, haptoglobin, C3, C4, and serum amyloid A.¹ Urinalysis may show albuminuria and microhaematuria. Abdominal X-rays may be characterised by bowel oedema with air–fluid levels in the small intestine.¹

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The successful cloning of the gene has important consequences, as a PCR can now be employed to establish the diagnosis of FMF in suspected patients.³ Prophylactic colchicine therapy may be offered to patients with FMF, as the attacks under colchicine therapy are milder, of shorter duration, and may prevent renal failure.¹

Final diagnosis

Familial Mediterranean fever.

Keywords: familial Mediterranean fever; abdominal pain

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Small bowel obstruction in a young adult

D W Harkin, G Blake

A 21-year-old man presented to hospital with a 3-day history of increasing vomiting, abdominal pain and distension, and constipation. On questioning, he gave a 3-month history of poor appetite, intermittent abdominal cramps, intermittent diarrhoea and weight loss of approximately 13 kg. He had no relevant medical or family history, and had no previous surgery. He was apyrexia clinically anaemic, with a centrally distended abdomen, but no abdominal scars or external hernia. Bowel sounds were obstructive but there were no obvious signs of peritonism. Positive blood results showed a microcytic hypochromic anaemia (haemoglobin 7.9 g/dl) and a low serum albumin (corrected albumin 26 g/l), his inflammatory markers were also grossly elevated (C-reactive protein (CRP) 112 IU/l; erythrocyte sedimentation rate 77). Erect and supine abdominal X-rays are shown in figures 1 and 2.

Figure 1 Erect abdominal X-ray

Figure 2 Supine abdominal X-ray

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Questions

- 1 What do the abdominal X-rays show (figures 1 and 2)?
- 2 What is the differential diagnosis?
- 3 What is the most appropriate treatment?

Answers

QUESTION 1

The erect abdominal X-ray (figure 1) shows a large air-filled viscus in the upper abdomen with two long fluid levels. The supine abdominal X-ray (figure 2) shows several grossly dilated small bowel loops in the central upper abdomen. No obvious free intra-peritoneal gas is seen outlining the ligamentum teres, major viscus, paracolic gutters, or between adjacent bowel loops (Riggler's sign) on either X-ray. An erect chest film also showed no subdiaphragmatic air.

QUESTION 2

The differential diagnosis is small bowel obstruction (adhesions, hernia, tumour, inflammatory stricture, foreign body, gallstone, congenital bands or stenosis, intussusception, meconium ileus or meconium ileus equivalent, mid-gut volvulus), large bowel obstruction (tumour, volvulus, inflammatory stricture), or gastric dilation (acute, outlet obstruction, volvulus).

The distribution of the distended bowel loop in the central upper abdomen, the presence of valvulae conniventes, and the absence of gaseous distension of the caecum implies small bowel obstruction. The size of the distended bowel loop may imply an acute or chronic obstruction.

QUESTION 3

He underwent a surgical laparotomy which revealed an obstructed and grossly dilated 25 cm segment of mid small bowel twisted 360° clockwise about its mesentery (figure 3). The segment of small bowel was grossly dilated with diameter in excess of 10 cm, but was not acutely ischaemic, and there were many large reactive lymph nodes in its draining mesentery. There was no evidence of malrotation or situs-inversus, and there were no abnormal fibrous or Ladd's bands. We performed a wide segmental resection and side-to-side anastomosis of his small bowel. He made an uncomplicated post-operative recovery.

Histopathology showed a gross specimen of 25 cm of dilated small bowel, diameter in excess of 10 cm, with four large ulcerated areas on the mucosal surface and unremarkable mucosa in between. The mesentery also contained two large reactive lymph nodes. On histological examination the areas of mucosal ulceration contained fissure ulcers, transmural chronic ulceration, lymphoid follicle forma-

tion, and submucosal fibrosis. Areas of normal mucosa separated the involved segments. Despite the absence of granulomata, histopathological features were consistent with Crohn's disease.

Our patient is presently under review on sulphasalazine treatment, and has had no major disease flare-ups or symptoms one year post operation.

Discussion

Crohn's disease is a chronic, transmural, inflammatory, disease of the intestinal tract most frequently involving the terminal ileum and colon. The disease can affect any part of the gastrointestinal tract from lips to anus, and also can manifest itself as various systemic complications such as finger clubbing, large joint arthritis, erythema nodosum, iritis, pyoderma gangrenosum, episcleritis, uveitis and conjunctivitis, sclerosing cholangitis and bile duct carcinoma, although liver problems are much more common in ulcerative colitis.^{1,2} There is a wide geographical variation in the incidence of Crohn's disease, and although the aetiology is unknown, there does appear to be some genetic susceptibility as there is a 30-fold increase in sibling incidence compared to the general population. The most common symptoms of small bowel Crohn's disease are diarrhoea (90%), abdominal pains (55%), anorexia, nausea and weight loss (22%).^{1,2} Our patient exhibited all these symptoms, and also showed typical nutritional disturbance of anaemia (iron, folate or vitamin B12 deficiency), hypoalbuminaemia and weight loss. Acute phase reactants are also often raised in active disease and our patient's CRP was grossly elevated. Small bowel stenosis is common in Crohn's disease, at time of diagnosis a bowel stenosis was documented in 37% in one series.³ However, acute first presentation of Crohn's disease with small bowel segmental volvulus has not previously been reported. Closed loop obstruction such as this can also lead to accelerated mucosal permeability changes with bacterial translocation and portal endotoxaemia which may lead to multiple organ dysfunction syndrome. Also grossly distended bowel is at risk of ischaemic necrosis and/or perforation.³ Therefore, early diagnosis and expedient treatment is a priority to prevent the development of these complications. Small bowel volvulus (midgut volvulus) is in itself rare and usually presents in childhood, being due to an unusually narrow based mesentery to the small bowel caused by malrotation of the bowel and persistent embryological peritoneal bands (Ladd's bands). In the absence of this embryological abnormality, volvulus of small bowel is extremely rare. However, in our case, there was no malrotation and rather the volvulus occurred by twisting of a grossly dilated loop of small bowel about an area of inflammatory stenosis of the small bowel. With short segment stenosis due to Crohn's disease, the conservative procedure of stricturoplasty has been very effective with a low associated morbidity and mortality.⁴ In our patient however, due to the

Figure 3 Operative field at laparotomy, showing a grossly dilated segment of small bowel, the base of the dilated segment is seen to be twisted 360° in a clockwise direction, forming a closed loop obstruction

extent of the disease in the involved segment and the lack of a prior histological diagnosis, a segmental resection was felt to be appropriate. Clinicians should be aware of this rare presentation, demonstrated on abdominal X-ray, which required quick diagnosis and urgent treatment. This report adds to the known literature on both Crohn's disease and small bowel volvulus.

Final diagnosis

Crohn's disease presenting as a segmental small bowel volvulus.

Keywords: Crohn's disease; volvulus; small bowel obstruction

Learning points

- Crohn's disease can present in a variety of ways and mimic many other disease processes. It should be part of every clinician's differential diagnosis of acute or chronic abdominal pain
- a closed loop bowel obstruction is a surgical emergency which requires rapid diagnosis and early intervention, if a successful outcome is to be obtained
- true midgut volvulus not only presents in children, but although rare, has been reported in young adults and even geriatrics
- in the absence of congenital abnormalities, a volvulus can occur around any pivotal point; common axes for the volvulus are tumours, adhesive bands, and stenoses

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Atrial flutter in a young man with a highly competitive and stressful occupation

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A previously fit 41-year-old man presented in March 1997 with palpitations and shortness of breath. Initial symptoms consisted of paroxysmal palpitations occurring after exercising; however, over the course of 6 months, he became aware that his pulse was consistently irregular and that even mild exertion made him short of breath. The patient was on no medicines. Coffee, tea and caffeine-containing beverages were only consumed in moderation. He was a life-long non-smoker and consumed approximately 5 units of alcohol per week. His occupation was competitive with a mentally stressful environment; he found his performance was helped by the use of a dietary supplement. Examination was unremarkable apart from an irregularity of the arterial pulse. The patient appeared euthyroid and was normotensive (blood pressure 110/700 mmHg) with no signs of heart failure. An electrocardiogram showed atrial flutter, at a rate of 148 beats/min, with variable block. Haematological and biochemical analyses, including thyroid function were normal as were a chest radiograph and echocardiogram. The patient was anticoagulated with warfarin and commenced on flecainide (200 mg bid) in anticipation of precipitating a pharmacologic cardioversion to sinus rhythm.

Administration of flecainide resulted in a deterioration in symptoms due to increased irregularity of heart rhythm and a reduction in exercise capacity. This was discontinued and an elective DC cardioversion was performed with a return to sinus rhythm at a rate of 68 beats/min.

Questions

- 1 What is the most probable diagnosis ?
- 2 What would be your next investigation ?
- 3 In what cardiovascular circumstance might you have chosen to avoid flecainide because of its pro-arrhythmic potential ?

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Answers

QUESTION 1

Atrial flutter precipitated by the combination of stimulant herbal constituents in the dietary supplement used as an aid to performance at work.

QUESTION 2

An electrocardiogram with the patient back in sinus rhythm looking for evidence of an accessory conduction pathway.

QUESTION 3

The risk of pro-arrhythmic effects are always present but are most likely in patients with structural heart disease and/or significant left ventricular impairment. Flecainide should therefore be avoided in the presence of haemodynamically significant valvular heart disease and/or heart failure. Flecainide should also be avoided post-myocardial infarction and in cases where ischaemia is suspected as the underlying aetiology of the arrhythmia.

Comment

The current trend for alternative or complementary medicine, in particular, a proliferation of 'herbal remedies' and 'dietary supplements', has led to concern being expressed in both the lay and medical press.¹ Such products may contain numerous compounds, including cocktails with western synthetic medicines.² They are often untested, unregulated by medicine review bodies and are available to anyone.³ In a clinical context the problem is compounded by undisclosed use, use by patients already on conventional medicines and use by those with underlying medical conditions.⁴

Several components of the dietary supplement used by this patient (table) are individually reported as having cardiovascular and/or central nervous system effects; of particular note the use of guarana, ginseng, ginger and liquorice are cautioned in those with existing heart disease.⁵ It appears probable that our patient developed his arrhythmia as a consequence of a combination of these actions. The use of traditional herbal medicines over centuries has led to a widespread feeling that they are

Learning points

- herbal preparations are frequently heterogeneous and lack quality controls
- risk is usually due to contamination, to an added drug or to falsification of constituents
- potential interactions with conventional orthodox medicines need to be considered
- constituents may be unknown, undisclosed and could contain illegal (ie, amphetamines) and/or prescription only (ie, steroids) components
- an awareness of toxic effects should include those due to heavy metals and to mega-vitamin over-dosage

innocuous. Whilst atrial flutter was relatively well tolerated in this patient, a previously healthy individual was subjected to several potential complications including tachycardia-related cardiomyopathy, thrombo-embolic events, trial of anti-arrhythmic therapy, anticoagulation and DC cardioversion.

Table 1 Constituents of the herbal blend component of the single dietary supplement used in this case and their potential for clinical effects

Component	System affected
Guarana	cardiovascular
Astragalus root	
<i>Rhizoma ligusticum</i>	cardiovascular
White willow bark (weidewinde)	
Bladderwrack (<i>Fucus vesiculosus</i>)	endocrine
Peppermint	
Lemon verbena	
Goto kola	CNS
Siberian ginseng	cardiovascular
Licorice	endocrine
Cinnamon	
Chamomile	cardiovascular, CNS
Ginger root	cardiovascular
Bee pollen	
<i>Pericarpium citri reticulatae</i>	cardiovascular
Rehmannia root	
Chicory	
Reishi mushroom (<i>Ganoderma lucidum</i>)	

CNS = central nervous system

Final diagnosis

Atrial flutter secondary to stimulant components of a compound dietary supplement.

Keywords: dietary supplements; herbal remedies; arrhythmia; atrial flutter

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Sore mouths and itchy wrists

J A G Buchanan, J M Zakrzewska

Oral soreness is a frequently encountered complaint in clinical practice with a large number of possible causes. Figures 1 and 2 below are clinical photographs taken of the mouths of two different late-middle-aged patients complaining of long-standing oral soreness, particularly associated with the ingestion of acidic, spicy foods and drinks. On direct questioning, both admitted to having pruritic rashes on the flexor aspects of the wrists and forearms which had appeared several months previously (figure 3). Both patients have oral manifestations of the same mucocutaneous condition. Study the photographs below and say whether the following statements are true or false.

Figure 1

Figure 2

Figure 3

Questions

- The oral lesions are:
 - caused by *Candida albicans*
 - associated with an elevated titre of IgG autoantibodies to the intercellular substance of the epithelium
 - typically bilateral
 - usually painless and associated with urethritis, conjunctivitis and arthritis
 - a recognised marker of internal malignancy.
- Cutaneous manifestations of this condition include:
 - alopecia
 - nail pitting
 - violaceous papules with Wickham's striae
 - photosensitive rash
 - an association with a positive Koebner's sign.
- In the management of this condition:
 - the oral lesions rapidly respond to oral metronidazole at doses of 200 mg tid for 7 days
 - biopsy will typically show features of dysplasia
 - liver function tests should be considered
 - a careful drug history should be taken
 - topical steroids are curative.

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Answers

QUESTION 1

A False Whilst the white lacy appearance might be mistaken for lesions of acute pseudomembranous candidiasis or thrush, the faint white striae present on the buccal mucosa have the classical appearance of reticular lichen planus and, unlike thrush, are not rubbed off to leave a red area of mucosa. Lesions can become secondarily infected with *Candida* with resultant exacerbation of oral soreness.

B False This is found in pemphigus vulgaris.

C True Both the oral and cutaneous manifestations of lichen planus are classically symmetrical. In the mouth, the tongue, gingivae, buccal and labial mucosa may be affected. In addition to the *reticular* (figure 1) and *erosive* (figure 2) lesions shown here, *papular*, *plaque*, and *atrophic* types of oral lichen planus are recognised and may coexist. Pigmentation of the mucosa can occur on healing and is most marked in patients with pigmented skin.

D False The oral lesions of lichen planus may be asymptomatic but are not associated with Reiter's syndrome in which the classical oral lesions are painless superficial ulcers.

E False Both pemphigus vulgaris and benign mucous membrane pemphigoid have been suggested to be associated with internal malignancy in a small number of patients. As one might expect given its high prevalence, lichen planus can coexist with neoplasia at other sites in about 6% of cases, but it cannot be said to be a marker of internal malignancy.

QUESTION 2

A True Permanent scarring alopecia is a recognised complication of lichen planus.

B True Nail involvement is thought to occur in up to 10% of patients and varies from longitudinal grooving and pitting to permanent nail loss.

C True The cutaneous lesions of lichen planus tend to start on the limbs, particularly affecting the forearms and wrists as pruritic, flat-topped, polygonal papules a few mm in diameter which may have a delicate lace-like pattern of white Wickham's striae on their surface. The papules are initially red but subsequently become violaceous. The skin of the neck, genitalia, palms and soles may also be affected. The skin lesions subside within 9 months in about 50% of cases and in 85% have cleared within 18 months.¹

D False Lichen planus, unlike lupus erythematosus, is not associated with a photosensitive rash.

E True Lichen planus shows the Koebner phenomenon, ie, lesions appear in an area of linear trauma such as a scar or a scratch. Other dermatological conditions exhibiting this phenomenon include psoriasis, molluscum contagiosum, warts, and vitiligo.

QUESTION 3

A False Oral metronidazole is of no recognised therapeutic use in the treatment of lichen planus.

B False In the reticular type of lichen planus

the histological appearance classically shows hyperpara- or ortho-keratosis, saw-tooth-like rete ridges and a band-like lymphocytic infiltrate. There is typically no dysplastic change. The premalignant potential of oral lichen planus is a contentious issue but some have suggested a malignant transformation rate of 1–10%.²

C True Associations of lichen planus with chronic active hepatitis and primary biliary cirrhosis have been reported.³

D True To exclude a lichenoid drug reaction which may resemble lichen planus but is usually not symmetrically distributed. Drugs associated with oral lichenoid reactions include gold salts, nonsteroidal anti-inflammatory agents, antimalarials, and methyldopa.

E False Topical steroids may reduce the oral symptoms but are not curative.

Discussion

Lichen planus is a relatively common chronic mucocutaneous disorder of uncertain, possibly autoimmune, aetiology which, if untreated, in the mouth may give rise to prolonged oral soreness and on the skin may cause an intensely pruritic symmetrical rash. The prevalence of oral lichen planus in the general population is approximately 2%⁴ with a wide variation (4–44%) in the proportion of patients with oral lesions having concurrent cutaneous lesions.⁵ It is predominantly a disease of late middle age and is rarely encountered at the extremes of age. Before the age of 50 years both sexes appear to be affected equally; after this there is a slight female predominance.⁶

There is a wide variation in the extent of discomfort associated with oral lichen planus: complaints of oral discomfort exacerbated by acidic or spicy foods are more common with the atrophic or erosive types. The natural history of the oral disease is variable with periods of exacerbation which may be associated with times of stress. In addition to an association with autoimmune liver disease, lichen planus has been linked with diabetes mellitus and impaired glucose tolerance. In such cases it seems likely that high blood glucose levels lead to candidal superinfection of pre-existing lichen planus lesions and oral soreness. Oral lesions can exist in isolation and may persist for many years after the resolution of cutaneous lesions. In one study only 32% had cutaneous lesions when oral lichen planus was initially diagnosed.

The differential diagnosis of oral lichen planus includes candidiasis, leukoplakia, squamous cell carcinoma, lichenoid reactions and lupus erythematosus. A thorough drug history is of paramount importance where a lichenoid reaction is considered a possibility. Definitive diagnosis requires a biopsy and is most suitably performed by an oral physician. Few hospitals have access to a Department of Oral Medicine and should this be the case a suitable alternative opinion should be sought from either the oral and maxillofacial surgeons or the dermatologists.

Where lichen planus is asymptomatic and a chance finding, management may merely involve confirmation of the diagnosis and reassurance of the patient. In others with symptoms, advice to avoid highly spiced foods and to use a nonflavoured toothpaste may be beneficial. Candidiasis should be considered and treated with topical antifungal agents if present. Topical steroid applications, eg, triam-

cinolone in Orabase or betamethasone mouthwash are used to reduce inflammation. Tetracycline mouthwash may be useful in the management of erosive lesions. Experience suggests that lesions with an atrophic nature are the most likely to undergo malignant transformation and should be closely monitored.

Keywords: lichen planus; alopecia; oral lesions

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A complication of intensive care

Mark Melzer, Sarah Craven, Robert Bagg

A 44-year-old woman with non-insulin-dependent diabetes mellitus presented with severe respiratory distress secondary to a suspected pulmonary embolus. She required immediate intubation, thrombolysis was administered and she was transferred to the Intensive Care Unit for ventilatory and inotropic support. A ventilation perfusion scan confirmed ventilation perfusion mismatch and she was subsequently anticoagulated. She appeared to be making an uneventful recovery until 7 days later when she developed a temperature. An abnormality of her right eye was noted and on ophthalmological review visual acuity was 6/36; funduscopy revealed multiple choroidal lesions.

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Figure

Questions

- 1 What is the abnormality seen in the right eye?
- 2 What are the possible causes?
- 3 What investigations were undertaken to confirm the diagnosis?
- 4 How was this condition managed?

Answers

QUESTION 1

A right eye hypopyon.

QUESTION 2

Bacterial endophthalmitis, whether endogenous or exogenous, may give rise to a hypopyon. Non-infectious causes include Beçhet's syndrome and, on occasions, the HLA B27 arthritides that are associated with anterior uveitis.

QUESTION 3

A fully sensitive *Staphylococcus aureus* was grown from blood taken centrally and peripherally and from a central line tip which had been inserted 5 days previously. As pathogens found in blood cultures and ocular fluid occur with equal frequency, no intravitreal specimen was obtained, although sampling the anterior chamber and vitreous is of importance when the diagnosis is in doubt.¹

QUESTION 4

The patient was treated for 6 weeks with flucloxacillin, initially intravenously then orally, and oral fusidic acid, and her hypopyon and choroidal lesions resolved. When last seen the patient was clinically well and visual acuity in her right eye was normal. Treatment with high-dose intravenous therapy is generally sufficient as the passage of organisms is thought to disrupt the blood-ocular barrier, although in severe cases intravitreal antibiotics and vitrectomy are advocated.^{2,3} As the condition is uncommon there are no controlled data suggesting that either intravitreal antibiotics or vitrectomy is better than more conservative treatment.

Discussion

Bacterial endophthalmitis is a rare but severe sight-threatening form of ocular infection. Exogenous endophthalmitis following ocular

surgery or trauma is more common than metastatic blood-borne infection (endogenous endophthalmitis). If left untreated, progressive reduction in vision and ultimately blindness will occur. In recent years the most common organisms causing metastatic endophthalmitis have become Gram-positive bacteria, replacing *Neisseria meningitidis*, the incidence of which decreased in the 1940s with the introduction of antibiotics. Certain organisms have a clear predilection for particular parts of the eye, with *S aureus* commonly originating in the posterior segment. It is, on occasions, associated with a reactive hypopyon (figure). With early systemic intravenous treatment, as in this case, focal posterior involvement has a good prognosis. This is in marked contrast to diffuse posterior involvement and panophthalmitis.⁴ Similar cases, though community acquired, have been reported in diabetics,⁵ dialysis patients,⁶ and in patients with lymphoma⁷ who, because of recurrent breaks in the skin, intravenous access and immunocompromised states, are more prone to staphylococcal bacteraemia. In addition to these predisposing factors concurrent non-ocular infection such as urinary tract infections,⁸ endocarditis and osteomyelitis, should be considered and may not present until after the onset of ocular infection.

In any patient with staphylococcal bacteraemia, metastatic infection of heart valves, joints and bones are well documented. Rarely, the posterior chamber of the eye may become infected and a hypopyon and choroidal lesions should not be overlooked.

Final diagnosis

Nosocomially acquired right eye endophthalmitis caused by a *Staphylococcus aureus* bacteraemia secondary to an infected central line.

Keywords: endophthalmitis; *Staphylococcus aureus* bacteraemia

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A neonate with an unusual pulse discrepancy

Martial M Massin, Geneviève Franckart

A 38-week gestational age boy was admitted after birth by Caesarean section to a neonatal unit. At 6 hours of life, a dextrose infusion was started because of hypoglycaemia. At 36 hours he developed cyanosis and tachypnoea. Physical examination revealed tachycardia, 2/6 systolic murmur, weakly palpable limb pulses, hepatomegaly and pulmonary rales. Laboratory tests were within the normal range, except blood gas analysis which showed respiratory and metabolic acidosis. Management entailed fluid resuscitation, mechanical ventilation and antibiotic administration. Because of recurrent metabolic acidosis and unstable haemodynamics, the infant was transferred at 48 hours to our neonatal intensive care unit with a diagnosis of probable sepsis. On admission all limb pulses were absent but carotid pulses were weakly palpable and became strong after establishing stable haemodynamics with inotropic support. Chest X-ray showed cardiomegaly and pulmonary oedema. Echocardiography confirmed the clinical diagnosis. The clinical condition of the patient improved quickly after initiation of treatment. Twenty-four hours later he was catheterized because of associated lesions. Left ventricular angiography is shown in figure 1. Retrograde aortography with a balloon-tipped catheter passed from the main pulmonary artery through the ductus arteriosus into the descending aorta (figure 2) confirmed the diagnosis. He was then prepared for surgery.

Figure 1 Left ventricular angiography: lateral view

Figure 2 Retrograde aortography, frontal projection

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Questions

- 1 What is your diagnosis ?
- 2 What do left ventricular angiography and retrograde aortography demonstrate ?
- 3 What is the present drug of choice for treatment ?

Answers

QUESTION 1

Physical findings of radial, carotid and femoral pulse discrepancy are typical of interrupted aortic arch or ductal-dependent coarctation. In this situation, where all limb pulses are very weak or impalpable and while both carotid pulses are strong, one would suspect interrupted aortic arch with obstruction proximal to the left subclavian artery with aberrant origin of the right subclavian artery from the descending aorta. Ductal-dependent coarctation with involvement of the left subclavian artery in the coarctation, its origin below the lesion, or a localised stenosis of the vessel's origin, associated with aberrant origin of the right subclavian artery, is the second possible diagnosis.

QUESTION 2

Left ventricular angiography (figure 1) confirms that both carotid arteries arise proximal to the interruption. The appearance of contrast in the descending aorta through an associated malalignment-type ventricular septal defect and the ductus arteriosus makes the site of interruption evident. A balloon-tipped catheter with proximal side holes is passed from the main pulmonary artery through the ductus arteriosus into the descending aorta and a retrograde aortography with inflated balloon shows that both subclavian arteries arise distal to the interruption (figure 2).

QUESTION 3

Standard therapy with prostaglandin E1 must be started immediately for induction and maintenance of ductal patency.

Discussion

Interrupted aortic arch is a rare congenital heart disease with a prevalence of 1% of critically ill cardiac infants. It is defined as a complete separation of ascending and descending aorta. It comprises several different anomalies that relate to the pattern of branching of the brachiocephalic arteries.¹ Patients typically present with acute cardiovascular collapse after spontaneous closure of the ductus arteriosus in

Learning points

- ductal-dependent left heart obstructive lesions (interrupted aortic arch and severe form of coarctation) are the main causes of cardiac failure in the neonate and the only congenital heart defects for which clinical examination with analysis of the pulse discrepancy suggests the exact diagnosis
- anomalous origin of the right subclavian artery from the aorta distal to the normally positioned left subclavian artery is one of the more frequent congenital anomalies. It is frequently associated with congenital heart disease
- when an aberrant right subclavian artery is associated with interruption between carotid and subclavian arteries, only the palpation of the carotid pulses is helpful to differentiate interrupted arch from critical aortic stenosis or sepsis

the first days of life. Interrupted aortic arch and severe forms of coarctation are the main causes of cardiac failure in the neonate and are often at the root of multiple organ failure which worsens the prognosis.²

Anomalous origin of the right subclavian artery from the aorta distal to the normally positioned left subclavian artery is one of the more frequent congenital anomalies. Zapata *et al*³ reported associations of aberrant right subclavian artery with aortic arch anomalies, and found this anomaly in 3% of cases of interrupted aortic arch and 1% of coarctation of the aorta.

Ductal-dependent left heart obstructive lesions are the only congenital heart defects for which clinical examination suggests the exact diagnosis with the consequence that initial management may be optimal. Physical findings of radial, carotid and femoral pulse discrepancy, depending on branching pattern, are typical of interrupted aortic arch or ductal-dependent coarctation (table).^{4,5} Differential cyanosis, although theoretically possible, is uncommon.⁵ Retro-oesophageal right subclavian artery is not uncommon and absence of right radial pulse does not exclude aortic arch anomalies. When an aberrant right subclavian artery is associated with interruption between carotid and subclavian arteries, only the palpation of the carotid pulses is helpful to differentiate interrupted arch from critical aortic stenosis or sepsis.⁴

In this case the diagnosis should have been suspected before clinical deterioration; quick transfer under prostaglandin E1 therapy would have avoided the development of acute cardiovascular collapse.

Final diagnosis

Interrupted aortic arch.

Keywords: congenital heart disease; neonate; aortic arch abnormality

Table Diagnosis according to the pulse discrepancy

Right arm pulses	Right carotid pulse	Left carotid pulse	Left arm pulses	Femoral pulses	Diagnosis
+	+	+	+	–	IAA type A or COA
+	+	+	–	–	IAA type B or COA
+	+	–	–	–	IAA type C
–	+	+	+	–	IAA type A+ARSA or COA+ARSA
–	+	+	–	–	IAA type B+ARSA or COA+ARSA
–	+	–	–	–	IAA type C+ARSA
–	–	–	–	–	sepsis or aortic stenosis or IAA or COA in agonal condition

Abbreviations: IAA = interrupted aortic arch, type A = interruption distal to the left subclavian artery, type B = interruption between the left common carotid artery and the left subclavian artery, type C = interruption between the innominate artery and the left common carotid artery; COA = coarctation of the aorta; ARSA = aberrant right subclavian artery; + = strong pulse, – = weak or impalpable pulse.

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Pericardial tamponade in a 65-year-old woman

Celalettin Usalan, Enver Atalar, Filiz Kulb Vural

A 65-year-old woman with a one-month history of weakness and malaise was admitted to hospital because of chest pain, confusion, sweating and severe dyspnoea. Body temperature, blood pressure, pulse rate, and respiratory rate were 35.7°C, 80/60 mmHg, 62 beats/min and 38 breaths/min, respectively. Physical examination showed tachypnoea, jugular venous distension, pulsus paradoxus, kussmaul sign, hepatomegaly and diminished heart sounds. Chest X-ray disclosed a symmetrical globular enlargement of the heart (figure 1). Electrocardiogram revealed a reduction in amplitude of the QRS complex and sinus rhythm. Echocardiogram showed a massive pericardial effusion with right atrial and ventricular diastolic collapse. The diagnosis of pericardial tamponade was suggested, and emergency treatment was performed.

Haematological studies revealed a haemoglobin level of 11.6 g/dl, a leucocyte count of $11.8 \times 10^9/l$, and erythrocyte sedimentation rate of 52 mm/h. Serum biochemical profile was in normal range, and tests for viral, rheumatic and collagen disease were negative. Mantoux test was also negative. After stabilizing the patient's clinical condition, further studies were performed to establish the aetiology. Pericardial fluid examination was unremarkable except for the high protein content (4 g/dl), and microbiological cultures and cytologies were negative.

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Figure 1 Admission chest X-ray

Questions

- 1 What is the most probable cause of the cardiac tamponade in this patient?
- 2 What are the major causes of pericardial tamponade?
- 3 How should the patient be managed?

Answers

QUESTION 1

The association of hypotension with relative bradycardia in this case was interesting and suggested the possibility of hypothyroidism complicated by pericardial effusion. The results of thyroid function tests were as follows; serum thyroxine 1.2 µg/dl (normal range 5–12 µg/dl), triiodothyronine 8.8 ng/ml (80–120) and serum thyroid-stimulating hormone 102 µU/ml (0.4–4.8). Thyroid function studies were diagnostic of primary hypothyroidism. Although hypothyroidism is a rare cause of pericardial tamponade, it should be included in the differential diagnosis of cardiac tamponade.

QUESTION 2

Pericardial tamponade may occur in association with pericarditis of almost any cause. The most frequent causes of cardiac tamponade are malignancies followed by idiopathic or viral pericarditis and uraemia (box).

QUESTION 3

The patient should be managed with pericardiocentesis and thyroid replacement therapy.

Outcome

After the diagnosis of pericardial tamponade, percutaneous pericardiocentesis was performed immediately with a catheter and after removal of 250 ml of fluid from the pericardial sac the blood pressure gradually returned to normal and a considerable improvement in haemodynamics was seen. Because the aetiology of our patient was primary hypothyroidism, thyroid replacement treatment was started with levothyroxine 0.025 mg/day, with progressive increase of dosage. When the patient's thyroid function reached an euthyroid state after 2 months of therapy, chest X-ray showed marked diminution of cardiac size (figure 2). Echocardiography was repeated and showed minimal pericardial fluid.

Figure 2 Chest X-ray in the euthyroid state, after 2 months of thyroid replacement therapy

Common causes of cardiac tamponade

- malignant disease
- idiopathic pericarditis
- uraemia
- bacterial
- tuberculosis
- cardiomyopathy (receiving anticoagulants)
- acute myocardial infarction (receiving heparin)
- diagnostic procedures with cardiac perforation
- dissecting aortic aneurysm
- postpericardiotomy syndrome
- radiation
- myxoedema (a rare cause of pericardial tamponade)

Discussion

Hypothyroidism is associated with increased capillary permeability and impaired lymphatic drainage with subsequent leakage of protein into the interstitial space, resulting in pericardial effusion, a common clinical finding in overt hypothyroidism. The incidence has been reported as between 3% and 80% in several studies.^{1,2} No correlation appears to exist between the development of pericardial effusion and severity or duration of hypothyroidism. Pericardial effusion in hypothyroidism is rarely complicated by pericardial tamponade, and may be partly accounted for by slow fluid accumulation. The presentation and clinical courses of pericardial effusion in hypothyroidism are extremely variable. It may rarely be the major presenting manifestation of thyroid disease.^{3,4} Most pericardial effusions due to hypothyroidism slowly regress after thyroid replacement. Rarely, pericardial effusion persists despite adequate thyroid therapy. And more rarely recurrent tamponade can be seen despite adequate thyroxine therapy.⁵ The classical clinical picture in pericardial tamponade includes chest pain, confusion, and dyspnoea associated with hypotension and tachycardia. The association of hypotension with relative bradycardia in this case was of interest and suggested the possibility of hypothyroidism complicated by pericardial effusion.

The diagnosis of hypothyroidism is frequently overlooked. It is important therefore, to carry out appropriate tests for thyroid function as well as echocardiography in patients with an enlarged cardiac silhouette of undetermined origin.

Final diagnosis

Hypothyroidism complicated by pericardial tamponade.

Keywords: hypothyroidism; pericardial tamponade

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Postural hypotension and electrolyte disturbances in a 61-year-old man

L R Ranganath, S R Gould

A 61-year-old man, in apparent previous good health, presented to hospital with persistent dizziness and two attacks of postural syncope, all with a duration of less than a month. His blood pressure was 100/70 and 80/55 mmHg in the recumbent and upright postures, respectively. His pulse was 72 beats/min, regular, and all accessible peripheral pulses were palpable; the rest of the cardiovascular system examination was normal. He denied any drug therapy or gastrointestinal fluid losses. His serum electrolytes are shown in table 1.

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Table 1 Serum and urinary electrolytes

	<i>Serum (ref range)</i>	<i>Urine</i>
Sodium (mmol/l)	120 (133–149)	<10
Potassium (mmol/l)	2.5 (3.6–5.2)	21
Chloride (mmol/l)	72 (96–108)	—
Bicarbonate (mmol/l)	33 (24–30)	—
Urea (mmol/l)	26.3 (2.3–6.3)	—
Creatinine (μmol/l)	162 (50–130)	12 800
Osmolality (mOsm/kg)	266 (285–295)	401

Questions

- 1 What diagnoses would the serum and urine electrolytes suggest?
- 2 What treatment should this man receive?

Answers

QUESTION 1

The combination of hyponatraemia, hypokalaemia, raised bicarbonate (indicative of probable metabolic alkalosis but blood gases not performed) and uraemia is indicative of sodium, potassium and fluid loss. The uraemia in our patient is most likely to be pre-renal since urine sodium is undetectable, fractional sodium excretion is <0.1%, urine to serum (U:S) creatinine ratio is 79, and U:S osmolality ratio is 1.51 (pre-renal uraemia is generally characterised by urine sodium <10 mmol/l, a fractional sodium excretion of <1%, a U:S creatinine ratio of >25 and a U:S osmolality ratio of >1.5).

The diagnosis of Addisonian crisis is suggested by the hypotension, uraemia and hyponatraemia; however, the absence of clinical features suggestive of Addison's disease, as well as the absence of hyperkalaemia and increased renal sodium loss, makes this diagnosis extremely unlikely. The urinary results do not support a primary renal loss of fluid and electrolytes as the cause of hypotension in this man. In health, hyponatraemia (and plasma hypotonicity) leads to suppression of antidiuretic hormone secretion; this appropriate homeostatic response leads to the production of dilute urine, increased free water excretion and restoration of plasma sodium to normal. However, when intravascular volume depletion co-exists with hyponatraemia, the hypovolaemia produces a marked increase in antidiuretic hormone secretion over-riding the suppressive effect of hyponatraemia (as exemplified by our patient); this leads to high urine osmolality in the face of hypotonic serum, highlighting the body's attempts to maintain blood volume and tissue perfusion in preference to maintaining electrolyte balance.

In our patient, in the absence of obvious gastrointestinal losses, unadmitted diuretic or laxative abuse must be considered. The urine

measurements do not exclude the possibility of recent diuretic abuse.

QUESTION 2

This man should be given isotonic saline with potassium supplements to restore euhydration and electrolyte balance. A search for the cause of his electrolyte and fluid losses must continue.

Further clinical course

Soon after the initiation of fluid and salt repletion as an in-patient, a mucous liquid (approximately 800 ml per day) rectal discharge was noted. He admitted that he had noticed mild mucoid rectal discharge averaging 3–4 times per day for the previous 6 months. The composition of the faecal fluid is shown in table 2.

Table 2 Composition of serum and faecal fluid

	Serum	Faecal
Sodium (mmol/l)	124 (133–149)	159
Potassium (mmol/l)	3.3 (3.6–5.2)	34
Chloride (mmol/l)	74 (96–108)	157
Bicarbonate (mmol/l)	37 (24–30)	—
Urea (mmol/l)	27.4 (2.3–6.3)	14.5
Creatinine (μmol/l)	179 (50–130)	19
Osmolality (mOsm/kg)	272 (285–295)	408

The main source of the fluid and electrolyte losses in this man is probably the lower gastrointestinal tract. The lack of a positive faecal osmolal gap probably excludes osmotic diarrhoea. The secondary hyperaldosteronism, following rectal loss of fluid and electrolytes, leads to further renal potassium loss, compounding the faecal potassium loss. Sigmoidoscopy revealed a villous adenoma whose extent was delineated by a barium enema (figure). Tumour fragments obtained by biopsy following sigmoidoscopic examination did not reveal a malignant change. A fasting gut hormone profile for vasoactive intestinal polypeptide, pancreatic polypeptide, gastrin, glucagon, somatostatin and neurotensin was negative. This man is currently awaiting surgery for excision of the tumour.

Discussion

The short duration of mucoid diarrhoea and occult faecal fluid and electrolyte losses in this man with villous adenoma is similar to that described in previous studies.¹ Most modern standard textbooks do not highlight the profound hyponatraemia that can occur in patients with villous adenomata, although hypokalaemia secondary to these tumours continues to be emphasized. The entire clinical picture in this man is attributable to the sudden development of sodium, potassium and fluid losses, reversed entirely by isotonic saline and potassium. We found no evidence of a humoral-mediation of faecal losses of fluid and

Figure Barium enema studies of colonic villous tumour showing (A) coating of the tumour surface by residual barium following evacuation, and (B) barium-filled rectosigmoid colon showing the outline of the tumour mass. The arrows indicate the site of the tumour

electrolytes such as those reported in tumours secreting excessive vasoactive intestinal polypeptide secretion. Our patient had no symptoms attributable directly to a local effect of the tumour, either as tenesmus or rectal bleeding, which may have contributed to the late clinical presentation.

Villous adenomata arise mainly in the rectum and the rectosigmoid, with equal sex distribution, usually in persons over the age of 50 years.² Malignancy is a common complication in these tumours and multiple histological sections may be required to exclude this possibility in any given patient. Diarrhoea of varying duration (3 months to 15 years) and volume (0.3–3.4 l/24 h) is commonly seen with these tumours; an average of 120, 44 and 123 mmol/l of sodium (range 40–120), potassium (range 15–107) and chloride (80–163), respectively, has been described in the faecal fluid.³ Vague abdominal pain, anorexia, weight loss, excessive thirst, nausea and vomiting may have been present for some time prior to total collapse.¹ Not all of these tumours produce fluid and electrolyte depletion⁴ but those that do may cause marked dehydration, lethargy, weakness, oliguria, metabolic acidosis, mental confusion, and hypotension. Ability to compensate for loss of fluid and electrolytes may extend over many years until the tumour enlarges sufficiently, intake is decreased or fluid loss increased to the point that compensatory mechanisms become ineffectual; inability to compensate may develop rapidly and dramatically, the previously asymptomatic patient presenting as an emergency.¹ Symptoms such as rectal bleeding, change in bowel habit, tenesmus, prolapse of the tumour, and elimination of tumour tissue have also been described.¹ Lesions can be over-

looked on rectal palpation because of their softness or a more proximal location. These tumours are usually single and located within reach of a sigmoidoscope, as was the case in our patient, although multiple and more proximal lesions have been described.⁵ Typically the tumour arises in the rectum, is sessile, reddish-grey, bulky and may involve the entire circumference of the bowel. Barium enema studies are helpful, as seen in our patient, in outlining the extent of the lesions as well as establishing the presence or absence of multiple lesions. Definitive diagnosis must be confirmed by histological examination.^{5–6} Lack of awareness has been credited with fatal outcome, up to 20% in some series^{1–3}; such fatal outcome is invariably secondary to the incomplete correction of fluid and electrolyte imbalance produced by these tumours. Complete excision of the lesion with a margin of normal tissue is curative and the treatment of choice in benign lesions. If the tumour is shown to be malignant, the type of surgery should be the same as for any other carcinoma of colon or rectum.

We were unable to find recent publications describing the electrolyte and fluid imbalance that may occur with villous adenoma. This case is a reminder that severe electrolyte and fluid disturbances may occur with these tumours and energetic replacement is required in the management of these patients.

Final diagnosis

Villous adenoma causing severe electrolyte and fluid disturbances.

Keywords: villous adenoma; hyponatraemia; hypokalaemia; electrolyte imbalance

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