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Contents

Management of complicated parapneumonic effusion

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Introduction

Pneumonia ranked the third of leading causes of death in Hong Kong from 2001-2004 [1]. Complicated parapneumonic effusion or empyema thoracis complicates pneumonia in 44 to 57% of all the pneumonia cases [2,3]. The overall mortality rate among patients with complicated parapneumonic effusion is 15-20%. Most cases of parapneumonic effusion resolve with appropriate antibiotics, but a significant proportion develops complicated parapneumonic effusion or empyema thoracis. Apart from antibiotics, other treatment modalities for pleural infections consist mainly of drainage of the infected pleural fluid, administration of intrapleural fibrinolytic agents and surgical intervention.

Pathophysiology

An exudative effusion occurs in up to 57% of patients with pneumonia, and consists initially of the formation of a sterile “simple parapneumonic effusion”. The mechanisms contributing to the formation of effusion include increased vascular permeability and leakage following neutrophil migration into pleural space, and the production of pro-inflammatory cytokines including interleukin-8 (IL-8) and tumour necrosis factor (TNF-α). Simple parapneumonic effusions are clear, sterile exudates. Most simple parapneumonic effusion resolve with antibiotics and drainage is not usually required [4].

A minority of patients are complicated with secondary bacterial infection of the pleural effusion, leading to the development of a complicated parapneumonic effusion. The pleural fluid findings fulfilling the criteria for complicated parapneumonic effusion include pH <7.2, LDH >1,000 IU/L, glucose <2.2 mmol/L, and positive Gram stain or culture [2]. Such effusion seldom resolves without drainage. Persistence of infected pleural effusion may eventually result in the accumulation of pus in the pleural space (empyema thoracis). A key feature of this “fibrinopurulent stage” of infection is the result of inhibition of fibrinolysis (depressed levels of tissue-plasminogen activator) and activation of the coagulation cascade (elevated levels of plasminogen-activator inhibitors-2). Such disturbances result in fibrin formation which coats the pleural surfaces and forms adhesions and fluid loculations. Intrapleural fibrinolysis might have a role in breaking down the fibrinous adhesion at this stage.

Bacteriology

In general, the overall pleural fluid culture positivity rate ranges from 54 to 76%. In a local case series [5], Gram-positive bacteria accounted for 52.7% among all culture positive specimens whereas Gram-negative organism contributed 47.3%. Anaerobic pathogens (29.9%) were also common. Commonly isolated bacteria were *Streptococcus milleri* group (19.3%) and *Bacteroides* (14%), followed by *Klebsiella pneumoniae* (12.3%) and *Peptostreptococcus* (7.0%). When compared with the study by Maskell *et al* [6], we found a higher frequency of anaerobes (29.9% vs 8.13%). However, the proportion of *Streptococcus* species (31.2%) was greater in the study by Maskell et al then ours. Among the *Streptococcus* species, *Streptococcus milleri* group is the commonest group of organisms identified. Similar figure has been noted in the study by Maskell et al (15.6%). These findings contrasted with the findings in 1960s when pneumococcus had been the commonest pathogen [7]. Such change of microbial pattern may be attributed to the accessibility of patients worldwide to broad spectrum antibiotics. It was postulated that pneumonia due to virulent organism such as *Streptococcus pneumoniae* often manifests with prominent symptoms at very early stage of the disease. Hence, it is often treated earlier and reducing the chance of progression to pleural infection.

Streptococcus milleri group (SMG), a subgroup of viridans streptococci, is well known to be associated with pulmonary empyema or abscess formation [8]. SMG includes 3 species — *Streptococcus intermedius, Streptococcus anginosus* and *Streptococcus constellatus*. They possess proteolytic enzymes that predispose to necrosis of tissue and abscess formation [9]. Moreover, recent data in mice model showed that certain capsular material produced by SMG might be a pathogenic factor in terms of inhibiting the phagocytosis by polymorphonuclear neutrophils [10]. It has been postulated that SMG have relationship with underlying periodontal disease. In a local case series, 64% of cases with SMG were co-infected with anaerobes [5]. Studies in mouse model of pneumonia demonstrated that the abscess forming ability and the bacteria numbers of SMG were augmented when they were co-inoculated with other anaerobes (e.g. Fusobacterium) in vitro [11]. Another study suggested that *Prevotella intermedia* may interact with *Streptococcus constellatus* in the production of pulmonary infections by stimulating the growth of the latter and suppressing bactericidal activity of the host [12]. All these studies demonstrated the synergistic effect of anaerobes on SMG infection.

Gram-negative pathogens are commonly encountered among patients with diabetes mellitus. 44% of culture-positive empyema patients had diabetes mellitus in both Taiwan and local studies [13]. In the Taiwan study, the mortality rate was highest among those infected with aerobic Gram-negative bacilli (22%), followed by those with mixed pathogens (15.7%), aerobic or facultative Gram-positive pathogens (6.4%) and anaerobes (0%). Hence, more aggressive initial antimicrobial chemotherapy such as third generation cephalosporin is recommended for immunocompromised patients such as those with diabetes mellitus, malignancy or alcoholism.

Treatment

Apart from background co-morbidities, empirical antibiotics should have adequate coverage against common pathogens causing community-acquired pneumonia and should have favourable pharmacokinetics in pleural fluid. Penicillin was considered to have good penetration through infected pleura, followed by metronidazole, ceftriaxone, clindamycin, vancomycin and gentamicin in a rabbit model of empyema [14]. Penicillin levels remain elevated in pleural fluid at 240 minutes after serum levels had decreased [14]. However, in a recent Taiwan study [15], high proportion of anaerobes and SMG pathogens isolated in patients with lung abscess were resistant to penicillin and clindamycin. Beta-lactam / beta-lactamase inhibitor or 2nd / 3rd generation cephalosporin with clindamycin or metronidazole were suggested as empirical antibiotic therapy for community-acquired lung abscess. In the British Thoracic Society (BTS) guidelines of 2003 for pleural infection, beta-lactam / beta-lactamase inhibitor and cephalosporin were recommended as empirical antibiotics for complicated parapneumonic effusion [2]. Taking into account of the daily cost of each antibiotic and its anti-microbial coverage, amoxicillin / clavulanic acid appears to be the most cost-effective agent for use in this situation.

It is worth noting that a wide range of Gram-positive, Gram-negative and anaerobic organisms have been implicated in complicated parapneumonic effusion. It is therefore imperative that empirical antibiotics should have broad coverage. A broader spectrum coverage than is currently recommended for uncomplicated community-acquired pneumonia (CAP) seems warranted if parapneumonic effusion or empyema thoracis complicates CAP [16,17]. In those patients with poor clinical response with initial antibiotic (beta-lactam / beta-lactamase inhibitor or cephalosporin), a combination of antibiotics appears useful. Tuberculous effusion / empyema has to be excluded if fluoroquinolone is used. For critically ill patients, carbapenem group could be considered. Aminoglycosides should be avoided as

they penetrate poorly into pleural space and may be inactive in the presence of pleural fluid acidosis [18].

Sterilisation of the empyema cavity with appropriate antibiotics for at least 4-6 weeks is required. A longer course may be necessary unless there is prompt resolution of fever and leukocytosis.

The American college of Chest Physicians (ACCP) consensus in 2000 categorised parapneumonic effusions according to the risks of unfavourable outcome [3]. Those with either one or more of the followings were categorised into moderate risk group: (1) size of effusion greater than one hemithorax, (2) thickened pleura on CT thorax, (3) presence of loculations, (4) positive microbiological results and (5) pH <7.20 in pleural fluid. Those with frank pus in pleural fluid were categorised into high risk group. Prompt drainage was recommended apart from antibiotics. Fibrinolytics and surgery were recommended as acceptable approaches for moderate to high risk group patients and were believed to be associated with lowest mortality (level C evidence).

In the British Thoracic Society (BTS) guidelines of 2003 for pleural infection [2], patients with frank pus aspirated or pleural fluid results fulfilling the criteria for complicated parapneumonic effusion were recommended to receive a combination of chest tube drainage and 3 days course of intrapleural fibrinolytics. It was not known if such combination reduces mortality and / or the need for surgery.

On the other hand, a recently published multi-centre randomised controlled trial suggested that intrapleural streptokinase was ineffective in reducing mortality, the need for surgery or length of stay [6]. Besides, it carried a modest adverse event profile and should be generally avoided in pleural infection. In the accompanying editorial, the study was criticised for late administration of the intrapleural fibrinolytics, absence of ultrasonographic assessment at enrolment, relative advanced mean age of patients and large proportion of patients with coexisting illness which might adversely influence some of the study endpoints more strongly than did the potential benefits of fibrinolytic therapy.

In a local study [5], it appeared that drainage with intrapleural fibrinolytic and concordant initial antibiotic usage was associated with improved mortality and surgery-free survival. In a subgroup analysis, it was further shown that early use of intrapleural urokinase (≤ 4 days of diagnosis) reduced mortality, need for surgery and length of hospital stay. Such findings contrasted with the conclusion in the study by Maskell et al in which no benefit was found with intrapleural streptokinase [6].

The findings of our local study supported the hypothesis that intrapleural fibrinolytics have to be given early in the “fibrinopurulent stage” of complicated parapneumonic effusion so as to minimise the subsequent fibroblast proliferation and inelastic fibrous pleural thickening in the “organising stage” which might compromise drainage, impair the control of sepsis, and limit lung expansion.

Surgical intervention for complicated parapneumonic effusion includes thoracoscopy, rib resection with drainage of pleural space and decortication. Surgical interventions are usually indicated for multiloculated parapneumonic effusions, or uncontrolled pleural sepsis despite chest tube drainage.

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Pancreatic tuberculosis in a HIV-infected patient

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Introduction

Abdominal infection with tuberculosis (TB) commonly affects the spleen, liver and ileocecal region. Pancreatic tuberculosis is an extremely rare disease, especially when it is isolated in the pancreas.

The case

A 32-year-old gentleman, who was an ex-intravenous drug user, enjoyed good past health. He presented to a regional hospital with fever, cough with whitish sputum and right upper quadrant pain. CXR showed right lower zone haziness. Blood test showed neutrophilia (13.6 x 10^9/L) and lymphopenia (0.3 x 10^9/L). Liver and renal function tests were unremarkable and amylase was normal. Cefuroxime was started empirically. Sputum culture showed commensals only and sputum for AFB smear was negative. Urgent CT abdomen showed subsegmental collapse / consolidation of right middle lobe and no feature of liver abscess or acute cholecystitis. Subsequently blood culture grew methicillin-sensitive *Staphylococcus aureus* and cloxacillin was added. Echocardiogram was arranged. The patient, however, discharged himself 5 days after admission when fever just came down.

Six months later, the patient presented with fever, anorexia and epigastric pain again. Peripheral total white cell count was 10.7 x 10^9/L (Neutrophil 11.2 x 10^9/L and lymphocyte 0.5 x 10^9/L). Haemoglobin was 10.7g/dL. Liver and renal functions were again unremarkable. Albumin was reduced to 25 g/L while globulin was increased to 50 g/L. Amylase was normal. Urgent CT abdomen showed multiple small hypodense areas in the region of pancreatic head with the radiological diagnosis of pancreatic head abscess. Drainage of the pancreatic abscess was performed under ultrasound guidance during which a 4 cm x 3 cm x 3.5 cm heterogenous hypoechoic multiloculated mass at the pancreatic head was seen. Culture of the pancreatic abscess aspirate grew no organism but the AFB smear was positive and then confirmed to be *Mycobacterium tuberculosis* by PCR. Anti-tuberculosis treatment including isoniazid, rifampicin, pyrazinamide and ethambutol was started. Patient's symptoms improved. He was later diagnosed to have HIV infection which was also complicated by suspected pneumocystis pneumonia. He responded well to cotrimoxazole although BAL showed no evidence of pneumocystis infection. BAL and blood culture results later showed *Mycobacterium tuberculosis* as well.

Discussion and literature review

In 2005, WHO estimated that one third of the world's population is infected with tuberculosis and around 8% of the total global population burden of tuberculosis occurs in people with HIV infection. However, pancreatic involvement by tuberculosis is uncommon. In 1941, Auerbach reported 1656 consecutive autopsies on persons with tuberculosis [1]. Miliary tuberculosis was noted in 297 cases and of these, evidence of spread to the pancreas was found in only 4.7%. Paraf reported a similar review of autopsy studies in patient with miliary tuberculosis in 1966, pancreatic involvement was observed in 2% of 526 patients [2]. In a review of 300 cases of abdominal tuberculosis over 12 years in India, none of the patients had pancreatic involvement [3].

The pancreatic tuberculosis is likely to occur either by contiguous spread from peripancreatic lymph nodes or haematogenous spread. It can also represent reactivation of a latent pancreatic tuberculous focus after initial disseminated primary infection. Pancreas seems to be very resistant to invasion by tuberculosis. Antimycobacterial effect from pancreatic

extracts and purified lipases and deoxyribonucleases has been reported before.

The most common manifestation of pancreatic tuberculosis is a pancreatic mass found on imaging study and sometimes mimicking pancreatic carcinoma. Patient can also present as pancreatitis with epigastric pain, hyperamylasaemia, associated with ultrasound or CT findings of enlargement of the pancreas. This presentation occurs most commonly with disseminated tuberculosis. Patient may rarely present with obstructive jaundice. Crowson et al described a case of a 36-year-old man with a history of a paravertebral tuberculous abscess presented with jaundice and biochemical evidence of extrahepatic cholestasis [4]. An ultrasound revealed enlargement of the pancreas. At laparotomy, a 5-cm mass was found in the head of the pancreas and a clinical diagnosis of carcinoma of the pancreas was made. Histopathology revealed caseating granulomas and *Mycobacterium tuberculosis* was isolated. Three months after antituberculosis medications, an endoscopic retrograde cholangiopancreatography showed resolution of the obstruction.

At least three local cases of pancreatic tuberculosis have been reported. In 1986, a 48-year-old man with history of pulmonary tuberculosis was later found to have pancreatic tuberculosis [5]. He presented with epigastric pain and melaena for 10 days. An abdominal ultrasound showed a 6 cm x 7 cm mass in the head of the pancreas, the appearance of which was suggestive of hemorrhagic pancreatitis with necrosis. The patient, however, died of massive bleeding into the abdominal cavity. Autopsy revealed extensive tuberculous foci intermingled with normal pancreatic acini and erosion of one of the major pancreatic arteries. Another 2 cases occurred in two ladies aged 29 and 27 who presented with ascites and epigastric pain respectively [6]. The 29-year-old lady showed strongly positive tuberculin skin test while the other showed a negative result. CT abdomen showed pancreatic head lesion in both cases and the diagnosis of pancreatic tuberculosis was made from histology by fine needle aspiration. Both had good response to antituberculosis treatment.

Most published materials on pancreatic tuberculosis are confined to case reports and literature reviews. In one review, the author studied 37 cases of pancreatic TB [7]. Seven of them were reported as HIV antibody-negative and the result of the test was not stated in the remaining patients. The method of diagnosis of TB consisted of either histological appearance being consistent with TB, or finding organisms which were positive for acid-fast staining or culture of *Mycobacterium tuberculosis*. The mean age was 46.1 years (range 22-73). 19 (55.9%) were male and 15 (44.1%) were female. The duration of symptoms prior to presentation ranged from 7 days to 24 months (mean 3.8 months). The most common symptoms were abdominal pain or discomfort (69.7%), weight loss (57.5%), fever (45.5%) and anorexia (36.3%). Other symptoms included jaundice in 5 cases (15.1%) and per rectum bleeding in 2 (6.1%). CXR abnormalities were found in 26.1% of 23 cases with CXR appearance reported. These abnormalities included bilateral pleural effusion, reticulonodular pattern, bilateral diffuse alveolar infiltrates, miliary TB and old TB changes. Two cases had past history of tuberculosis. 87.5% of the 16 cases who had undergone tuberculin skin test were positive. Needle aspiration under CT or ultrasound guidance was attempted in 14 cases and succeeded in making the diagnosis in half of these cases. 2 cases were diagnosed in post-mortem biopsy. Combinations of 3 drugs were used for 21 patients and the agents most commonly used were isoniazid, rifampicin and ethambutol or pyrazinamide. The duration of treatment was recorded in 13 cases ranging from 2 to 18 months. 90.9% survived TB of the pancreas. One died from disseminated TB after treatment had been commenced and 2 died before treatment could be started.

58 cases of pancreatic TB reported in Chinese language literature were also reviewed [8]. 15 of these 58 patients were stated to be HIV antibody-negative, and the HIV status of the other

patients was not confirmed. 20 patients were male and 36 were female. The mean age was 43.5 years (from 14 to 73). The main symptoms were still epigastric pain and discomfort (37 cases), fever (31 cases), weight loss (23 cases) and anorexia (21 cases). The duration of symptoms prior to presentation ranged from 5 days to 5 months (mean 2.6 months). 22% had past history of TB. 21 out of 34 patients had positive tuberculin skin test. 23 patients were found to have abnormalities on CXR. 15 patients had TB in other organs. Initial provisional diagnosis of pancreatic tumour was made in up to 60% of these cases. Ultrasound-guided fine needle aspiration was performed in 21 cases and was successful in diagnosis of pancreatic TB in 14 cases. The duration of treatment was recorded in 28 cases, ranging from 3 to 12 months. 24 patients were reported to have resolution after treatment for 3 to 12 months and only one death was reported among the 58 cases.

Worldwide, an estimated 11% of new adult tuberculosis cases are infected with HIV. While only one out of ten immunocompetent people infected with *Mycobacterium tuberculous* will develop active TB in their lifetime, one in ten per year will developed the disease in patient infected with HIV. However, only a small number of pancreatic TB has been reported in HIV patients. 19 cases of documented or presumed pancreatic TB associated with HIV infection was reviewed in 1995 [9]. The common presenting symptoms were epigastric discomfort, fever and weight loss. Pancreatic TB was diagnosed during autopsy in 6 patients and patient details were fully documented in 9 patients who were diagnosed to have pancreatic TB while they were alive. The mean age of these 9 patients was 41 years. 66% were male. Duration of symptoms ranged from a few hours to 4 months (mean 42 days). 8 of the 9 patients were diagnosed to have HIV after the diagnosis of pancreatic TB was made. The CD4 counts were recorded only for 3 patients, ranging from 0 to 718/mm^3. Percutaneous pancreatic fine needle aspiration was performed in 5 patients and was able to establish the diagnosis in 2 patients. Exploratory laparotomy was required by 8 patients to make the diagnosis. 8 patients improved with anti-TB therapy. 1 died of massive GI bleeding. Two died 6 and 12 months later of disseminated cryptococcosis and non-Hodgkin's lymphoma respectively. The authors concluded that the combination of fever and abdominal pain in an HIV infected patient, particularly in association with pancreatic mass lesion identified on imaging, should raise the possibility of tuberculous abscess. Follow-up CT at 2 weeks, 4 weeks and 8 weeks after the start of anti-TB treatment was recommended to monitor the pancreatic TB abscess.

So far, no randomised controlled clinical trial on the management of pancreatic tuberculous abscess has been reported to help us to decide the optimal treatment for these patients. Moreover, major guidelines on tuberculosis do not mention specifically the regimen and duration of anti-TB treatment for pancreatic tuberculosis. However, based on those case reports, standard anti-TB treatment with or without drainage should be started once the diagnosis of pancreatic tuberculosis was made and the clinical and radiological response by serial imaging studies should then be monitored.

In summary, pancreatic tuberculosis is uncommon in both HIV and non-HIV patients. The most common presenting symptoms include epigastric pain, weight loss, fever and anorexia. Around 50% of these patients can be diagnosed by fine needle aspiration. Prompt diagnosis and timely anti-TB treatment with or without drainage give favourable outcome in majority of patients with pancreatic tuberculosis.

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A child with torticollis

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The case

A 32 months old boy was referred to a hospital for suspected mumps. He presented with tender right facial swelling leading to difficulty in swallowing for 1 day. The associated symptoms included high fever (up to 39°C) for 2 days, cough and runny nose for 1 week and vomiting. There was no skin exanthema, abdominal or testicular pain. Vaccination was up to date with measles, mumps and rubella vaccine. There was no history of infectious disease contact and no travel history outside Hong Kong.

Physical examination showed the child was febrile (38.5°C) with tachycardia (pulse rate 150/min). His head was tilted to the right side. A tender swelling was present on the right parotid region with surface erythema. The right tonsil was erythematous and enlarged. Bimanual palpation of both parotid glands showed no tenderness or signs of sialolith and no abnormal discharge from the Stensen's duct opening. Examination of the abdomen, respiratory and cardiovascular systems were normal. There was no testicular pain or swelling.

Investigations included WBC 56.6 $\times$ 10^9/L (93.3% neutrophil), C-reactive protein 148 mg/L (reference <8), a normal serum amylase level (which argue against a diagnosis of parotitis). Computed tomography of the neck showed the presence of right retropharyngeal abscess measured 15 mm $\times$ 20 mm $\times$ 22 mm. Emergency operation by otorhinolaryngologist was performed and the operative diagnosis was right peritonsillar and retropharyngeal abscess. Incision and drainage of the abscess was done. Intravenous augmentin and cloxacillin were given. The pus aspirated for culture grew *Streptococcus pyogenes* which was sensitive to penicillin and ampicillin but resistant to erythromycin. The recovery of the patient was good and the torticollis resolved.

Retropharyngeal abscess in children

Retropharyngeal space is a virtual space behind the pharynx, limited by the buccopharyngeal fascia anteriorly, the prevertebral fascia posteriorly, and the carotid sheaths laterally. It extends from the skull base to the level of the 4th thoracic vertebra. The retropharyngeal space contains the retropharyngeal lymph nodes and some fat. These nodes are organised into a lateral and a medial chain and are typically found between the internal carotid artery and the prevertebral muscle. They receive drainage from the nasopharynx, adenoids and posterior paranasal sinuses. These retropharyngeal lymph nodes are prominent in early childhood but atrophy at puberty.

The cause of retropharyngeal abscess (RPA) is usually the result of suppuration of retropharyngeal lymph nodes, secondary to infection in adenoid, nasopharynx, posterior pharyngeal wall, sinuses and tonsils. Trauma in the pharynx as a consequence of endotracheal intubation, endoscopy, foreign body ingestion and removal may also be the cause. Rarely, a RPA may arise from vertebral osteomyelitis. Patients at increased risk include those who are immunocompromised or chronically ill e.g. patient with diabetes, cancer, alcoholism or AIDS.

RPA is virtually an exclusive disease for children as the lymph nodes in the retropharyngeal space disappear after 4-5 years of age; abscess due to naso-oropharyngeal infection is rare after this age. A review in Sydney, Australia found that 55% of paediatric cases were under 1 year of age and 32% were less than 6 months [1]. A 10-year review of RPA cases at

Hospital for Sick Children in Toronto revealed that 66% of paediatric cases occur in children younger than 6 years old [2]. A 5-year review of RPA cases at Primary Children's Medial Center in Utah revealed that 75% of patients were younger than 5 years [3]. RPA is not common nowadays with the increasing use of antibiotics in the treatment of upper respiratory tract infection.

Delay in diagnosis and treatment can lead to risk of complications. Mortality of RPA is due to the association with airway obstruction, mediastinitis, aspiration pneumonia, epidural abscess, jugular venous thrombosis, carotid artery erosion, pericarditis and airway compromise.

The presenting symptoms of RPA may be different for adult and children. Children may present with or without fever, cough, sore throat, difficult in swallowing, stridor, neck pain and stiffness. In adults, shortness of breath and dysphagia may be more prominent. The physical signs of RPA may include fever, cervical lymphadenopathy, neck mass, torticollis, drooling of saliva, unilateral swelling seen in the posterior pharyngeal wall with signs of inflammation, neck stiffness and respiratory distress. These signs may be absent in newborn or early infancy as they may only present with fever and irritability.

Organisms implicated in RPA include *Streptococcus pyogenes*, *Staphylococcus aureus*, *Haemophilus* species, *Klebsiella* species, oral anaerobes e.g. *Bacteroides*, *Peptostreptococcus* and *Fusobacterium* species.

Investigations in a patient suspected to have RPA include complete blood count, C-reactive protein, blood and pus culture (if aspirated). Imaging studies include lateral neck x-ray and CT scan of the neck.

Lateral neck x-ray is used to document the widening of the retropharyngeal soft tissues. It was defined as soft tissue swelling of more than 7 mm at C2 and more than 14/22 mm at C6 in different studies. Other experts defined that the anterorposterior diameter of the prevertebral soft tissue space in children should not exceed that of the contiguous vertebral bodies. In addition to showing widening of the prevertebral space, lateral neck x-ray may show foreign body or gas in tissue subsequent to infection caused by gas forming bacteria.

CT scan of the neck is helpful in diagnosis as RPA will show up as hypodense lesion in the retropharyngeal space with peripheral ring contrast enhancement. It can also permit accurate estimation of the extent of the abscess and involvement of adjacent spaces such as its relation to great vessels. Other findings on CT include soft tissue swelling, obliterated fat planes and mass effect.

A chest x-ray is indicated to look for complications e.g. aspiration pneumonia and mediastinitis.

Pre-hospital care includes supplemental oxygen and attention to upper airway patency. Children in respiratory distress may adopt the sniffing position. In case of emergency, endotracheal intubation or cricothyrotomy may need to be performed. In-patient management includes close monitoring of oxygen saturation and emergency consultation to otorhinolaryngologist.

Because a variety of organisms can be found in nasopharyngeal space infection, obtaining an adequate microbiological culture is important in RPA. Throat swab is usually not adequate because of contamination with normal oropharyngeal flora. Pus obtained after aspiration or

drainage should be properly transported in anaerobic medium e.g. in anaerobic transport medium or sealed syringe and cultured for the presence of anaerobic organisms. The culture result obtained can guide the subsequent antibiotic treatment.

Intravenous antibiotics and surgical drainage are the main modalities of treatment. The choice of antibiotics should target organisms most commonly present in the nasopharynx. A combination of beta-lactamase resistant antibiotics with additional coverage for anaerobic organisms is useful.

Surgical treatment includes incision and drainage of central abscess transorally in a head low position to avoid aspiration. For lateral abscesses, drainage may be done by external incision in neck anterior or posterior to the border of sternocleidomastoid muscle.

Conclusion

Literature suggests that the incidence of retropharyngeal abscess is declining due to the availability of better antibiotics and their frequent use for upper respiratory tract infection. Physicians should however maintain high vigilance when encountering children with torticollis or unexplained neck pain or swelling, and to perform the necessary investigations to avoid delay in diagnosis which may lead to serious consequences.

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Journal review

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Although a number of different antiviral agents possess activity against hepatitis B virus (HBV), their utility has been limited by low efficacy, development of adverse effects and the emergence of viral resistance during therapy. Entecavir, a new potent inhibitor of HBV DNA polymerase, is highly effective against HBV. Researchers globally have been conducting a number of studies comparing the efficacy of entecavir with lamivudine, and the results of 2 major studies were recently published in the New England Journal of Medicine. All enrolled patients were 16 years or above and were naïve in terms of previous nucleoside analogue therapies.

In the study by Chang and colleagues, 628 HBeAg-positive patients with chronic hepatitis B infection were randomised to receive entecavir or lamivudine for 52 weeks. At 48 weeks, significantly more entecavir recipients showed improvement in liver histology (72% vs 62%), had undetectable HBV viral loads (67% vs 36%), and had normalised alanine aminotransferase levels (68% vs 60%). Use of entecavir was associated with a greater reduction in mean HBV DNA level (6.9 vs 5.4 log copies/mL). Six entecavir and 63 lamivudine recipients experienced a rebound in HBV viral load; evidence of drug resistance was found only in those taking lamivudine. Both agents were found to be safe in the study population.

Lai et al performed a similar trial in 638 HBeAg-negative patients with chronic hepatitis B infection. At 48 weeks, significantly more entecavir recipients showed histologic improvement (70% vs 61%), had undetectable viral loads (90% vs 72%), and had normalised alanine aminotransferase levels (78% vs 71%). The mean reduction in HBV DNA level was significantly greater with entecavir (5.0 vs 4.5 log copies/mL). No evidence of viral resistance to entecavir was found, and again both drugs were found to have good safety profiles.

Points to note: These findings suggest that entecavir is more efficacious than lamivudine for chronic hepatitis B. With the availability of three well-tolerated oral agents for HBV (adefovir, lamivudine and entecavir), as well as interferon, combination antiviral regimens similar to those used for HIV disease should now be contemplated. Further trials are obviously needed before a firm conclusion can be made in this area.

Schildgen O, Sirma H, Funk A, et al. Variant of hepatitis B virus with primary resistance to adefovir. N Engl J Med. 2006; 354: 1807-12.

Lamivudine is often used to treat chronic hepatitis B virus (HBV) infection, but the emergence of resistance during therapy is problematic. Another reverse-transcriptase inhibitor, adefovir, is also effective for chronic HBV infection, and most lamivudine-resistant strains seem to remain sensitive to adefovir despite extended therapy. Investigators in Germany now describe three patients with lamivudine-resistant HBV infection whose viraemia failed to respond to adefovir treatment.

Before initiation of adefovir therapy, the three patients already harboured a mutant virus that

is substantially less susceptible to adefovir. In this mutation (rtI233V), valine replaces isoleucine at position 233 of the reverse-transcriptase domain. All three patients responded virologically to treatment with an alternate agent, tenofovir. It was subsequently found that the rtI223V mutation was previously reported in only 3 of the 500 genome-sequenced HBV strains.

Points to note: Drug resistance in HBV is commonly induced by prolonged courses of treatment, as in the case with lamivudine. This report describes a form of primary resistance to adefovir that occurs in some HBV strains. Should these naturally occurring rtI233V variants spread, the usefulness of adefovir in treating chronic HBV will be hampered. Further surveillance is indicated for drug-resistant HBV viral strains to determine the magnitude and extent of the problem.

Treanor JJ, Campbell JD, Zangwill KM, et al. Safety and immunogenicity of an inactivated subvirion influenza A (H5N1) vaccine. N Engl J Med. 2006; 354: 1343-51.

The rapid spread of avian influenza A (H5N1) among birds in Asia and Europe this winter has raised the possibility of an imminent pandemic among humans. A safe and effective H5N1 vaccine will be important for control of the pandemic should the virus acquires the ability to have effective human-to-human transmission. Researchers from the US recently evaluated the safety and immunogenicity of one such vaccine.

The vaccine was prepared from an egg-grown recombinant virus composed of the hemagglutinin and neuraminidase genes from a human H5N1 isolate and other genes derived from a laboratory influenza A strain commonly used as a platform for vaccine production. The investigators randomised 451 healthy adults to receive two doses of the vaccine or a placebo. The vaccine appeared to be safe. Side effects were pain and tenderness at the injection site. Neutralising antibodies against the H5N1 virus were induced in a dose-dependent fashion. Among subjects who received 90 µg vaccine doses, up to 54% achieved a presumably protective antibody titre of 1:40.

Points to note: The good news is that researchers have produced a potentially protective H5N1 vaccine that is similar to licensed vaccine. Unfortunately, protection was achieved only by administering high doses of the vaccine (~12 times that contained in seasonal influenza vaccine). It is also unclear whether this vaccine could induce cross-protection against other H5N1 strains. A safe and effective H5N1 vaccine is urgently needed.