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EDITORIAL COMMENT

Although bronchiolar disorders like bronchiolitis are important causes of morbidity and mortality in children, they are no less important in adults. Most of the airways resistance lies in the peripheral airways in children that shift towards larger airways as the age advances. Bronchioles can be involved in a large variety of conditions including infections to inhalation injuries to the most important condition of bronchiolitis obliterans with organizing pneumonia. They can be involved in almost all types of disorders of the lung although to varying extent. Recognition of these problems are important as the treatment will depend upon the underlying disorder.

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BRONCHIOLAR DISORDERS IN ADULTS: DIAGNOSTIC APPROACH AND MANAGEMENT

Introduction

Airways with an internal diameter of 2 mm or less that do not contain cartilage in their walls are termed bronchioles. These airways consist of membranous and terminal bronchioles, which are purely air conducting and respiratory bronchioles, which contain alveoli in their walls. Normally bronchioles contribute to only approximately 10% of airway resistance because the total cross-sectional area of the small airways is much greater than the total cross-sectional area of the central airways. In disease states, however, abnormalities at the level of small airways contribute disproportionately to increased airway resistance¹.

Bronchiolar involvement is relatively common and occurs in a variety of clinical settings including infections, connective tissue diseases,, inhalational injuries, drug reactions, organ transplantation and many others. In addition bronchiolar abnormalities may at times represent a component of a pathologic process primarily affecting more distal lung parenchyma (e.g. hypersensitivity pneumonitis and sarcoidosis) or larger, proximal airways (e.g. COPD, bronchiectasis)².

Classification of bronchiolar disorders

A number of classifications have been proposed for bronchiolar disorders though none has gained wide acceptance. Perhaps the most useful one from a pulmonologist's perspective is the computed tomographic classification though knowledge of the aetiologic, pathologic and clinico-pathologic classifications is important for a thorough understanding of the wide spectrum of conditions associated with bronchiolar inflammation.

I) Aetiologic classification³

- a) Inhalational injury : (toxic gases, cigarette smoke, mineral dusts, organic dusts, fire smoke)
- b) Postinfectious : (RSV, adenovirus, Mycoplasma, Mycobacterium tuberculosis, others)
- c) Drug induced : (amphotericin B, amiodarone, bleomycin, carbamazepine, cephalosporins, interferon alpha, methotrexate, penicillamine, Paraquat)
- d) Idiopathic : No associated disease (Idiopathic bronchiolitis obliterans, cryptogenic organising pneumonia, diffuse panbronchiolitis)

Associated with other disease (organ transplantation, CTD, radiation pneumonitis)

II) Pathologic classification⁴

Histologically bronchiolitis can be classified into 4 broad categories:

- a) Cellular bronchiolitis which is characterised by the presence of an inflammatory cellular infiltrate involving both the bronchiolar lumen and wall. Included under this are infectious bronchiolitis, hypersensitivity pneumonitis, follicular bronchiolitis, diffuse panbronchiolitis and aspiration bronchiolitis.
- b) Respiratory bronchiolitis, characterised by the accumulation of pigmented macrophages within respiratory bronchioles

and alveoli. Respiratory bronchiolitis, respiratory bronchiolitis-associated interstitial lung disease (RB-ILD) and Desquamative Interstitial Pneumonia are part of the spectrum of smoking-related interstitial lung diseases.

- c) Constrictive bronchiolitis / bronchiolitis obliterans
- d) Proliferative bronchiolitis / bronchiolitis obliterans with organising pneumonia

III) Clinico-pathologic classification²

- a) Primary Bronchiolar Disorders: Constrictive Bronchiolitis/Bronchiolitis Obliterans, Acute bronchiolitis, Diffuse Panbronchiolitis, Respiratory Bronchiolitis, Mineral Dust Airway Disease, follicular bronchiolitis and aspiration bronchiolitis.
- b) Interstitial Lung Diseases with a Prominent Bronchiolar Component : Hypersensitivity Pneumonitis, RB-ILD and DIP, Cryptogenic Organizing Pneumonia/ Idiopathic BOOP, Others (Langerhans' cell histiocytosis, sarcoidosis, idiopathic pulmonary fibrosis).
- c) Bronchiolar Involvement in Large Airway Diseases : Bronchiectasis, cystic fibrosis, COPD.

IV) HRCT classification⁵

- a) Bronchiolar disease with tree-in-bud pattern
Asthma, ABPA, Infections (bacterial, Mycoplasma, Chlamydia, TB, CMV, PCP), Diffuse panbronchiolitis
- b) Bronchiolar disease with diffuse centrilobular nodules
HP, RB-ILD, follicular bronchiolitis, sarcoidosis, LIP, CTD
- c) Bronchiolar disease with decreased lung attenuation (includes all the causes of BO)
- d) Bronchiolar disease with ground-glass opacity and/or consolidation (includes all the causes of BOOP)

General Approach to Diagnosis

1. **HISTORY AND PHYSICAL EXAMINATION** : The usual history in most bronchiolar disorders is that of subacute onset of gradually progressive dyspnoea and non-productive cough. Onset may be relatively acute in bronchiolitis obliterans while copious expectoration may be seen in diffuse panbronchiolitis. A detailed history of symptoms suggestive of connective tissue disease as well as exposure to inhalational irritants, drugs and radiation should be elicited in order to identify a possible aetiology. It is important to note that while BOOP is most commonly idiopathic, in patients with BO an aetiological agent can be identified in all but a few cases. Physical examination is usually unremarkable except for inspiratory wheeze (c.f. COPD and bronchiectasis in which wheeze is most often expiratory) and/or crackles. Clubbing is not a feature of primary bronchiolar disorders³.
2. **PULMONARY FUNCTION TESTING** : In patients with primary bronchiolar disease PFT usually reveals an obstructive pattern with no significant bronchodilator reversibility except in patients of diffuse panbronchiolitis who may show some response to bronchodilator testing. In those bronchiolar diseases which occur as part of ILDs (e.g. BOOP, DIP) a restrictive pattern with reduced DLCO and lung volumes is seen. Tests of small airway function (FEF_{25-75%}, closing volume, frequency dependence of compliance) may be performed in order to detect small airway disease earlier and to follow up patients on treatment².
3. **RADIOLOGIC EVALUATION** : Though CXR is the initial radiologic investigation performed in almost all patients with bronchiolitis it is not very informative since it is usually normal. Less commonly one may find hyperinflation, attenuation of peripheral vascular markings and reticulonodular infiltrates. The advent of HRCT

has revolutionized our ability to diagnose bronchiolitis. A two step approach should be used in evaluating HRCT for this purpose⁵.

Step 1: Does the patient have bronchiolar disease?

Features of bronchiolar disease on HRCT can be broadly categorized into direct and indirect signs.

a) Direct CT findings of bronchiolar disease include bronchiolar wall thickening, bronchiolar dilatation (bronchiolectasis), and luminal impaction that render affected airways directly visible either as centrilobular nodules or a tree-in-bud pattern.

b) Indirect signs of bronchiolar disease on CT include subsegmental atelectasis and air trapping. Air trapping often results in a "mosaic pattern" of lung attenuation (multilobular, geographic density differences of the lung parenchyma). This mosaic pattern is caused by hypoventilation of alveoli distal to bronchiolar obstruction which leads to secondary vasoconstriction and is seen on CT scans as areas of decreased attenuation. Paired CT scans performed in inspiration and expiration are useful for distinguishing bronchiolar disease from pulmonary vascular disease and some diffuse infiltrative diseases that may also cause a mosaic pattern. In bronchiolar disease, the lucent regions of lung seen at inspiration remain lucent at expiration due to air trapping and show little increase in lung attenuation or decrease in volume as seen in primary vascular lung disease.

Step 2: What is the pattern of involvement? (See HRCT classification of bronchiolar disorders)

4. **ROLE OF LUNG BIOPSY (TBLB/OLB/ VATS)**

After a detailed history, physical examination, pulmonary function testing and HRCT most patients can be placed in a single clinico-pathological category of bronchiolitis and appropriate treatment initiated. In a number of

cases however, especially those with an atypical presentation histopathological confirmation is necessary. Since most diseases associated with bronchiolitis exhibit patchy involvement of the lungs even in patients who are severely disabled clinically the diagnosis can be missed if lesions are inadequately sampled. Transbronchial lung biopsy is therefore a relatively insensitive diagnostic tool, and for those patients in whom histologic confirmation is required, a surgical or thoracoscopic lung biopsy is necessary².

TREATMENT

Treatment of bronchiolitis is based on its aetiology in addition to supportive measures like bronchodilators and early treatment of infective exacerbations. Those disorders secondary to inhalational injury such as RB-ILD and mineral dust airway disease require removal from exposure and occasionally short courses of steroids.. Cryptogenic organizing pneumonia is a corticosteroid-responsive disorder. Clinical improvement may be rapid and dramatic, and prognosis is generally excellent with more than two-thirds of these patients experiencing complete resolution of their lung disease⁶. In diffuse panbronchiolitis low-dose macrolide therapy with erythromycin, 400 to 600 mg per day or azithromycin 250 mg thrice/ week is the preferred therapy and has shown some efficacy⁷.

Figure 1 : Summary of diagnostic approach to bronchiolar disorders

History (connective tissue disease, inhalational irritants, drugs etc.)



Physical exam (inspiratory wheeze, absence of clubbing)

CXR (normal/hyperinflation/reticulonodular infiltrates)

PFT (primary bronchiolar disorders: obstruction with no BDR ILDs with bronchiolar involvement: restriction)

HRCT Is there bronchiolar disease? (direct and indirect signs) What is the pattern? (tree-in-bud/centrilobular nodules/ decreased attenuation/ground glassing and/or consolidation)

BAL, TBLB/OLB

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EDITORIAL COMMENT

Respiratory system in general and lungs in particular play important part in the physiological alterations during and after administration of anaesthesia. It is crucial to have adequate pulmonary reserve for the patient to tolerate anaesthesia that requires a detailed pre-anaesthetic assessment. Similarly during induction till administration and maintenance of anaesthesia pulmonary physiology is to be maintained for proper oxygenation and maintenance of carbon dioxide and acid-base balance. More important is the prevention of postoperative complications following anaesthesia as a number of pathophysiological changes occur during the course of anaesthesia and as a result of certain surgical procedures. Recognition of these problems and their successful management are important for early and uneventful recovery.

ANAESTHESIA AND LUNG: PULMONOLOGIST'S PERSPECTIVE

Introduction

Pulmonary complications are major cause of postoperative morbidity and mortality and lead to prolongation of hospital stay and health care costs. (1) Pulmonologists are often consulted for the management of postoperative complications. Thus understanding the changes in respiratory physiology with anesthesia and surgery and factors associated with increased risk of pulmonary complications would be of great value in prevention and management of these complications

Physiologic alterations with anesthesia & surgery Wide-ranging effects occur during administration of anesthesia and surgery that alter respiratory physiology.

Firstly, due to the General Anesthesia (GA) there is a loss of diaphragmatic and intercostals muscle tone leading to reduced transverse diameter of thorax and decreased vital capacity (VC) and functional residual capacity (FRC) leading to dependent atelectasis. The pattern of pulmonary function following thoracic and abdominal surgery is restrictive. Secondly, diaphragmatic dysfunction also contributes to the reduced lung volumes and this is thought to arise due to inhibitory reflexes from vagal, sympathetic and splanchnic receptors, which depress the phrenic

nerve activity. Thirdly, alteration of ventilation perfusion relationships leads to post operative hypoxemia. This is due to anesthetic induced respiratory depression in the initial hours after surgery and dependent atelectasis and pneumonia in the subsequent days to weeks. Lastly, lung defence mechanisms are suppressed as the cough reflex and mucociliary clearance mechanisms are compromised. Thus increased amount of respiratory secretions are retained, which predispose the postoperative patient to increased risk of lower respiratory tract infections (2)

Postoperative pulmonary complications Clinically significant postoperative pulmonary complications (PPC) are as common as postoperative cardiac complications. They lead to prolongation of the hospital stay by one to two weeks and are responsible for increased health care costs (3)

Major categories of PPC

The various types of postoperative pulmonary complications encountered in practice. (1,2). The most frequently encountered PPC are atelectasis, pneumonia, and respiratory failure due to exacerbation of underlying chronic lung disease. The PPC are depicted in table 1

- Atelectasis
- Infections-pneumonia, tracheobronchitis
- Exacerbation of chronic lung disease
- Respiratory failure
- Thromboembolic diseases
- Pulmonary edema
- Aspiration of gastric contents
- Bronchospasm
- Pneumothorax/hemothorax
- Bronchopleural fistula
- Pleural effusion/ Chylothorax/empyema
- Air embolism
- Rib fracture
- Phrenic nerve palsy
- Mediastinitis

Risk factors for Post operative Pulmonary Complications

The presence of the certain risk factors increases

the risk of PPC (2). The risk factors are depicted in table 2.

1. Preoperative factors

Chronic lung disease

Smoking

General health status

Age

Nutritional status

Obesity

Preceding respiratory tract infection

2. Intraoperative factors Type of anesthesia

Duration of surgery

Emergency surgery

Site of surgery

Type of incision

blood transfusion

3. Post operative factors Immobilization

Inadequate pain control

PREOPERATIVE RISK FACTORS : Preexisting chronic obstructive lung disease increases the incidence of PPC by 25-40% in various studies. (1) The risk increased to more than 50% when FEV1 <65% of predicted and hypercapnia was present (4). Smoking is a known risk factor for PPC and prolonged ventilatory support. The effects of smoking are independent of the pulmonary impairment (1) In a study of 200 smokers undergoing CABG (5) the risk of PPC diminished in those abstinent for 08 weeks as compared with current smokers (14.5% vs 33%)

Studies from 1970s had suggested an increased risk of PPC with older age. When the data of these studies was stratified according to the ASA class, overall perioperative mortality for class II to V was found to be the same in all age groups. (6) ASA classification correlates with the development of PPC Patient in ASA Class II or higher undergoing abdominal surgery is at high risk of PPC Poor exercise capacity also identifies patients at high risk for PPC. (2)

Recent URTI is associated with increased airway reactivity and resistance for several weeks. Diaphragmatic dysfunction may also occur during viral URTI. Most authorities recommend that elective abdominal /thoracic surgery should be deferred following an episode of URTI. (1)

Intraoperative Factors

There are advantages of regional (spinal/epidural) anesthesia over GA. The respiratory compromise is minimal due to preservation of diaphragmatic function, and hypoxic pulmonary vasoconstriction. There are lower risk of PPC than GA in most comparative studies. and these modalities are recommended to be used in high risk cases undergoing surgery, (1). Long acting neuromuscular blocking agent pancuronium was associated with higher complications than short acting agents, vecuronium / atracurium due to prolonged postoperative block causing hypoventilation. Authors recommended that this drug should be avoided in patients with high risk for PPC(7).

Surgical procedure lasting more than 3h increases risk of PPC. When duration exceeds 4h patients are five times more likely to suffer post operative pneumonia than surgery shorter than 2h. In addition the surgical site also affects the risk of PPC. The alteration of respiratory function increases as the incision approaches the diaphragm. The risk of PPC is highest with thoracic and upper abdominal surgery 10-40% as compared to lower abdominal surgery < 5%. (1).

Laparoscopic surgery is associated with lower risk of PPC (0.3-0.4%) as compared to conventional cholecystectomy (13-33%). Video assisted thoracoscopic surgery (VATS) offers the advantages of reduced post operative pain and hospital stay compared to conventional thoracotomy.(2)

Postoperative Factors

Pain inhibits deep breathing and coughing and delays mobilization leading to increased risk of atelectasis and pneumonia due to retained secretions. Epidural analgesia with morphine lowers the risk of PPC as compared with parenteral narcotics (8). During postoperative immobilization,

the FRC decreases by 500-1000ml thereby increasing the risk of atelectasis Ambulation not only enhances clearance of respiratory secretions but also reduces the risk of venous thromboembolism.

PREOPERATIVE PULMONARY ASSESMENT

Preoperative pulmonary assessment includes thorough history & physical examination, and wherever relevant investigations such as chest radiograph, pulmonary function testing, arterial blood gas analysis. Certain specialized tests such as cardiopulmonary exercise testing, predicted post operative FEV1 and diffusion capacity for carbon monoxide (DLCO) are used in assessment prior to lung resection surgery (9)

History of smoking, respiratory symptoms, exercise intolerance, preexisting lung disease/sleep apnea and recent URTI should be elicited. Those with signs of obstructive airway disease, collapse, pneumonia and pleural effusion should be investigated further prior to clearance for surgery.

Chest radiograph is not routinely indicated except when there is an underlying cardio pulmonary disease, and for those undergoing thoracic surgery. Contrary to the existing practice in most centers, routine pre operative PFT is not indicated except in following circumstances, underlying chronic lung disease, unexplained cough or dyspnea, smoking>20 pack years, and planned lung resection, CABG or upper abdominal surgery.

Findings of FEV1 or FVC <70% predicted or FEV1 / FVC < 65% are associated with high risk for PPC. There are no threshold values beyond which risk of surgery is prohibitive The PFT must not be used to deny a patient surgery, but it should serve as a useful guide to the clinician to provide diligent care following surgery in high-risk cases. This fact was elegantly demonstrated by Kroenke et al, who followed patients with severe COPD (FEV1<50% predicted) undergoing surgery. and observed that among 107 operations, PPC occurred in 29% and only one death among 97 cases undergoing non-coronary surgery(4)

Arterial blood gas analysis is not recommended for preoperative evaluation except in patients with chronic lung disease, recently diagnosed pulmonary disease and prior to lung resection surgery. Hypercapnia (PaCO₂> 45 mmHg) indicates substantial airway obstruction and high risk for PPC. These patients require stabilization prior to surgery (1,9)

Preventive strategies for PPC Preoperative measures

Cessation of smoking 08 weeks prior to surgery reduces the risk for PPC. and smokers should be counseled to quit smoking Patient education regarding lung expansion maneuvers in the preoperative period was found to be better than postoperative period in reducing atelectasis as the patients are more receptive. Optimization of treatment of underlying chronic obstructive lung disease prior to surgery reduced the risk of PPC by more than 50 %. Steroids upto 60mg prednisolone may be added to optimize pulmonary function without any increase in infection post operatively(1)

Intra operative measures

The duration of surgery should be limited to less than three hours, if feasible to minimize the PPC. Less invasive procedure such as laparoscopic / thoracoscopic procedure must be contemplated in those at high risk for PPC.

Anesthetic measures

Anesthetist must try and avoid airway injury during intubation. Adequate nebulized bronchodilators are to be administered during anesthesia to prevent bronchospasm. Use short acting narcotics /sedatives/anesthetics to minimize .respiratory depression Avoid using pancuronium as it has prolonged duration of neuromuscular blockade and causes postoperative hypoventilation. Use regional anesthesia in cases at high risk for PPC. Post

operative measures

Lung expansion maneuvers such as deep breathing exercises and incentive spirometry reduce the

relative risk of PPC by 50%. There was no difference in efficacy among these methods. Non invasive ventilation with application of continuous positive airway pressure (CPAP) to prevent post operative atelectasis, was found to be as effective and not dependant on patient's efforts. Nasal bilevel positive airway pressure (BiPAP) minimizes the decline in lung volume after surgery, and may be effective in postoperative atelectasis and respiratory failure(1)

Postoperative analgesia

Epidural morphine-reduced the rates of PPC and is recommended in high risk cases of thoracic, abdominal and major vascular procedures. Intercostal nerve block reduces the incidence of PPC, however, the reduction does not reach statistically significant levels. This modality is recommended if epidural morphine is ineffective.

Conclusions

Anesthesia and surgery have profound effects on respiratory physiology which makes the patients prone for PPC. The knowledge of risk factors associated with PPC should enable clinicians to evaluate patients prior to surgery and prevent morbidity and mortality associated with postoperative pulmonary complications

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Announcement

1st National Conference of the Indian Society for Study of Lung Cancer

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