Pulmonary complications of intravenous drug misuse · 2

Infective and HIV related complications

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Pulmonary infections in HIV negative drug users

The reasons for the increased risk of pulmonary infection in HIV negative intravenous drug misusers¹ have already been referred to in the first article (November, p 890). Pneumonia may be acquired via the upper respiratory tract (community acquired or after aspiration of vomit) or be secondary to septic pulmonary emboli. Lung abscesses may complicate pneumonia of any type. The main types of infection²⁻⁷ may be summarised as:

- Community acquired pneumonia
- Aspiration pneumonia
- Septic pulmonary emboli
- Lung abscess
- Empyema
- Fungal pneumonia
- Tuberculosis

COMMUNITY ACQUIRED PNEUMONIA

Intravenous drug users have a 10 fold increased risk of community acquired pneumonia. For example, the annual attack rate for *Streptococcus pneumoniae* pneumonia in this group is 21/1000, compared with 0.7-2.6/1000 for the general population.⁸ This susceptibility seems to correlate with the duration of heroin addiction, but not apparently with periods of debility or unconsciousness.¹² The range and frequency of microbiological agents are essentially similar to those found in people not misusing drugs.⁹ In one series pneumonia accounted for 38% of hospital admissions of intravenous drug users who were febrile.¹⁰

The history and findings on examination are similar to those of community acquired pneumonia in non-drug users. The pneumonia does not appear to be more severe and the infection usually responds to conventional antibiotic treatment.

SEPTIC PULMONARY EMBOLI

Haematogenously acquired pneumonia or septic pulmonary infarcts in intravenous drug users are the result of recurrent emboli of infected material, which almost invariably contains *Staphylococcus aureus* (80%) or *Staphylococcus albus* (19%)—or occasionally *Candida* species or Gram negative organisms. The source of the infection is either a subcutaneous infection at the site of the injection (intravenous, or occasionally intradermal—"skin popping") or tricuspid endocarditis, or both.¹¹⁻¹⁸ In one series endocarditis with septic pulmonary emboli accounted for

13% of hospital admissions of febrile intravenous drug users.¹⁰

The clinical features are dominated by the symptoms of recurrent pulmonary emboli (chest pain, dyspnoea, haemoptysis) with high fever (fluctuating up to 39-40°C). The tricuspid murmurs are often absent (38%) in tricuspid endocarditis or barely audible (12%). Signs of left sided endocarditis are rare, though tricuspid and coexisting left sided valve endocarditis were seen in 4% of cases of endocarditis in addicts in one series.¹⁶ Tricuspid endocarditis is suggested by the sequential appearance of lesions in different parts of the lungs in the absence of peripheral thrombophlebitis, and can usually be confirmed by echocardiography.

Blood cultures are usually positive. The chest radiograph will usually show diffuse infiltrates (80%) and sometimes peripheral nodules (40%), which may be round or wedge shaped, with or without cavitation, and a pleural effusion may be present (20%). Hilar and mediastinal lymphadenopathy, resolving with antibiotic treatment, has been described.¹⁸ The infection may be complicated by lung abscess, empyema, gangrene, tension pneumothorax, bronchopleural fistula, or the adult respiratory distress syndrome.

With the conventional four to six weeks' intravenous treatment, septic pneumonia due to right sided *Staphylococcus aureus* endocarditis has a favourable prognosis, mortality rates ranging from zero to 16%. Because of the difficulty in obtaining prolonged intravenous access in such patients, and their desire to leave hospital quickly, a combination of oral antibiotics may be given for four weeks, and this is equally effective (for example, ciprofloxacin and rifampicin).¹⁹ Through its effect on hepatic metabolism rifampicin may induce signs of methadone withdrawal.²⁰ In patients with pneumonia secondary to peripheral thrombophlebitis and with no echocardiographic evidence of tricuspid endocarditis one or two weeks' intravenous treatment is thought to be adequate.^{2,17}

Mycotic aneurysms of the pulmonary arteries have been diagnosed at necropsy in association with embolic pneumonia.²¹ The diagnosis was not made or suspected clinically, though one patient had complained of haemoptysis.

FUNGAL PNEUMONIA

Several cases of pulmonary candidiasis have been reported in intravenous drug users

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taking heroin.²²⁻²⁵ These result from contamination by *Candida albicans* of the lemon used to acidify their "fix."

Patients may present with an apparent community acquired lobar pneumonia several days after their last self injection. Alternatively, the pulmonary disease may be part of a systemic candidiasis arising six to 12 hours after the last injection, and associated with the development of endocarditis, chorioretinitis, hepatitis, and bone or cartilaginous infection with abscess formation. This more generalised form may be complicated by the adult respiratory distress syndrome and carries a poor prognosis.

Contamination of street heroin by other fungi has also been found. The high prevalence of serum precipitins to fungi such as *Aspergillus* species in intravenous drug users suggests that this form of misuse may be a potential vehicle for other types of fungal pneumonia.²⁶

PULMONARY TUBERCULOSIS

Not surprisingly, tuberculosis is more common in intravenous drug users than in the general population owing to the risk factors associated with their life style, such as close contact, alcoholism and depressed immunity.²⁷ In a recent prospective study among 303 HIV negative drug misusers in New York 20% had a positive skin response to tuberculin testing.²⁸ During a two year follow up 13% of the tuberculin negative individuals became positive, though none developed active tuberculosis during this time. Other retrospective surveys in the United States have reported an incidence of active tuberculosis of 1.3-4% among HIV negative drug misusers, the disease accounting for 2% of the deaths in this group.²

The clinical, radiographic, and microbiological features of tuberculosis and the response to standard antituberculous chemotherapy are similar to those seen in people not misusing drugs. The increasing incidence of tuberculosis among HIV positive drug misusers (see below) has prompted some centres to consider adding prophylactic isoniazid to their oral methadone treatment programme in tuberculin positive intravenous drug users.²⁹

MISCELLANEOUS

Pulmonary melioidosis has also been described in intravenous drug users returning from highly endemic areas, such as South East Asia. The usual mode of presentation is as an acute pulmonary infection varying in severity from mild bronchitis to overwhelming pneumonia. The chest radiograph may simulate the appearance of post-primary tuberculosis. Definitive diagnosis is made by isolating *Pseudomonas pseudomallei* from the sputum.³⁰

Pulmonary complications in HIV positive intravenous drug users without AIDS

In Western countries and the United States the rate of HIV infection is increasing dis-

proportionately faster among intravenous drug users than among other risk groups.³¹ In the United States, for example, the seroprevalence rate of HIV antibody is increasing by up to 14% a year among intravenous drug abusers.³² In 1989 from 61 000 to 398 000 intravenous drug users in the United States were estimated to be HIV positive.

Within individual countries there is pronounced geographical variation in HIV positivity among drug addicts (in the United Kingdom 0-54% and in the United States 0-65%).³³⁻³⁶ Even within groups of intravenous drug users in individual cities HIV prevalence varies (in San Francisco, for example, 26% of black, 10% of Hispanic, and 6% of white drug users are HIV positive³⁷). Other independent predictors of HIV infection include intravenous injection of cocaine (often taken up to 10 times a day) or speed ball (a mixture of heroin and cocaine), sharing drug injection equipment (for example, at "shooting galleries"), and "booting" (withdrawing blood into the syringe to mix with the drug).^{37 38}

BACTERIAL PNEUMONIA

Several prospective studies have shown a higher incidence of community acquired pneumonia among HIV positive intravenous drug users (9.7%) than among their HIV negative counterparts (2.1%) or HIV positive homosexuals who are not drug misusers (4%).^{8 39} This excess is not due to increased intravenous drug use, cigarette smoking, or alcohol abuse. It would therefore appear to be a direct reflection of their being infected with HIV rather than a consequence of any aspect of behaviour.

Bacterial pneumonia usually occurs early in the course of the natural history of HIV infection and is responsible for the sharp rise in deaths from non-AIDS pneumonia among intravenous drug users since 1981.⁴⁰

The range of organisms is similar to that of community acquired pneumonia in the general population (*Streptococcus pneumoniae*, *Haemophilus influenzae*; group B streptococci and *Moraxella* (formerly *Branhamella*) *cattarrhalis* have also been reported); the infection is usually more severe, however, as judged by the initial presentation, chest radiographic findings, length of stay in hospital, and mortality.^{9 41}

The increased risk and severity of infection has prompted a call for prophylactic treatment in this group;⁴² there is also some evidence that bacterial infection may accelerate the progression to AIDS in HIV positive individuals.⁴³ Prophylactic options suggested have included pneumococcal (and perhaps *Haemophilus influenzae*) vaccination (but the response is variable) and treatment with penicillin and immunoglobulin G.^{42 44-46}

EMPHYEMA

Empyema may complicate community acquired or aspiration pneumonia and septic pulmonary emboli. In one surgical series of 61

cases, 40 recovered after the insertion of one or two intercostal drains. The other 21 had multiple loculations and required thoracotomy with extensive debridement or decortication (95%) and in three instances lobectomy or pneumonectomy. There were three deaths and no recurrent empyemas.⁴⁷

PULMONARY TUBERCULOSIS

HIV is an important risk factor for tuberculosis. This is why in 1986 the number of cases of tuberculosis in the United States (where most HIV positive patients are intravenous drug users) increased for the first time in over 30 years.⁴⁸ Though HIV positive intravenous drug users have a prevalence and incidence of tuberculous infection similar to those of their HIV negative counterparts, their risk of developing tuberculosis is considerably higher.^{8,49} The aggressive use of isoniazid chemoprophylaxis has been adopted in HIV positive intravenous drug users with a positive tuberculin skin test response who are enrolled in methadone maintenance programmes in New York. Compliance rates of 76% and a reduction in frequency of active tuberculosis cases have been reported as a consequence.²⁸

The diagnosis of tuberculosis in HIV positive intravenous drug users usually precedes the diagnosis of AIDS (by 4 months to 5 years) or occurs concurrently, as in other risk groups. The clinical and radiological features and the response to treatment are the same in intravenous drug users with HIV infection or AIDS as in other risk groups, and have been the subject of several recent reviews.⁴⁹⁻⁵¹

Pulmonary complications in intravenous drug users with AIDS

Intravenous drug use is the second leading risk category for AIDS in developed countries. It accounted for 23% of the cases of AIDS reported in the United States in the first six months of 1989, compared with 2% in 1983 and 15% in 1985. Half the patients were female. It has been estimated that there will be 65 000 cases of AIDS among intravenous drug misusers in the European Community by the end of 1990.^{36,37,52} Despite these dramatic increases in numbers, non-HIV associated death rates still exceed HIV related death rates in intravenous drug users.⁵³ For example, in a cohort of intravenous drug users in Rome drug overdose, violence, or trauma accounted for 65% of the deaths, AIDS for 7.4%, and endocarditis and bacterial infections for 5.2%.⁵⁴

The range of pulmonary disease associated with AIDS in intravenous drug users is the same as that in other HIV positive groups.⁵⁵⁻⁶²

INFECTIONS

The range and clinical features of opportunist and non-opportunist pulmonary infections in individuals with AIDS have been the subject of many recent review articles. Many of the principles of management of an intravenous drug user with AIDS are the same as those of a patient with AIDS who is not an intravenous drug user and are therefore not discussed

here.⁶²⁻⁶⁷ There are, however, a few differences that will be highlighted.

Non-opportunist pulmonary infections

Bacterial infections Although the primary defect in AIDS affects T cells, HIV also infects B lymphocytes and macrophages and alters B cell functions.⁶⁸⁻⁷⁰ Opportunist infections account for over 90% of all pulmonary infections in homosexuals with AIDS not using intravenous drugs. The proportion among heterosexual intravenous drug users appears to be less and in some areas, such as Edinburgh, non-opportunist infections are more common than opportunist ones.⁷¹ Infection with community acquired organisms (for example, *Streptococcus pneumoniae*, *Haemophilus influenzae*) may closely mimic *Pneumocystis carinii* pneumonia in this group and some bacterial infections (especially those caused by *Staphylococcus aureus*) may occur with *Pneumocystis carinii* pneumonia or pulmonary Kaposi's sarcoma.³⁹ An aggressive diagnostic approach, including bronchoscopy, is used to establish a microbiological diagnosis in such cases in centres dealing with intravenous drug users with AIDS. Such centres also routinely add ampicillin or erythromycin when pentamidine is used instead of co-trimoxazole as empirical treatment for *Pneumocystis carinii* pneumonia.

Community acquired pneumonia tends to occur early in the clinical course of intravenous drug abusers with AIDS, to be readily recognisable, and to have a good prognosis.^{39,45} In contrast, nosocomial infections (especially with *Staphylococcus aureus* and Gram-negative bacteria) occur late, frequently in association with a pre-existing opportunist infection, are often unsuspected, and carry a high mortality.^{45,56}

Mycobacterial infection As in HIV positive intravenous drug users, the prevalence of *Mycobacterium tuberculosis* infection in intravenous drug users with AIDS is considerably higher than in homosexuals with AIDS who do not misuse drugs. In contrast, infection rates for *Mycobacterium avium-intracellulare* and other non-tuberculous mycobacteria are similar in the two groups.^{28,48,72-76}

Opportunist lung infections The range of organisms, clinical features, and management of opportunist lung infection in HIV positive intravenous drug users are essentially similar to those of other HIV positive groups.^{55-62,77} There are, however, a few differences that should always be borne in mind. For example, pulmonary "mainline" talc granulomatosis must be considered in the differential diagnosis of pulmonary infiltrates in an HIV positive drug misuser.^{78,79} Furthermore, the use of the carbon monoxide transfer factor as a screening test for pulmonary disease is less specific in HIV positive intravenous drug users, as it is often abnormal (first article, p 891) for reasons other than *Pneumocystis carinii* pneumonia.^{80,81} Similarly, a positive gallium-67 scan in an addict may result from pulmonary "mainline" talc granulomatosis as well as pneumocystis infection.⁸²

The observation that prevention of

Pneumocystis carinii pneumonia, the most common of the AIDS defining diseases, increases longevity has stimulated the inclusion of prophylactic treatments (such as co-trimoxazole, dapsone, or nebulised pentamidine) in methadone maintenance programmes.⁴²

MALIGNANCY

Two malignancies have an increased incidence in those infected with HIV—namely, Kaposi's sarcoma and non-Hodgkin's lymphoma.⁶⁵⁻⁸⁵ The lungs are affected by these tumours in about 15% of cases among intravenous drug users with AIDS.

Although the clinical presentations of HIV associated Kaposi's sarcoma are similar in intravenous drug users and in other risk groups, this malignancy is less common in drug misusers with AIDS than in homosexual men with AIDS. In New York, for example, half of the homosexual men who were not intravenous drug users had Kaposi's sarcoma as part of their original manifestations of AIDS, compared with only 5% of heterosexual intravenous drug users. The percentage of patients with AIDS who develop Kaposi's sarcoma at any point in their illness is declining in intravenous drug users in parallel with other groups at risk of AIDS. In addition, when pulmonary Kaposi's sarcoma does occur in an intravenous drug user with AIDS, it is usually not of the "poor risk" type (that is, pleural disease), and such individuals usually die from other complications of their HIV infection.⁸⁴⁻⁸⁶

Non-Hodgkin's lymphoma is also far less common in intravenous drug users with AIDS than in homosexual men. The clinical features of this high grade tumour are otherwise similar, thoracic lymphoma developing in less than a quarter. In contrast to Kaposi's sarcoma, non-Hodgkin's lymphoma appears to be increasing in frequency (1985 2.5%, 1987 5% of all cases of AIDS in the United States).⁸⁵⁻⁸⁷⁻⁸⁸ A recent report from Italy suggests that non-Hodgkin's lymphoma may now be more common than Kaposi's sarcoma in intravenous drug users with AIDS.⁸⁹

INTERSTITIAL PNEUMONITIS

HIV associated lymphocytic and non-specific interstitial pneumonitis have been reported in intravenous drug users, though they are very rare, occurring predominantly in blacks. The clinical features are similar to those seen in other patients with AIDS.⁶⁵⁻⁸⁵⁻⁹⁰

Conclusion

As both the numbers of intravenous drug users and the variety of self injected substances increase, the range of pulmonary complications will continue to widen. Chest physicians need to be aware of the ways in which such drug misuse results in pulmonary disease, and to remember that not all drug misusers will admit to their use of drugs.

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