Case report

Characterization and treatment challenges of pulmonary hypertension in methamphetamine users

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ARTICLE INFO

Keywords:
Pulmonary arterial hypertension
Systolic heart failure
Methamphetamine

ABSTRACT

The World Health Organization pulmonary hypertension classification scheme provides a framework for evaluation and management of patients with pulmonary vascular disease. Methamphetamine is a recreational stimulant which causes cardiac and pulmonary vascular toxicity. We discuss three cases of methamphetamine users who presented with left ventricular systolic failure but on heart failure therapy developed features more consistent with pulmonary arterial hypertension (PAH) or combined pre-capillary and post-capillary pulmonary hypertension. All three were started on PAH treatment and showed clinical improvement in symptoms. These cases illustrate the difficulty with treating methamphetamine users with pulmonary hypertension who have been left out of randomized controlled trials. Consideration should be given to creating a clinical registry for patients with methamphetamine associated pulmonary hypertension to assist with best treatment strategies.

There has been tremendous progress in understanding the pathophysiology and classification of pulmonary hypertension (PH) [3,5]. Updated guidelines from the 6th World Symposium on Pulmonary Hypertension continue to utilize a 5-diagnostic group classification scheme [11]. However, some patients have risk factors for multiple types of PH presenting challenges for clinicians.

Pulmonary arterial hypertension (PAH), group 1 disease, is a chronic and incurable disease of scarring in the small arterioles and capillaries of the lung that leads to progressive loss of effective vascular bed and right ventricular failure. However, most people with PH are found to have predominantly left sided heart disease (group 2) or lung diseases (group 3). Some patients are best characterized as combined pre-capillary and post-capillary pulmonary hypertension (Cpc-PH) in which the pulmonary vasculature is felt to be injured from long standing left atrial hypertension. Typically, therapies targeted to the pulmonary vasculature are reserved for patients with group 1 disease. Methamphetamine is an illegal stimulant and a known risk factor for both acute and chronic left ventricular systolic and diastolic dysfunction as well as PAH [1,2,7–9, 12].

We present three cases of methamphetamine associated PH with features of both group 1 and 2 disease or Cpc-PH. The clinical course of each patient is outlined in Table 1. Each of the three patients presented with signs of heart failure and initial echocardiogram demonstrating reduced left ventricular ejection fraction. None of these patients had invasive hemodynamic measurements on presentation. However, on standard heart failure treatment, follow up echocardiogram showed normalized left systolic function but worsened right ventricular failure associated with ongoing clinical deterioration. Work up excluded parenchymal and obstructive lung disease and chronic thromboembolic disease. Right heart catheterization for each patient showed normal pulmonary capillary wedge pressure (PCWP) and severe PH with marked elevation of pulmonary vascular resistance more consistent with a PAH phenotype. Right heart catheterization was performed in each case within 6 months of initial diagnosis. Each patient was started on treatment for PAH with combination oral therapy and clinically improved by walk test and functional class [4,6]. These three cases demonstrate the complexities of characterizing and treating PH patients with methamphetamine exposure.

1. Discussion

Evaluation of PH in patients with methamphetamine abuse presents unique challenges due to both acute and chronic toxicity of the left and right ventricle and the pulmonary vasculature causing features of both group 1 and 2 disease. It is possible that these patients experienced acute, transient systolic heart failure from methamphetamine exposure.
in the background of chronic methamphetamine induced pulmonary vascular injury [10]. Alternatively, these patients may best fit into Cpc-PH from long standing drug induced elevated left ventricular filling pressures but normal PCWP is atypical. However, fluid challenge was contraindicated in these patients due to decompensated right heart failure and clinical instability. The degree of pulmonary vascular resistance elevation with normal PCWP suggested these patients could benefit from medications typically used to treat group 1 disease. As many methamphetamine users have difficulty with access to health care, making consistent treatment difficult.

Optimal treatment strategies are not known for patients with PH associated with methamphetamine exposure as they are excluded from randomized trials and most observational studies. As the number of people with methamphetamine exposure continues to grow it will be important to better understand how they fit in the diagnostic groups. There is substantial risk to this population with both under and over treatment of pulmonary vascular disease. In general, there is a lack of data and consensus on treatment strategies for patients with Cpc-PH and no specific data for patient with methamphetamine exposure. Consideration should be given towards a clinical registry of patients with methamphetamine associated PH to increase our knowledge base and experience with these challenging patients.

### Table 1
**Characteristics of each patient and clinical time course with treatment.**

| Patient 1                          | Patient 2                          | Patient 3                          |
|-----------------------------------|------------------------------------|------------------------------------|
| **Initial Presentation**          |                                    |                                    |
| Chief complaint                   | Dyspnea                            | Dyspnea                            |
| Physical Exam                     | Bilateral LE edema                 | Trace LE pain                       |
|                                  | Cracks at bilateral lung bases.    | Normal lungs sounds                 |
| ECHO:                            | Normal LV size                     | Normal LV size                      |
| LVF:                             | 35%                                | 40%                                |
| RVSP:                            | 51–56 mmHg                         | 68–73 mmHg                         |
| TAPSE:                           | 1.45 cm                            | 1.1 cm                             |
| Treatment                         | Carvediolol, Lisinopril, furosemide| Carvediolol, Lisinopril, furosemide|
| Follow up #1                      |                                    |                                    |
| Chief complaint                   | Dyspnea                            | Dyspnea                            |
| Physical Exam                     | No LE edema                        | No LE edema                        |
|                                  | Bilateral lung crackles            | Clear lungs                        |
| ECHO:                            | Normal LV size                     | Normal LV size                      |
| LVF:                             | 60%                                | 50%                                |
| RVSP:                            | 64–70 mmHg                         | 61–66 mmHg                         |
| TAPSE:                           | 1.2 cm                             | 1.5 cm                             |
| Right/Left heart catheterization: | Normal coronary artery anatomy.    | Normal coronary artery anatomy.    |
| PAP:                             | 71/35 (45 mmHg)                    | 60/19 (40 mmHg)                    |
| PCWP:                            | 12 mmHg                            | 2 mmHg                             |
| PVR:                             | 8.2 wood units                     | 10.8 wood units                    |
| 6 minute walk test               | 308m                               | 330m                               |
| Ventilation-perfusion scan       | Normal                             | Normal                             |
| CT Chest                         | Normal                             | Normal                             |
| Spirometry                       | Normal                             | Normal                             |
| Polysomnography                  | Normal                             | Normal                             |
| Treatment                         | Sildenafil and ambrisentan         | Tadalafil and macitentan           |
| Follow up #2                      |                                    |                                    |
| Chief complaint                   | Improved dyspnea                   | Improved dyspnea                   |
| Physical exam                     | No LE edema                        | No LE edema                        |
|                                  | Improved lung crackles             | Clear lungs                        |
| ECHO:                            | Normal LV size                     | Normal LV size                      |
| LVF:                             | 70%                                | 60%                                |
| RVSP:                            | 82 mmHg                            | 69 mmHg                            |
| TAPSE:                           | 1.1 cm                             | 1.9 cm                             |
| 6-min walk test                  | 360m                               | 219m                               |
| Course                           | Periods of improved symptoms and   | LV function has remained normal,   |
|                                  | periods of worsening symptoms      | additional hospitalizations for     |
|                                  | largely related to ongoing         | right heart failure in              |
|                                  | methamphetamine use.              | conjunction with ongoing           |
|                                  |                                    | methamphetamine use.              |

**Declaration of competing interest**

Neither author has any competing interests or conflicts of interest.

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