Successful Management of Patient with Treatment Resistant Schizophrenia and Swyer–James–Macleod Syndrome with Clozapine

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ABSTRACT
Swyer–James–Macleod syndrome (SJMS) is a rare disorder characterized by infective bronchiolitis. It typically presents with a history of recurrent chest infections during childhood. Cardinal sign of the disease includes the hyperlucency of the lung fields. Till date, only a few cases have been reported of this syndrome. We report a very unusual case of SJMS along with comorbid schizophrenia in a 20-year-old female and the successful management using clozapine.

Key words: Clozapine, Swyer–James–Macleod syndrome, treatment-resistant schizophrenia

INTRODUCTION
Swyer–James–Macleod syndrome (SJMS) is a rare disorder first described by George James and Paul Swyer in the 1950s. The incidence of this disease is reported to be 0.01% as per 17,450 surveyed chest radiographs. It is characterized on radiographs by unilateral small lung with hyperlucency. It is thought to follow repeated childhood viral infections and is considered as a postinfectious form of bronchiolitis obliterans. Till date, only few cases have been reported of this rare entity in the literature. More importantly no case has been reported in the literature where SJMS has been comorbid with schizophrenia.

We hereby present an unusual case of 20-year-old female with a comorbid diagnosis of SJMS and schizophrenia and difficulties faced in management.

CASE REPORT
Miss S, 20-year-old female presented to us with a history of psychiatric illness of 5-year duration. It started after the excessive worries related to her health. She started reporting that her neighbors were trying to harm her. Over a span of few months, she would remain fearful most of the day. On being asked, she reported camera being fitted in her room to spy on her. She also reported hearing voices of her neighbor abusing her and making plans to harm her. She could hear these voices clearly during awake state. Though her family members could not hear such voices and reassured her frequently stating that it is not possible, she continued to believe...
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so to an extent that she complained to police about the same. After about a year, she would mutter even when no one was around. She tried to run away from home repeatedly, and hence family members had to keep a constant watch on her. Her predominant mood was irritable during this time. As she did not improve even after treatment with multiple antipsychotics (including olanzapine, haloperidol, risperidone, valproate, etc.), the patient was referred to us for further management.

On elaborating the past medical history, it was found that she suffered from multiple respiratory tract infections during her infancy and childhood leading to multiple hospital admissions. Over the years, she developed progressively decreased exercise tolerance. Investigations were performed after a consultation with chest medicine department. Her hematological and biochemical parameters were normal. Pulmonary function tests revealed an obstructive pattern along with air-trapping. X-ray chest revealed hyperlucency in the left lung field [Figure 1]. Computed tomography (CT) scan of the chest showed emphysematous changes with central bronchiectatic changes in the left lung. Magnetic resonance (MR) angiography was also performed which suggested hypoplasia of left pulmonary artery with decreased left lung volume, ipsilateral mediastinal shift, and compensatory herniation of the right lung. Echocardiogram (ECHO) suggested congenital hypoplasia of left pulmonary artery with no cardiac abnormalities. Her electrocardiogram was normal, and bronchoscopy revealed no airway obstruction.

Based on these findings, the patient was diagnosed as a case of paranoid schizophrenia (treatment resistant) with SJMS. She was prescribed tablet clozapine, started with 25 mg, very slowly builds up to 300 mg over 6 weeks and was managed conservatively for the SJMS. The patient showed sedation and constipation while building up dose to 300 mg, but her blood parameters were within normal range. The patient started showing a response on positive symptom on similar 300 mg doses of clozapine. Side effect of medication was managed conservatively, and dose was adjusted accordingly. The patient followed up regularly for a period of 10-month during which her positive symptoms improved substantially. However, she continued suffering from intermittent productive cough, dyspnea, and shortness of breath. Frequent complete blood counts and other routine investigations were done owing to patient’s proneness to infections and clozapine treatment.

DISCUSSION

Our patient suffered from schizophrenia along with a rare disease SJMS. SJMS is characterized by hyperlucency of one lung field along with pulmonary vascular abnormalities, alveolar overdistension and bronchiectasis, bronchiolitis obliterans, or emphysema. Although the exact etiology of this disorder is not clear, recurrent respiratory infections are speculated as a cause. These infections include Mycoplasma pneumonia, Bordatella pertussis, influenza A, tuberculosis, measles, respiratory syncytial virus, etc. However, infection with adenoviruses (especially types 3, 7, and 21) are most commonly associated. This is evident in our patient who also suffered from repeated chest infections during her infancy and childhood. SJMS is usually diagnosed based on the radiological findings. Our patient showed all the cardinal features on the radiograph (unilateral hyperlucency with bronchiectatic changes) and also on the CT scan, MR angiogram and ECHO.

Schizophrenia is among the common psychiatric disorders with prevalence around 1% worldwide. Although neurodevelopmental model of schizophrenia has long been accepted, recently infectious (especially viral) etiology has gained popularity. Various in-utero infections are linked with subsequent development of schizophrenia during adulthood which includes influenza, measles, toxoplasma, adenovirus, etc. This might be a possible common etiological link between these two entities presenting together in our patient.

Figure 1: Chest X-ray showing unilateral hyperlucency (left lung) with decreased volume

The management of the patient posed an important challenge. The patient was already tried on multiple antipsychotics (including a second-generation antipsychotics such as risperidone and olanzapine in an adequate trial) without much improvement. Because of these, she was a suitable candidate to be started on clozapine. However, comorbid SJMS posed a challenge for management with clozapine. SJMS is itself a risk factor for recurrent chest infections, and
so it was supposed to complicate the treatment of schizophrenia with clozapine. Previous cases suggest that serious respiratory infections may increase levels of clozapine, which may lead to clozapine toxicity.\cite{7,8}

This has been attributed to decrease metabolism by cytochrome P450 1A2 (caused by downregulation by cytokine interleukin 6) because of the severe respiratory infections. However, no such signs of clozapine toxicity were observed during the treatment course and subsequently no major dosage changes were needed in our case (sequential serum clozapine levels were measured). Clozapine, being a sedating drug may also complicate the respiratory conditions. Possible reasons for the increased predisposition to infections include agranulocytosis and impaired swallowing along with sialorrhea leading to aspiration pneumonia. However, our patient responded well to the treatment with clozapine without significant worsening of recurrent infections. A symptomatic management along with antibiotics was advised for the chest infections by the pulmonologists as and when required.

In summary, this is may be the first case of SJMS comorbid with a psychiatric illness (schizophrenia) in author’s knowledge. The present case highlights the difficulties faced in the management of schizophrenia with clozapine because of comorbid SJMS.

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**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. Fregonese L, Girosi D, Battistini E, Fregonese B, Risso FM, Bava GL, et al. Clinical, physiologic, and roentgenographic changes after pneumonectomy in a boy with Macleod/Swyer-James syndrome and bronchiectasis. Pediatr Pulmonol 2002;34:412-6.

2. Moore AD, Godwin JD, Dietrich PA, Verschakelen JA, Henderson WR Jr. Swyer-James syndrome: CT findings in eight patients. AJR Am J Roentgenol 1992;158:1211-5.

3. Tortajada M, Gracia M, García E, Hernández R. Diagnostic considerations in unilateral hyperlucency of the lung (Swyer-James-MacLeod Syndrome). Allergol Immunopathol (Madr) 2004;32:265-70.

4. Marchevsky AM, Guintu R, Koss M, Fuller C, Houck W, McKenna RJ. Swyer-James (MacLeod) syndrome with placental transmogrification of the lung: A case report and review of the literature. Arch Pathol Lab Med 2005;129:686-9.

5. Schlesinger C, Veeraraghavan S, Koss MN. Constructive (obliterative) bronchiolitis. Curr Opin Pulm Med 1998;4:288-93.

6. Fruntes V, Limosin F. Schizophrenia and viral infection during neurodevelopment: A pathogenesis model? Med Sci Monit 2009;14:RA71-7.

7. de Leon J, Diaz FJ. Serious respiratory infections can increase clozapine levels and contribute to side effects: A case report. Prog Neuropsychopharmacol Biol Psychiatry 2003;27:1059-63.

8. Darling P, Huthwaite MA. Infection-associated clozapine toxicity. Clin Schizophr Relat Psychoses 2011;5:159-60.