



## TOTAL SITUS INVERSUS AND PSYCHOSIS IN CONTEXT OF VITAMINS B12 AND D DEFICIENCY: A CASE REPORT

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### Abstract

**Rationale:** Situs inversus totalis, vitamin B12 and D deficiency have been individually described to be associated with schizophrenia. This case is a patient, who had situs inversus totalis, showing psychotic features after a psychosocial stressor, together with underlying vitamin B12 and D deficiency. **Patient concerns:** A 22-year-old gentleman was admitted in a psychiatric hospital for further assessment of altered behavior in the form of receiving message from God to clean the earth and to save human beings. **Diagnoses:** Incidental finding of dextrocardia on electrocardiogram and chest radiograph. Ultrasound abdomen revealed situs inversus totalis. He had a low level of vitamin D and B12, 9 ng/ml and 136 pmol/l respectively. Brain computed tomography was unremarkable. Urine for illicit drugs was negative for amphetamines, cannabis, cocaine, and opiate. Whole genome array CGH (180k) did not identify any DNA copy number changes of known clinical significance. **Interventions:** He was treated with risperidone 2 mg tablet daily and vitamin D2 50,000 tablet weekly. **Outcomes:** His sleep and appetite improved, however, he remained withdrawn, anxious and in low mood. He travelled back to his home country on his fifth day of hospitalization. **Lessons:** Situs inversus totalis and schizophrenia is rare. In this particular case, vitamins B12 and D deficiency may have precipitated the onset of psychotic features in this otherwise healthy young gentleman.

**Keywords:** Situs inversus totalis, Schizophrenia, Vitamin B12 deficiency, Vitamin D deficiency, Case report.

### INTRODUCTION

Situs inversus totalis (SIT) is a rare congenital anomaly with an incidence which appears to be 1:10,000 live births in which all thoracic and abdominal organs are laid out in a mirror image of their usual pattern.<sup>1</sup> A large number of genes influencing node and ciliary structure have been identified as a probable cause of SIT.<sup>2</sup> Although Kartagener syndrome was formerly known as a classical type of primary ciliary dyskinesia (PCD) with the Kartagener triad - situs inversus, chronic sinusitis and bronchiectasis - the situs inversus appears to be observed in 40 to 50% of patients with PCD.<sup>3-5</sup> The aim of this communication is to report the case of a young gentleman with psychotic features who had SIT and vitamins B12 and D deficiency as well, and to discuss the possible significance of such an association. Although there have been reported cases of patients with Kartagener syndrome presenting with psychotic features,<sup>6</sup> the literature on neuropsychiatric abnormalities in patients with SIT and psychotic features in context of vitamins B12 and D deficiency is lacking, thus, our interest in highlighting this case. This study was approved by the ethics committee and Institutional Review Board of Hamad Medical Corporation (MRC-04-19-450), and the written informed consent was obtained from the patient.

### CASE REPORT

A 22-year-old Nepalese gentleman, single, with no past medical and psychiatric history, was admitted to the Mental Health Services at Hamad Medical Corporation for further

assessment of altered behavior in the form of receiving message from God to clean the earth and to save human beings, which had also resulted in inability to sleep for a week, together with loss of occupational and social functioning. The patient is employed as a cleaner and has been working in Qatar for three years. After admission, positive psychopathology noted were: irritability, labile affect, formal thought disorder, and religious preoccupations and delusions. Review of symptoms was negative for chronic sinusitis. The patient reported that the symptoms started after experiencing severe guilt feelings after consuming meat products which is, in fact, against his religious values. Physical and neurological examination was unremarkable except for the presence of strabismus. He had a BMI of 18.5 and smokes cigarettes occasionally, but does not consume alcohol. He denied the use of recreational products. Possible family history of mental illness in mother and siblings; he refused to elaborate. Our working diagnosis was brief psychotic triggered by a psychosocial stressor. He was incidentally found to have dextrocardia on routine ECG and CXR. No features of bronchiectasis on CXR. Ultrasound abdomen revealed situs inversus totalis. Blood chemistry levels were unremarkable, including normal lipid levels and HbA1c. He had a low level of vitamin D and B12, 9 ng/ml and 136 pmol/l respectively. TSH and FT4 were within normal limits, but FT3 was slightly elevated to 7.5 pmol/l. CT Scan brain was unremarkable. Urine for illicit drugs was negative for amphetamines, cannabis, cocaine, and opiate. Whole genome array CGH (180k) did not identify any DNA copy number changes of known clinical significance. Chromosomal analysis (G-banding technique) was normal - 46, XY. The patient was kept on Risperidone 2 mg tablet daily and weekly Vitamin D2 50,000 units tablet. He required as needed (PRN) Promethazine 20 mg PO once only for insomnia.

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Table 1

Case Number	Author(s)	Year	Age	Gender	Remarks
1	Kartagener and Horlacher <sup>9</sup>	1935	34	Male	
2	Wuhrman (reported by Kartagener and Stucki) <sup>10</sup>	1960	Not reported	Not reported	Cases 1 to 4: Associated with Kartagener's syndrome
3	Finkelstein <sup>11</sup>	1962	23	Female	
4	Glick and Graubert <sup>6</sup>	1964	34	Male	
5	Ponzano C, Piora P, Ollino S <sup>12</sup>	1978	Not available	Not available	
6	Dixit, S. Khanna, R. <sup>8</sup>	1993	18	Male	WAIS-R: IQ 70
7	Mohan, I., Lowe, M., Sundram, S. <sup>13</sup>	2013	18	Male	Intellectually normal
8	UlusoyKaymak, S. et al. <sup>14</sup>	2017	Not available	Not available	Associated with Tetralogy of Fallot
9	Khodoruth MAS, Khodoruth WNC	2019	22	Male	Vitamins D and B12 deficiency, and esotropia

One to one nursing interaction noted that he was withdrawn, anxious, and in low mood; on a positive note, patient had adequate sleep and appetite. On his 5th day of hospitalization, patient requested to go back to his home country. Social Services and Case Management liaised with his company and parents. The latter made travel arrangements and the patient was then transferred to a step-down facility awaiting travel.

## DISCUSSION

As a disorder of laterality, SIT has also involved the CNS. CNS defects such as hydrocephalus, meningomyelocele, cerebellar hypoplasia, and arrhinencephaly have been documented in cases of SIT.<sup>7</sup> There is also a report of developmental dyslexia and psychosis in a patient with SIT further highlighting the link between disruptions in neuronal migration and assembly serving an example of the neurodevelopmental origin of a schizophrenic illness.<sup>8</sup> A summary of data reported in previous cases and our case can be found in Table 1. On a clinical imaging standpoint, data published on schizophrenia and SIT show that findings are not comparable. An anatomical and functional MRI study of three individuals with SIT showed that frontal and occipital petalia are reversed in individuals with SIT.<sup>1</sup> Even though MRI studies have suggested functionally significant petalia and occipital bending among patients with schizophrenia, there is no evidence yet of petalia reversal.<sup>15</sup> Similarly, the former study has demonstrated that the volume of the planum temporale was larger on the left in two of the three SIT subjects, whereas radiological studies have consistently showed reversal of the normal left-larger-than-right asymmetry of planum temporale surface area in patients with schizophrenia.<sup>16</sup> Nevertheless, this case implies that signaling abnormalities in SIT, which may also be affected in schizophrenia, might not require to involve planum temporale dysfunction<sup>17</sup> or cortical lateralization, and that indeed further studies are needed to explore the role of abnormal lateralization in schizophrenia. One limitation in this case is that we could have determined handedness using the Edinburgh handedness inventory, as there is supportive evidence of lateralization abnormalities in schizophrenia with a change in handedness frequency.<sup>18</sup> On a side note, this case also reports a rare occurrence of strabismus in situs inversus totalis. We will not dwell extensively on this issue as it is beyond the intent of this case report. However, it is discerning to highlight that strabismus is more common in schizophrenia than the general population.<sup>19</sup> Elevated rates of strabismus have also been found in children who later develop schizophrenia.<sup>20</sup>

Recent work has suggested that one type of strabismus, exotropia, is a risk factor for mental illness,<sup>20,21</sup> and in particular, schizophrenia.<sup>19,22-24</sup> Our patient had esotropia, which is an inward deviation whereas exotropia is an outward deviation. This new insight raises questions about a common neurodevelopmental link between schizophrenia, SIT, and strabismus. Lately there has been significant interest between vitamin D and mental illness<sup>25,26</sup> and cognitive decline in the elderly.<sup>27</sup> Blood levels of 30 ng/ml or higher are generally considered to be optimal while less than 20 ng/ml and 12 ng/ml are considered insufficient and deficient respectively. Our patient's vitamin D level was 9 ng/ml. In a Dutch study of 320 psychiatric outpatients, 30% had vitamin D deficiency and around 69% of these had schizophrenia or schizoaffective disorder; 23% had bipolar disorder.<sup>28</sup> Similar findings are also echoed in inpatient studies.<sup>29,30</sup> Some studies have tried to figure out the pathophysiology of the association between vitamin D deficiency and schizophrenia. For example, in animal studies vitamin D has been shown to promote gamma-glutamyltranspeptidase gene expression, thereby stimulating the generation of glutathione, the most important antioxidant in the brain.<sup>31</sup> Furthermore, the neonatal vitamin D status has been associated with the risk of schizophrenia,<sup>32</sup> where low vitamin D levels have been found.<sup>33</sup> The evidence of the association between vitamin B12 and schizophrenia is disputatious.<sup>34-36</sup> A meta-analysis of 13 studies concluded that patients with schizophrenia had a higher level of vitamin B12 compared to healthy controls, but without significant difference.<sup>37</sup> On the other hand, a recent study with 189 patients with schizophrenia showed that prevalence of vitamin B12 deficiency, usually a level less than 200 pmol/l, was significantly higher in the schizophrenia group.<sup>38</sup> One possible explanation for the ambiguous findings could be that patients with schizophrenia undergo regular blood work and thus receive vitamin supplementation as needed. Another argument is that drug therapy may change the level of vitamin B12 in patients with schizophrenia.<sup>39</sup> A proposed mechanism linking vitamin B12 deficiency to schizophrenia has been suggested by previous studies whereby high homocysteine level was associated with schizophrenia,<sup>39,40</sup> and in fact vitamin B12 and folate deficiency may lead to increased homocysteine level in one-carbon metabolism pathway.<sup>34,41</sup>

## CONCLUSION

So far there have been no report of a psychotic illness occurring in an individual with SIT with underlying vitamins B12 and D deficiencies. The purpose of this case report is to renew psychiatric interest in the association between neuronal

misconnections, vitamin B12 and D deficiencies, and psychiatric disorders. We describe here for the first time the comorbid presentation of psychotic features, situs inversus totalis, and vitamins B12 and D deficiency in an otherwise healthy young gentleman without PCD. There is a need for further studies to establish a link between SIT and schizophrenic illness in context of vitamins B12 and D deficiency for the early identification of vulnerable individuals and for possible therapeutic implications.

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