**International Journal of Medical Science in Clinical Research and Review**
Online ISSN: 2581-8945
Available Online at http://www.ijmscrr.in Volume 3|Issue 01 (January-February) |2020 Page: 25-28

Case Report

# H1N1 illness related secondary hypothyroidism : A rare case report and a brief review of literature

**Authors:**
**Dr. Mahendra Wawhal[1], Dr. Vajed Mogal[2]**
*[1]Associate Professor-Senior Consultant, MD (Medicine) , Department of Medicine*
*[2]Assistant Professor- Consultant Nephrologist, D.M. (Nephrology) Department of Nephrology*
*M.G.M. Medical College & Hospital, Aurangabad, Maharashtra, India*
**Corresponding Author**:
Dr. Vajed Mogal

Article Received: 04-January-2020, Revised: 24-January-2020, Accepted: 14-February-2020

**ABSTRACT**:
Viral infections have been frequently associated with thyroid diseases. In the present case report we document a rare case of H1N1 influenza infection related secondary hypothyroidism. A 32-year-old female, known case of hypothyroidism since 3 years & since 2 months developed an influenza-like syndrome. Polymerase chain reaction assay confirmed the diagnosis of H1N1 virus infection. Serum thyroid stimulating hormone was suppressed to zero while the levels of thyroxine (T4) and triiodothyronine (T3) were also decreased, below normal. She was treated & improved with oseltamivir and supportive treatment, including antibiotics and steroids.

***Keywords: H1N1 Virus, Secondary hypothyroidism***

## INTRODUCTION:

Viral infections are frequently implicated in thyroid diseases[1]. A few years ago, Dimos et al published a rare case of Sub-acute thyroiditis in the course of acute novel H1N1 influenza infection[2].In the recent pandemic, influenza A H1N1 virus has been estimated to cause approximately 18.449 deaths in 214 different countries until 2010[3]. Adult respiratory distress syndrome (ARDS), along with bacterial co-infections were the direct causes of death in most cases[4]. The patient was diagnosed with acute novel H1N1 influenza infection related secondary hypothyroidism when evaluated for a 7-day history of gradually worsening fever, and sore throat and ARDS with respiratory failure. Here, we report a rare case of H1N1 illness related secondary hypothyroidism.

## CASE REPORT:

A 32-year-old, Known case of hypothyroidism since 3 years & stopped treatment since 3 months, was admitted to the hospital complaining of gradually worsening fever, myalgia, dryness of mouth and sore throat over 7 days.. The patient's symptoms were initially attributed to pharyngitis by her primary care physician, and she was already being treated with azithromycin 500 mg OD when she was admitted to the hospital. The patient was not a smoker and did not mention any previous health problems.

On examination, she was conscious, oriented febrile ($101^0$ F),Physical examination revealed tachycardia (130 beats per minute); respiratory rate was 18 /min & SPO2 was 82% on room air. The patient denied the presence of palpitations in the past. Her blood pressure was within normal range (110/70 mmHg), while her temperature was 38.9 °C. The thyroid was soft, with no alterations of the overlying skin and there were no nodules felt. The chest was clear and the abdomen was soft to palpation. ABG was indicative of hypoxia and ALI. Chest x-ray showed features of bilateral infiltrates suggestive of ARDS and ECG were negative for pathological findings. The diagnosis of H1N1 viral infection was based on polymerase chain reaction testing of nasopharyngeal / oropharyngeal swabs.

Laboratory workup showed haemoglobin of 12.5mg/dl, WBC count of 19500/$mm^3$, platelet count of 220,000 /$mm^3$ . Kidney &liver function tests were mildly deranged. Urine examination were normal. Thyroid function tests showed significantly decreased levels of triiodothyronine (T3) 0.04ng/ml [normal values (NV) 0.6-1.85 ng/ml], free triiodothyronine (FT3) 1.2 pg/ml (NV: 2.3-4.2 pg/ml), thyroxine (T4) 2.2µg/dL (NV: 4.5-11 µg/dL), and free thyroxine (FT4) 0.04ng/dL (NV: 0.8-1.8 ng/dL), while thyroid-stimulating hormone (TSH) levels were suppressed to almost zero(0.01 mIU/L, NV: 0.5-5 mI U/L) suggestive of secondary hypothyroidism. Thyroid autoantibodies (thyroglobulin and thyroid peroxidase antibodies) were negative. Erythrocyte sedimentation

rate (ESR) was 110mm/h (NV: 0-20 mm/h) and C - reactive protein levels were elevated (CRP: 11.41 mg/dl, NV: <0.5 mg/dl).

On the basis of laboratory evaluation, we diagnosed the patient of H1N1 illness with ARDS with secondary hypothyroidism. She was treated with Paracetamol, I.V. antibiotics ( ceftriaxone, clindamycin ), Oseltamivir 150 mg BD, Steroids ( IV Methylprednisolone 125 mg OD for 3 days & shift to oral steroids and tapered off), Tab. Thyroxine 100ug OD, I.V. hydration with normal saline& supportive treatment. She improved with above treatment and was followed-up weekly with measurement of thyroid hormone levels. Her T3,T4 and TSH gradually recovered to normal levels in 2 months after discharge. Here, we present a rare first in india, perhaps and also in world case report of H1N1 illness related secondary hypothyroidism.

## DISCUSSION:

H1N1 virus is a RNA virus belonging to the family of Orthomyxoviridae. There are two ways of spread for influenza: the endemic form caused by the B group and the pandemic one supported by the A group, such as the "Spanish" occurred in 1918-1919, the "Asiatic" in 1957-1958 and the "Hong-Kong" in 1968-1969. The H1N1 virus is a type A influenza virus with swine origin (S- OIV, swine origin influenza virus). It infects wide varieties of warm-blooded animals, including birds, swine, horses, and humans, whereas influenza B and influenza C viruses almost exclusively infect humans and are also implicated in epidemics. The large, dynamic reservoir of influenza A subtypes in animals, as well as their evolutionary adaptability, help produce new influenza strains that cause new epidemics and pandemics[5]. The first inter-human infection was reported in Mexico in April 2009[6] and the rapid spread around the world was such that in June 2009 the WHO (World Health Organization) declared the pandemic state, as a scale 6 global emergency[7]. In Italy the spread of the H1N1 virus was observed in association with the spread of the virus that caused seasonal influenza in 2009-2010 and 2010-2011[8]. Children, young adults and elderly subjects represent the most affected groups, while the population at high risk of morbidity and mortality is represented by children, pregnant women, patients affected by heart disease, chronic respiratory diseases and immune-compromised subjects[9]. The 2009 global pandemic of the novel influenza A (H1N1) virus was characterized by significant clinical variations. The virus has genetic components from human, swine, and poultry influenza viruses a genetic combination that had not been previously identified[10]. The significant mortality related to this viral infection was due to a lack of prior immunity in the population, the virulence of the virus, and its transmissibility among humans[11,12].

In 2009, WHO originally called H1N1 influenza "swine flu" because its genetic appearance is similar to that of viruses that infect pigs in North America. However, further investigation revealed that this new virus is more complex. The new H1N1 virus is a quadruple human reassortant comprising 2 strains of avian and swine (North American and Eurasian) influenza virus[13,14].Overall, the symptoms of patients infected with H1N1 influenza are the same as those associated with seasonal flu, including fever up to 41 °C, cough, myalgia, malaise, appetite loss, sore throat, and headache. The clinical manifestations of the disease are various: asymptomatic forms, mild involvement of the upper airways (dyspnea, fever, coughing) and gastrointestinal system (diarrhoea and nausea), severe pneumonia with acute respiratory distress syndrome (ARDS), up to multi-organ failure and exit us. Thyroid diseases affects women more often than men[15].

Thyroid diseases is presumed to be caused by a viral infection or a post-viral inflammatory process and most patients have a history of an upper respiratory infection prior to the onset of thyroid disease (typically two to eight weeks). Clusters of cases have been reported in association with Coxsackie virus, EBV, mumps, measles, adenovirus, influenza and other viral infections[15]. The thyroid injury is considered to be the result of cytolytic T-cell recognition of viral and cell antigens present in an appropriate complex[16].For a long time, researchers have been interested in infection as a factor in the pathogenesis of thyroid illness. Valtonen et al. measured a broad spectrum of bacterial and viral antibodies in paired sera of 32 patients with thyroid disease of recent onset including subacute thyroiditis, Graves' disease and Hashimoto's disease and found evidence of a preceding infection in 44% of the patients[17].

Infections are frequently cited as a potential precipitating factor of thyroid diseases. Direct involvement of the thyroid gland with acute or subacute infection can precipitate a crisis[18]. However, the mechanism for precipitating a crisis in systemic illness is not well understood. It is well documented that the stress of systemic infections such as respiratory infections, endocarditis and urinary tract infections can precipitate a crisis[19]. Some researchers found acceleration of thyroxine and triiodothyronine turnover during systemic infection; this finding may partially explain the thyroid dysfunction during systemic illness, Wolf et al. studied the sera of patient recovering from Yersinia enterocolitica infections and observed that the immunoglobulin of these patients exhibited Graves' disease-like activity in human thyroid membranes[20].

Infections of viruses, including the hepatitis C, hepatitis B and Epstein-Barr virus infection were associated with increased incidence of clinical and

subclinical autoimmune thyroiditis, which may represent an Immunmodulation phenomenon[21]. An H1N1 diagnosis was confirmed by a positive result with reverse transcriptase-polymerase chain reaction in real time[22], and was presumed in individuals for whom it was not possible to collect clinical samples for laboratory diagnosis (or for whom samples were not feasible) and who had been in close contact with a laboratory confirmed case. The criteria for determining the severity of infection included the following[23] : mental confusion; respiratory rate of more than 30 breaths per minute; diastolic blood pressure of less than 60 mm Hg or systolic blood pressure of less than 90 mm Hg; and fever higher than 38 °C associated with cough and dyspnoea. The diagnosis of H1N1 infection is usually suspected basing on clinical data, but it must be confirmed by RT-PCR (reverse transcriptase polymerase chain reaction) on throat swab[7]. Diagnostic imaging based on chest radiography and computed tomography (CT) is very useful in the study of disease because it allows to assess the extent of lung parenchymal damage. Measures of hygiene and personal protection play an important role in order to limit the spread of the disease. Influenza vaccination represents an effective and safe way to prevent the disease and its complications in patients at risk. Antiviral treatments have been applied to patients with documented H1N1 infection[8] , but in case of severe clinical settings with respiratory failure, it is better to hospitalize the patient in order to get ventilator therapy[9]. Early treatment with oseltamivir[23] (75 mg orally, twice daily for 5 days) was defined as treatment initiated within 48 hours of the onset of symptoms, and late treatment was defined as that initiated after the first 48 hours. This seems to be, to our knowledge, the second case of subacute thyroiditis related to H1N1 influenza virus. It is worth noting that, as with the first case report, the viral infection was active and well documented. As far as the involvement of thyroid gland during viral infections is concerned, there is controversy regarding the exact nature of their possible relation. In many cases of thyroid diseases, the involvement of a viral infection was based on serology, i.e., on the presence of antibodies, which constitutes an indication of recent or past infection[24]. In the present case, the documentation of the presence of H1N1 virus by polymerase chain reaction assay indicates the active form of the infection, and reinforces the etio -pathogenetic role of influenza virus infection in the development of thyroid diseases[25]. It is interesting to mention that, in the literature, cases have been reported of thyroid storm triggered by H1N1 infection. Furthermore, recently, there was a case report of subacute thyroiditis following the H1N1 vaccine[26]. These two reported cases along with the documentation of H1N1 infection-induced thyroid storm support the hypothesis that the disorder of thyroid gland could be well included in the cluster of clinical complications that can occur in the course of H1N1 infection.

## CONCLUSION:

We report a very rare case of novel H1N1 virus related to secondary hypothyroidis. Cases of H1N1 virus infection related to subacute thyroiditis and thyroid strom have been reported in literature. However, we report here, probably the first case in literature in india and perhaps in the world of H1N1 virus infection associated transient secondary hypothyroidism which adds a new testimony to the hypothesis of infectious theory of pituitary and thyroid dysfunction, in this case by the novel H1N1 Virus.

## REFERENCES:


1. Prummel M, Strieder T, Wiersinga WM. The environment andautoimmune thyroid diseases. Eur J Endocrinol. 2004; 150: 605618.
2. Dimos G, Pappas G, Akritidis N. Subacute thyroiditis in thecourse of novel H1N1 influenza infection. Endocrine. 2010; 37:440-441.
3. Holvast A, Huckriede A, Wilschut J, Horst G, De Vries JJ, Benne CA, Kallenberg CG, Bijl M: Safety and efficacy of influenza vaccination in systemic lupus erythematosus patients with quiescent disease. Ann Rheum Dis 2006, 65:913-8.
4. Shieh WJ, Blau DM, Denison AM, Deleon-Carnes M, Adem P, Bhatnagar J, Summer J, Liu L, Patel M, Batten B, Greer P, Jones T, Smith C, Bartlett J, Montague J, White E, Rollin D, Gao R, Seales C, Jost H, Metcalfe M, Goldsmith CS, Humphrey C, Schmitz A, Drew C, Paddock C, Uyeki TM, Zaki SR: 2009 pandemic influenza A H1N1: Pathology and pathogenesis of 100 fatal cases in the United States. Am J Pathol 2010, 177:166-75.
5. G. Watts, "Pandemic Flu A/H1N1 Influenza Virus: The Basics," July 2009.
6. R. Perez-Padilla, D. de la Rosa-Zamboni, S. Ponce de Leon, *et al.*, "Pneumonia and Respiratory Failure from Swine-Origin Influenza A (H1N1) in Mexico," *The New England Journal of Medicine*, Vol. 361, No. 7, 2009, pp. 680-689.
7. World Health Organization, "Human Infection with Pandemic (H1N1) 2009 Virus: Updated Interim WHO Guidance on Global Surveillance," July 2009.

8. CircolaredelMinisterodella Salute, “Prevenzione eControlloDell’Influenza: Raccomandazioni per laStagione 2010-2011,” July 2010.
9. Centers for Disease Control and Prevention “People atHigh Risk of Developing Flu-Related Complications,” November 2009.
10. Machado AA. How to prevent, recognize and diagnose infection with the swineorigin Influenza A (H1N1) virus in humans. J Bras Pneum 2009;35(5):464–9.
11. Picone O, Ami O, Vauloup-Fellous C, Martinez V, Guillet M, Dupont-Bernabé C, et al. Pandemic influenza A H1N1 2009 flu during pregnancy: Epidemiology, diagnosis and management. J GynecolObstetBiolReprod 2009;38(8):615–28.
12. Dawood FS, Jain S, Finelli L, Shaw MW, Lindstrom S, Garten RJ, et al. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. N Engl J Med 2009;360(25):2605–15.
13. Greer LG, Abbassi-Ghanavati M, Sheffield JS, Casey BM. Diagnostic dilemmas in a pregnant woman with influenza A (H1N1) infection. ObstetGynecol 2010;115(2 Pt 2):409–12.
14. Shinde V, Bridges CB, Uyeki TM, Shu B, Balish A, Xu X, et al. Triple-reassortant swine influenza A (H1) in humans in the United States, 2005–2009. New Engl J Med 2009;360(25):2616–25.
15. Desailloud R, Hober D. Viruses and thyroiditis: an update. Virol J. 2009; 6: 5.
16. Kojima M, Nakamura S, Oyama T, Sugihara S, Sakata N, Masawa N. Cellular composition of subacute thyroiditis. An immunohistochemical study of six cases. Pathol Res Pract. 2002; 198: 833-837.
17. Valtonen VV, Ruutu P, Varis K et al. Serological evidence for the role of bacterial infections in the pathogenesis of thyroid disease. Acta Med Scand. 1986;219:105-11.
18. Al-kordi RS, Alenizi E, Elagazzar AH. Acute suppurative thyroiditis with abscess, gas formation, and thyrotoxic crisis. Nuklearmedizin. 2008;47:N44-6.
19. Desai B, Shukla A. Thyroid storm: An Atypical Presentation legionella and parainfluenza. 8 Oct 2007.
20. Wolf MW, Misaki T, Bech K et al. Immunoglobulins of patients recovering from Yersinia enterocolitica infections exhibit Graves’ disease-like activity in human thyroid membranes. Thyroid. 1991;1:315-20. Winter.
21. Tomer Y. Hepatitis C and interferon induced thyroiditis. J Autoimmun. 2010;34: 322-6.
22. Ministry of Health. Influenza A (H1N1): Protocol for Reporting and Investigation. http://portal.saude.gov.br/portal/arquivos/pdf/protocolo_investigacao_ notificacao08062009.pdf Published 2009.
23. Ministry of Health. Protocol for Clinical Management and Epidemiological Surveillance Of Influenza – Version III. http://portal.saude.gov.br/portal/arquivos/ pdf/protocolo_de_manejo_clinico_05_08_2009.pdfPublished 2009.
24. Volpé R, Row VV, Ezrin C. Circulating viral and thyroid antibodies in subacute thyroiditis. J ClinEndocrinolMetab. 1967; 27: 1275-1284.
25. Baharoon SA. H1N1 infection-induced thyroid storm. Ann Thorac Med. 2010; 5: 110-112.
26. Girgis CM, Russo RR, Benson K. Subacute thyroiditis following the H1N1 vaccine. J Endocrinol Invest. 2010; 33: 506.