

# Subacute thyroiditis in the course of novel H1N1 influenza infection

Georgios Dimos · Georgios Pappas ·  
Nikolaos Akritidis

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**Abstract** To describe the first documented case of subacute (De Quervain) thyroiditis in the course of novel H1N1 influenza infection. This is a case report of a patient diagnosed at the General Hospital “G. Hatzikosta” of Ioannina, Greece. A 55-year-old previously healthy male developed an influenza-like syndrome that was accompanied by severe neck pain, palpitations, weight loss, and disproportionately increased erythrocyte sedimentation rate. Polymerase chain reaction assay of pharyngeal swabs confirmed the diagnosis of novel H1N1 influenza infection. Serum thyroid-stimulating hormone was suppressed to zero and levels of free thyroxine and particularly triiodothyronine were increased. Technetium-99m-pertechnetate scintigraphy showed diffuse and inhomogeneous very low technetium trapping. The patient was treated with non-steroidal anti-inflammatory drugs and thyroid function gradually normalized without evolving to a hypothyroid phase. This is the first case of subacute thyroiditis associated with novel H1N1 influenza infection. Furthermore, this is the first case to definitely demonstrate active influenza infection of any type concurrent with thyroiditis, and one of the very rare similar cases for any active viral disease etiologically implicated in the pathogenesis of subacute thyroiditis.

**Keywords** H1N1 influenza · Subacute thyroiditis · Viral thyroiditis

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G. Dimos · G. Pappas · N. Akritidis  
Internal Medicine Department, General Hospital  
“G. Hatzikosta” of Ioannina, Ioannina, Greece

G. Pappas (✉)  
Institute of Continuing Medical Education of Ioannina,  
H. Trikoupi 10, 45333 Ioannina, Greece  
e-mail: gpele@otenet.gr

## Introduction

The pandemic of novel swine-origin H1N1 influenza virus, due to the sheer number of cases infected and the adequate surveillance that definitely diagnosed these cases, has resulted in recognition of rare clinical complications of the infection, which can implicate practically every organ of the human body. Herein, we report a unique case of subacute thyroiditis evolving during acute novel H1N1 influenza infection, the first such report in the literature, and briefly discuss the available literature relating other influenza virus strains with the thyroid gland.

## Patient report

A 55-year-old, previously healthy male was diagnosed as suffering from acute novel H1N1 influenza infection when evaluated for a 4-day history of gradually worsening fever, rinorrhea, sore throat, and neck pain. The patient also complained of rapid weight loss during this period, which he could not attribute to any loss of appetite. The diagnosis of novel H1N1 influenza was based on polymerase chain reaction testing of nasopharyngeal/oropharyngeal swabs by the reference center located in the University of Ioannina. The patient’s complaints of neck pain were initially attributed to the existing pharyngitis, but palpation of the bilaterally mildly enlarged thyroid gland elicited significant patient discomfort. The thyroid was soft, with no alterations of the overlying skin; there were no nodules felt, although a detailed palpation was not feasible due to patient discomfort. Clinical examination was also significant for the presence of tachycardia that was disproportionate to the degree of fever (130 beats per minute while temperature was 37.1°C); the patient had denied the

presence of palpitations in the past. His blood pressure was in normal limits (110/75 mmHg). Laboratory workup showed significantly increased levels of triiodothyronine (T3) (310 ng/dL, normal values 58–159 ng/dL), while free thyroxine levels (FT4) were also marginally above the upper normal limits (1.55 ng/dL, normal values 0.7–1.48 ng/dL) and thyroid-stimulating hormone (TSH) levels were suppressed to zero (normal values 0.35–4.95 mIU/L). Thyroid autoantibodies (thyroglobulin and thyroid peroxidase antibodies) were negative. Laboratory testing further showed an increase in erythrocyte sedimentation rate (ESR, 60 mm/h, normal values 0–20 mm/h) that was also disproportionate to the median values observed in other patients admitted with novel H1N1 influenza infection during the evolution of the pandemic in the region. Technetium-99m-pertechnetate scintigraphy showed diffuse and inhomogeneous very low technetium trapping, a finding compatible with subacute thyroiditis. The patient refused undergoing thyroid fine needle aspiration, or testing for human leukocyte antigen (HLA)-B35. Non-steroidal anti-inflammatory drugs were prescribed and the patient was followed-up weekly with clinical evaluation of thyroid tenderness and measurement of thyroid hormone levels. Administration of beta-blockers for symptomatic relief was further suggested to the patient, if needed (although these were not eventually used). Thyroid levels were restored in 4 weeks; further follow up for one more month showed that the patient did not progress to a hypothyroid phase.

## Discussion

Although subacute (De Quervain) thyroiditis is known to appear during an acute viral illness including Coxsackie viruses, Epstein-Barr virus, adenoviruses, echoviruses, influenza viruses, mumps, and measles, but also HIV [1], there are scarce cases in which this viral infection is documented; in most instances, the etiologic role of a virus in the development of De Quervain thyroiditis is based on serology. On the contrary, in the present case, active infection with the novel H1N1 influenza virus was documented, since polymerase chain reaction results document the presence of the virus itself and not antibodies against it, and moreover are positive only during the active phase of the infection. Serology on the other hand, for all kinds of viral infections implicated in subacute thyroiditis, may indicate a recent or past, but not active, viral infection [2]. Only in a single case of Coxsackie-related disease [3] and a recent Epstein-Barr virus related case [4] simultaneous viral presence has been demonstrated. Similar indirect evidence is also limited: there exists a single report of observation of virus-like particles resembling influenza in thyroid tissue sample [5]; there have also been reports of

presence of retroviruses or mumps or non-characterized viruses [6, 7]. These findings though are far from definite evidence of a specific viral etiopathogenetic role.

The concurrency of the influenza symptoms and the development of thyroiditis implicate a direct pathogenetic role of the virus, rather than an auto-immune-like process. Older reports of subacute thyroiditis have indicated an auto-immune process though, as for example in a case of subacute thyroiditis that has been associated with vaccination for seasonal influenza [8]: in that case thyroiditis was presumably due to molecular mimicry of thyroid autoantibodies by influenza antibodies generated by immunization.

Our case is instructive in a dual manner: first, it shows that in cases of pandemics when particularly large numbers of cases are documented, numerous rare complications can surface and, occasionally, perplex the diagnostic process. Second, it further shows that modern molecular diagnostic techniques may allow for better documentation of the etiopathogenesis of De Quervain thyroiditis, moving away from the ambivalence of serology results and towards a definite demonstration of active viral disease concurrent with the thyroiditis syndrome.

In conclusion, our case adds to the various clinical manifestations of novel H1N1 influenza infection the possible involvement of the thyroid gland as subacute thyroiditis. This is the first relevant report to be published in the literature.

**Conflict of interest statement** No conflicts of interest for any of the authors.

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