

CASE REPORT

Open Access

# Suppurative thyroiditis due to aspergillosis: a case report

Suemi Marui<sup>1\*</sup>, Ariella Cabral de Lima Pereira<sup>1</sup>, Raquel Maria de Araújo Maia<sup>2</sup> and Eduardo Ferreira Borba<sup>2</sup>

## Abstract

**Introduction:** *Aspergillus*, a nosocomial agent, is the most common fungal cause of suppurative thyroiditis. Most patients with *Aspergillus* thyroiditis have disseminated infection, primarily with lung compromise. Late diagnosis and treatment, severity of immunosuppressive state and thyroid hormone overload contribute to extremely high mortality rates.

**Case presentation:** We describe a 20-year-old Caucasian man receiving corticosteroid suppression therapy for systemic lupus erythematosus. He presented persistent fever with neck pain and pulmonary infection. Piperacillin/tazobactam was initiated but after 2 days he developed hypoxemia, vascular shock, severe anemia, lymphopenia, and high C-reactive protein. Thyroid ultrasound revealed well-defined hypoechogenic clusters in both lobes and laboratorial thyrotoxicosis but low triiodothyronine concentration. A purulent substance was obtained on fine needle aspiration and drained. Amphotericin B and fluconazole were added but he had unfavorable evolution and died. *Aspergillus fumigatus* was defined only 2 days after his death.

**Conclusions:** This case serves to alert clinicians to the possibility of infectious thyroiditis and reinforces the high risk of aspergillosis in immunocompromised patients. Therefore, management including voriconazole as first-line treatment or amphotericin B, in association with broad-spectrum antibiotic therapy, should be adopted to improve treatment outcome.

**Keywords:** *Aspergillus*, Suppurative thyroiditis, Thyrotoxicosis

## Introduction

Infectious thyroiditis is relatively rare because the thyroid is remarkably resistant to infection due to its high iodine content, hydrogen peroxide production, blood supply network, abundant lymphatic drainage, and encapsulated location [1]. The main routes of infection include hematogenous or lymphatic spread and directly from adjacent infected tissue. Predisposing factors include previous thyroid disease, earlier infection at distal site, local trauma, and particularly immunocompromised conditions, such as chemotherapy and high corticosteroid therapy. Suppurative or infectious thyroiditis is painful; subacute or acute etiology must be determined to define treatment and prognosis. Local signs and symptoms of infection are indistinguishable among infectious thyroiditis. Both present with painful thyroid and thyroid

enlargement, dysphagia and dysphonia. Transient thyrotoxicosis due to the release of thyroid hormone from follicular cell damage can occur. Corticosteroid therapy masks fever.

*Aspergillus*, a nosocomial agent, is the most common cause of fungal thyroiditis [2]. Most patients with fungal thyroiditis have disseminated fungal infection, primarily with lung compromise [2]. Delay in diagnosis and treatment, severity of immunosuppressive state and thyroid hormone overload contribute to extremely high mortality rates. We describe a patient on corticosteroid suppression therapy for systemic lupus erythematosus (SLE) diagnosed with *Aspergillus* thyroiditis with unfavorable evolution to alert clinicians to this rare and severe condition which is invariably overlooked.

## Case presentation

A 20-year-old Caucasian man was diagnosed with SLE due to polyarthritis, pleuritis, positive antinuclear antibodies (ANA on human epithelial type 2; HEp-2), positive

\* Correspondence: suemimar@usp.br

<sup>1</sup>Unidade de Tireoide-Disciplina de Endocrinologia e Metabologia, Avenida Dr Arnaldo 455 Sala 4305, 01246-903 Sao Paulo, SP, Brazil

Full list of author information is available at the end of the article

anti-double-stranded DNA, and biopsy-proven class IV glomerulonephritis. Methylprednisolone 1g/day was started for 3 days followed by prednisone 1mg/kg/day. After 1 month, active renal disease persisted and methylprednisolone treatment was repeated. Thereafter, severe pancytopenia and cytomegalovirus infection were identified. Gancyclovir was administered for 21 days with good response. Cyclophosphamide was started (500mg) but after 1 month he presented daily fever and neck pain. At physical examination, an anterior painful cervical prominence was observed; heart rate 122 beats per minute, temperature 37.9°C and oxygen saturation 91%. Piperacillin/tazobactam was started as pulmonary infection was detected. After 2 days, he developed hypoxemia, vascular shock, severe anemia, lymphopenia (300/mm<sup>3</sup>), and high C-reactive protein (137.5mg/L; normal range, NR, <5). Thyroid ultrasound revealed well-defined hypoechogenic clusters in both lobes. Thyroid-stimulating hormone (TSH) was suppressed, free thyroxine (T<sub>4</sub>) >74.6pmol/L (NR 7.7 to 18), total T<sub>4</sub> 189pmol/dL (NR 90 to 154), total triiodothyronine (T<sub>3</sub>) 1.15nmol/L (NR 1.23 to 1.85), and high serum thyroglobulin (650.6µg/L). A purulent substance was obtained on fine needle aspiration (FNA) and drained. Cytological analysis showed only pus cells. Thyrotoxicosis due to infectious thyroiditis was established. Fungal culture of thyroid abscess was partial positive. Amphotericin B and fluconazole were introduced. Tracheal and blood cultures were negative. Another thyroid ultrasound revealed persistent small clusters. He underwent drainage again but no secretion was obtained. He died at day 6 of hospital admission with suppressed TSH, lower free T<sub>4</sub> but still high (47.6pmol/L) and low total T<sub>3</sub> (0.60nmol/L). A culture of thyroid secretion took 10 days to reveal *Aspergillus fumigatus*, identified by septate hyphae, <5µm in thickness, with branching at acute angles, 2 days after his death.

## Discussion

Painful thyroid has two main causes: subacute thyroiditis and acute infectious thyroiditis [3]. Subacute thyroiditis is by far the most common cause of thyroid pain. Nevertheless, acute infectious thyroiditis or suppurative thyroiditis is a potentially life-threatening condition. As pain is the common presentation, clinical pictures can be used for differential diagnosis. Subacute thyroiditis frequently manifests with three classical phases: transient thyrotoxicosis, followed by transient hypothyroidism and usually euthyroidism. Patients report previous viral infection with low fever and malaise. Therapy aims to relieve pain; evolution is favorable and self-limited. Subacute thyroiditis rarely causes severe thyrotoxicosis [1].

Conversely, infectious acute thyroiditis is a potentially life-threatening disorder whose prognosis depends on prompt recognition and treatment [4]. Bacterial, fungal, and even parasitic organisms have been documented as

etiologic agents. Phlogistic signs are often seen. Abscess drainage and antimicrobial therapy, including antifungal, must be performed. In contrast to subacute thyroiditis, thyroid dysfunction is rarely noted in this condition.

Of interest, our case showed all the classical signs and symptoms of subacute thyroiditis and had a previous cytomegalovirus infection. However, he was already on corticosteroid therapy which is effective to treat subacute thyroiditis. Immunocompromised status that occurs in patients with human immunodeficiency virus, corticosteroid therapy, organ transplant and chemotherapy, is prone to atypical infections, rare etiologies, bizarre presentations and unusual primary infectious foci.

Common pathogens are encountered with greater frequency in a dose-dependent manner during therapy with glucocorticoids. Most patients present viral infections, herpes or cytomegalovirus, as our patient, but may also have *Staphylococcus*, candidiasis and *Strongyloides*. *Aspergillus* is increasingly recognized as an important nosocomial pathogen in immunocompromised patients but it is difficult to diagnose antemortem and typically has a fatal outcome. At autopsy, thyroid commitment is the result of a disseminated infection even in the absence of thyroid dysfunction [5]. Antemortem diagnosis is reached by direct microscopy and culture after FNA or by biopsy in most reported cases. Thyroid FNA is the easiest and fastest method of diagnosis, and cytological analysis reveals profuse purulent infiltration with hypha. In this regard, aerobic and anaerobic cultures of FNA specimens must also be performed, but fungal cultures are also mandatory. Unfortunately, fungal culture involves a lengthy process. Therefore, our management included broad-spectrum antibiotics and metronidazole. Amphotericin B and fluconazole however, were only added after positive fungal culture and, albeit unsuccessful, abscess drainage. Thyroidectomy should be performed only to debride necrotic tissue and to remove infected tissue if abscess persists. Surgery has more death risk as it requires a patient in better condition to tolerate surgery, as bleeding and hemodynamic instability are common.

Our service does not provide voriconazole, the best treatment to *Aspergillus* infection [6]. Some authors suggest that fluconazole should be added to treatment for immunocompromised infected patients, as well as *Aspergillus* serology [2]. As the primary site is frequently located in the upper respiratory tract, nasal or orotracheal samples must be collected for repetitive fungal culture, especially with mild lung infiltration. Growth of *Aspergillus* in blood cultures is rare but highly specific [7]. It is noteworthy that fungal cultures from orotracheal secretion and blood were negative in our patient. In our patient, fungal cultures took 10 days to reveal *Aspergillus* in colonies.

All but one anecdotal case of *Aspergillus* thyroiditis reported previously had unfavorable outcomes, which

suggest delays in diagnosis, representing a marker of poor prognosis [2,8-11].

Also of interest, our patient presented low T<sub>3</sub> concomitant with high T<sub>4</sub> level. After follicular thyroid damage, T<sub>4</sub> is disproportionately elevated relative to T<sub>3</sub>, reflecting intrathyroidal T<sub>4</sub>/T<sub>3</sub> ratio. Conversely, low T<sub>3</sub> observed in our patient could also reflect worse prognosis, as identified in euthyroid sick syndrome [12].

## Conclusions

This case alerts clinicians to the possibility of infectious thyroiditis and reinforces the high risk of aspergillosis in immunocompromised patients. Therefore, management including voriconazole and amphotericin B, in association with broad-spectrum antibiotic therapy, should be adopted to improve treatment outcome.

## Consent

Written informed consent was obtained from the mother of the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

## Abbreviations

FNA: Fine needle aspiration; NR: Normal range; SLE: Systemic lupus erythematosus; T<sub>3</sub>: Triiodothyronine; T<sub>4</sub>: Thyroxine; TSH: Thyroid-stimulating hormone.

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

SM attended, interpreted the patient data, wrote and submitted the manuscript. ACLP and RMAM attended the patient at our Intensive Care Unit. EFB performed diagnosis and treatment of systemic lupus erythematosus. All authors read and approved the final manuscript.

## Acknowledgements

The authors thank Shri Krishna Jayanthi, MD for the ultrasound examination and Lenine Garcia Brandao, MD, PhD for the abscess drainage approach.

## Author details

<sup>1</sup>Unidade de Tiroide-Disciplina de Endocrinologia e Metabologia, Avenida Dr Arnaldo 455 Sala 4305, 01246-903 Sao Paulo, SP, Brazil. <sup>2</sup>Disciplina de Reumatologia-LIM/17, Avenida Dr Arnaldo 455 Sala 3190, 01246-903 Sao Paulo, SP, Brazil.

Received: 11 September 2013 Accepted: 15 September 2014

Published: 21 November 2014

## References

1. Pearce EN, Farwell AP, Braverman LE: **Thyroiditis**. *N Engl J Med* 2003, **348**:2646-2655.
2. Goldani LZ, Zavascki AP, Maia AL: **Fungal thyroiditis: an overview**. *Mycopathologia* 2006, **161**:129-139.
3. Farwell AP: **Sporadic Painless, Painful Subacute and Acute Infectious Thyroiditis**. In *Werner and Ingbar's The Thyroid: A Fundamental and Clinical Text*. 10th edition. Edited by Braverman LE, Cooper DS. Philadelphia: Lippincott Williams & Wilkins; 2013:414-429.
4. Paes JE, Burman KD, Cohen J, Franklyn J, McHenry CR, Shoham S, Kloos RT: **Acute bacterial suppurative thyroiditis: a clinical review and expert opinion**. *Thyroid* 2010, **20**:247-255.
5. Hori A, Kami M, Kishi Y, Machida U, Matsumura T, Kashima T: **Clinical significance of extra-pulmonary involvement of invasive aspergillosis: a**

retrospective autopsy-based study of 107 patients. *J Hosp Infect* 2002, **50**:175-182.

6. Limper AH, Knox KS, Sarosi GA, Ampel NM, Bennett JE, Catanzaro A, Davies SF, Dismukes WE, Hage CA, Marr KA, Mody CH, Perfect JR, Stevens DA, and on behalf of the American Thoracic Society Fungal Working Group: **An official American Thoracic Society statement: treatment of fungal infections in adult pulmonary and critical care patients**. *Am J Respir Crit Care Med* 2011, **183**:96-128.
7. Denning DW: **Therapeutic outcome in invasive aspergillosis**. *Clin Infect Dis* 1996, **23**:608-615.
8. Ayala AR, Basaria S, Roberts KE, Cooper DS: **Aspergillus thyroiditis**. *Postgrad Med J* 2001, **77**:336.
9. Hornef MW, Schopohl J, Zietz C, Hallfeldt KJ, Roggenkamp A, Gartner R, Heesemann J: **Thyrotoxicosis induced by thyroid involvement of disseminated Aspergillus fumigatus infection**. *J Clin Microbiol* 2000, **38**:886-887.
10. Vogeser M, Wanders A, Haas A, Ruckdeschel G: **A four-year review of fatal Aspergillosis**. *Eur J Clin Microbiol Infect Dis* 1999, **18**:42-45.
11. Thada ND, Prasad SC, Alva B, Pokharel M, Prasad KC: **A rare case of suppurative aspergillosis of the thyroid**. *Case Rep Otolaryngol* 2013, **2013**:4.
12. Mebis L, Debaveye Y, Visser TJ, Van den Berghe G: **Changes within the thyroid axis during the course of critical illness**. *Endocrinol Metab Clin North Am* 2006, **35**:807-821.

doi:10.1186/1752-1947-8-379

**Cite this article as:** Marui et al.: Suppurative thyroiditis due to aspergillosis: a case report. *Journal of Medical Case Reports* 2014 **8**:379.

**Submit your next manuscript to BioMed Central and take full advantage of:**

- **Convenient online submission**
- **Thorough peer review**
- **No space constraints or color figure charges**
- **Immediate publication on acceptance**
- **Inclusion in PubMed, CAS, Scopus and Google Scholar**
- **Research which is freely available for redistribution**

Submit your manuscript at  
www.biomedcentral.com/submit

