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ASPERGILLUS SUPPURATIVE THYROIDITIS IN THE SETTING OF HYPOGAMMAGLOBULINAEMIA

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ABSTRACT

Thyroiditis is a condition characterised by the inflammation of the thyroid gland. Most cases of suppurative thyroiditis are caused by aerobic bacteria and present acute onset of symptoms. Hypogammaglobulinaemia associated with suppurative thyroiditis is extremely rare. This case relates to a diagnosis of *Aspergillus* suppurative thyroiditis in 78-year-old female patient in a setting of hypogammaglobulinaemia. The patient initially presented with dyspnoea following a recent diagnosis of chronic obstructive pulmonary disease. She developed worsening thyroid pain and swelling, and lab results confirmed hyperthyroidism. Imaging revealed a multinodular goitre, and fine-needle aspiration confirmed *Aspergillus fumigatus*. After discontinuing antibiotics, voriconazole was started. Due to immunologic workup showing low IgG, intravenous immunoglobulin was administered. Symptoms improved after a 12-week course. This case highlights the importance including differential diagnosis of fungal infection in patients present with acute suppurative thyroiditis and significance of conducting a comprehensive assessment for underlying immunodeficiency.

KEYWORDS

Suppurative thyroiditis, *Aspergillus fumigatus* infection, hypogammaglobulinaemia

LEARNING POINTS

- Although rare, fungal pathogens such as *Aspergillus* should be considered in patients with acute neck pain, swelling and signs of systemic infection, particularly in immunocompromised individuals.
- For infections caused by uncommon pathogens, immunology deficiency evaluation is important.
- Given the high mortality associated with *Aspergillus* thyroiditis, early identification and prompt treatment are essential to improved patient outcomes.

INTRODUCTION

Thyroiditis is characterised by inflammation of the thyroid gland; its potential causes include infection and autoimmune disease. Infectious thyroiditis is most commonly caused by skin or oropharyngeal organisms such as *Staphylococcus aureus* or streptococci. Patients with infectious thyroiditis may present with sudden onset of neck pain and tenderness, typically unilateral, along with fever and chills.

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Thyroiditis is complicated by abscess formation, most often seen in bacterial infection. Other organisms including mycobacteria, fungi and *Pneumocystis* usually cause chronic thyroiditis; this is seen primarily in individuals with severe immunocompromise due to acquired immune deficiency syndrome (AIDS), prolonged neutropenia, haematologic malignancy or immunosuppression in the context of chemotherapy or organ transplant. Acute fungal suppurative thyroiditis is extremely rare and *Aspergillus* is the most common cause of fungal thyroiditis[1]. Among these cases, *A. fumigatus* is the most common causative species[2]. The reported mortality rate for acute suppurative thyroiditis ranges from 3.7 to 9%, highlighting the importance of timely diagnosis and treatment[3]. We present a case of acute suppurative *Aspergillus* thyroiditis in a patient with hypogammaglobulinaemia, the first such case we were able to find in the literature.

CASE DESCRIPTION

A 78-year-old female with a history of right nodular thyroid hyperplasia diagnosed on partial thyroidectomy the year prior was admitted to the emergency department. Her chief complaint was recurrent dyspnoea following a recent diagnosis of, and admission for, chronic obstructive pulmonary disease. The patient's hospital course was complicated by atrial fibrillation and acute hypoxemic respiratory failure with an increasing oxygen requirement.

During this admission, the patient developed worsening thyroid pain and swelling. Laboratory investigation demonstrated thyroid stimulating hormone (TSH) of less than 0.1 and T4 was slightly elevated at 1.9, indicating a diagnosis of hyperthyroidism. Ultrasound was performed which demonstrated an enlarged heterogeneous left lobe of the thyroid with no normal thyroid tissue. The tissue appeared heterogeneous, measuring 6.8 × 5.7 × 4.4 cm, with numerous small echogenic foci. The patient was started on methimazole 5 mg daily for hyperthyroidism with the goal to maintain TSH in the range of 1 to 2, due to her atrial fibrillation. Lab tests also demonstrated a normal parathyroid hormone (PTH) level of 53 (pg/ml) and a low vitamin D level. A computed tomography (CT) scan of the neck with intravenous contrast showed a large mixed cystic and solid mass centred at the expected level of the left thyroid, extending anteriorly and slightly right of midline. This was thought to represent the progression of a multinodular goitre arising from the residual thyroid tissue. Ultrasound-guided fine-needle aspiration of a left thyroid mass yielded approximately 40 ml of purulent fluid and cytologic findings suggested acute inflammation. Empiric ceftriaxone and vancomycin were started pending further results. Pathology revealed fungal septate hyphae with features most consistent with *Aspergillus*. No malignant cells were identified, and the culture eventually grew *A. fumigatus*. The patient's serum galactomannan was also found to be positive (0.97).

Vancomycin and ceftriaxone were discontinued and voriconazole was started. Due to the unusual nature of this infection, a limited autoimmune workup was undertaken. Human immunodeficiency virus (HIV) screening was negative, and a lymphocyte profile and subset analysis was normal. However, evaluation of quantitative immunoglobulins showed a low IgG level of 279 (mg/dl). Haematology/Oncology was consulted. The patient was given one 500 mg/kg dose of intravenous immunoglobulin. Her symptoms improved after a week, and she was discharged home to complete a planned 12-week course of voriconazole. On follow-up evaluation after 12 weeks of therapy, the patient noted marked improvement in her neck pain and swelling.

DISCUSSION

Most cases of suppurative thyroiditis are caused by aerobic bacteria and present acutely with sudden onset of pain and a firm, tender, red, warm swelling in the anterior neck[1]. In contrast, infections caused by mycobacteria or fungi are rare and usually manifest as chronic infection. Disease due to *Aspergillus* is often clinically unapparent and is identified only on postmortem analysis[2]. In our case, the patient developed acute thyroiditis with pain and neck swelling during hospitalisation which is an unusual presentation for fungal thyroiditis.

Hypogammaglobulinaemia is an immune disorder in which the level of immunoglobulin, specifically gamma globulins, are low. Gamma globulins are antibodies that play an important role in preventing disease by facilitating the clearance of bacteria, viruses, fungi and other pathogens. This disease state can be caused by insufficiency in production or losses of immune globulin. Patients with hypogammaglobulinaemia can be completely asymptomatic or can present with recurrent and more severe infections such as rhinosinusitis or pneumonia[4].

Normally, fungal sensitisation occurs through activation of the immune system. T-helper 1 and T-helper 17 cells contribute to the development of protective immunity against fungal infections by releasing cytokines. These cytokines stimulate phagocytes and B-cells to produce specific IgG antibodies. Therefore, decreased gamma globulins levels may significantly increase susceptibility to fungal infections. The thyroid's abundant blood supply, high iodine concentration and capsule shape make it resistant to microbial invasion. While patients with hypogammaglobulinaemia have been reported to present with more serious infections such as osteomyelitis, meningitis, septicaemia and various skin infections, implication of the condition in the development of acute suppurative thyroiditis is exceedingly rare[5].

In *Aspergillus* thyroiditis, most patients maintain normal thyroid function. However, there have been reports of clinical and biochemical thyrotoxicosis. Early hypothyroidism is less common[6]. Recommended diagnostic testing includes thyroid fine-needle aspiration biopsy as well as culture. Serum galactomannan can be used for screening; the test has low sensitivity but one study had a 94% specificity in patients without proven invasive aspergillosis[7]. First-line treatment

for *Aspergillus* thyroiditis is voriconazole. Combination therapy with an echinocandin may improve survival[2]. Other azoles including posaconazole, isavuconazole and amphotericin B can also be used. In our case, given the rarity of acute suppurative thyroiditis caused by fungi, the initial treatment included ceftriaxone and vancomycin while awaiting pathology results. This case emphasises the important of conducting a thorough workup for less common infections to facilitate rapid, targeted antimicrobial therapy.

In patients with acute suppurative thyroiditis caused by fungal infection, evaluation for underlying immunodeficiency is crucial. In our case, the patient's newly diagnosed chronic obstructive pulmonary disease, along with a history of severe recurrent infections over a short period, raised the suspicion for an underlying immunocompromised state. Preliminary immunologic workup may include total serum IgG, IgA, IgM and IgE levels, IgG subclasses, HIV screening, lymphocyte count with quantitative subsets and complement levels. Management of hypogammaglobulinaemia, if identified, may require administration of intravenous immunoglobulin in addition to routine vaccination.

CONCLUSION

Although acute suppurative thyroiditis caused by fungi is rare, it should be considered in patients presenting with acute neck pain, swelling and systemic signs of infection. While bacterial pathogens are the most common cause, fungal pathogens – particularly *Aspergillus* – should be included in the differential diagnosis, especially in atypical cases and those involving immunocompromised patients. This case emphasises the importance of maintaining a high index of suspicion for uncommon pathogens as well as thorough evaluation for underlying immunodeficiency. Given the high mortality associated with *Aspergillus* thyroiditis, early recognition and timely initiation of appropriate treatment are critical for improving patient outcomes.

REFERENCES

1. 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.
2. Nguyen J, Manera R, Minutti, C. Aspergillus thyroiditis: a review of the literature to highlight clinical challenges. *Eur J Clin Microbiol Infect Dis* 2012;**31**:3259–3264.
3. Berger SA, Zonszein J, Villamena P, Mittman N. Infectious diseases of the thyroid gland. *Rev Infect Dis* 1983;**5**:108–122.
4. Herrod HG. Clinical significance of IgG subclasses. *Curr Opin Pediatr* 1993;**5**:696–699.
5. Hanson LA, Söderström R, Avanzini A, Bengtsson U, Björkander J, Söderström T. Immunoglobulin subclass deficiency. *Pediatr Infect Dis J* 1988;**7**:S17–21.
6. Ayala AR, Basaria S, Roberts KE, Cooper DS. Aspergillus thyroiditis. *Postgrad Med J* 2001;**77**:336–336.
7. Sulahian A, Boutboul F, Ribaud P, Leblanc T, Lacroix C, Derouin F. Value of antigen detection using an enzyme immunoassay in the diagnosis and prediction of invasive aspergillosis in two adult and pediatric hematology units during a 4-year prospective study. *Cancer* 2001;**91**:311–318.