Case Report

**Campylobacter jejuni** as a Cause of Acute Infectious Thyroiditis, on a Background of SLE-related End Stage Renal Failure and CMV Viraemia: A Case Report and Review of the Literature

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**Abstract**

Acute suppurative thyroiditis is a rare cause of thyroid disease; however it is capable of causing widespread systemic illness, with catastrophic complications. A large number of causative pathogens have been identified, the most common being *Staphylococcus* and *Streptococcal* species. We report a rare case of acute suppurative thyroiditis, caused by *Campylobacter jejuni* in a patient with systemic lupus erythematosus-related end-stage renal failure and excessive CMV viraemia. She developed severe respiratory compromise and required emergency total thyroidectomy and central neck clearance, which cured the local septic focus. The patient died from refractory sepsis due to *E. coli*.

**Keywords:** Thyroiditis; *Campylobacter jejuni*; SLE-related end stage renal failure

**Introduction**

Acute infectious thyroiditis is a rare condition, causing less than 0.1% of all thyroid disease [1]. The most common cause of acute suppurative thyroid infection is bacterial, but other causes also include fungal, mycobacterial and parasitic invasion [2,3]. The thyroid is thought to be protected from such infection by its own inherent properties, including its encapsulation, high vascularity and lymphatic drainage, its content of iodine and generation of hydrogen peroxide [2,4].

It is more common in those with coexistent thyroid disease or abnormalities, as well as immunosuppressed patients including patients with human immunodeficiency virus infection and those with congenital anatomical abnormalities, such as piriform sinus fistula (in particular in children) [4-6].

Prompt diagnosis is required for optimal management, with imaging, aspiration and Gram-staining, followed by institution of appropriate antibiotics, with surgical drainage of any abscesses [7]. Outcome is variable, and hinges on early recognition to reduce the risk of fulminant, life-threatening disease and complications [8-10].

We review the literature around acute infectious thyroiditis, and report a case of *Campylobacter jejuni* severe acute bacterial suppurative thyroiditis in a female patient with systemic lupus erythematosus (SLE). A detailed literature search (using PubMed, Medline and Google Scholar) revealed only a handful of documented cases of acute suppurative thyroiditis reported in a patient with SLE, and none due to this micro-organism.

**Case Report**

A 53 year-old African lady with end-stage renal failure secondary to SLE-related glomerulonephritis was admitted to the renal ward from the dialysis unit generally unwell, with pyrexia, general malaise and leg swelling; empirical antibiotic treatment was started for presumed cellulitis.

She had previously received a cadaveric renal transplant lost to chronic allograft nephropathy and was restarted on haemodialysis. Her renal physician had referred her to endocrine surgery for evaluation of a thyroid cyst approximately six months prior to her acute presentation, at which time she was asymptomatic. Imaging had shown a multinodular goitre with an asymptomatic cyst in the isthmus (measuring 5.7 cm). She had normal thyroid function and manageable chronic allograft nephropathy and was restarted on haemodialysis.

On initial presentation to the endocrine service she was comatose with acute renal failure (measuring 3x4x2.5 cm). 5 ml of thick purulent fluid was aspirated, of which equal volumes were sent for microbiological and cytological analysis. Curved Gram-negative rods were seen on microscopy. High-dose broad-spectrum intravenous antibiotics were commenced immediately, namely vancomycin, clarithromycin and metronidazole (owing to the patient’s penicillin allergy, and on microbiology advice).

Acute suppurative thyroiditis is a rare cause of thyroid disease; however it is capable of causing widespread systemic illness, with catastrophic complications. A large number of causative pathogens have been identified, the most common being *Staphylococcus* and *Streptococcal* species. We report a rare case of acute suppurative thyroiditis, caused by *Campylobacter jejuni* in a patient with systemic lupus erythematosus-related end-stage renal failure and excessive CMV viraemia. She developed severe respiratory compromise and required emergency total thyroidectomy and central neck clearance, which cured the local septic focus. The patient died from refractory sepsis due to *E. coli*.

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Microbiology confirmed the causative organism as *Campylobacter jejuni*.

Unfortunately, there was rapid local disease progression with development of airway obstruction. Computed tomography (CT) of the neck revealed retrosternal extension of the goitre to level of the aortic arch, with considerable tracheal compression to a nadir of 6 mm.

The patient hence underwent emergency neck exploration. Intra-operatively, elevated venous pressures within the neck and a massive enlargement of the thyroid (approximately 200 ml) were observed; the central compartment contained a 6 cm abscess and a phlegmone. Furthermore, the strap muscles were significantly compromised by the infection and the central compartment was filled with turbid fluid. Therefore, total thyroidectomy and total parathyroidectomy (all four of 2 cm diameter or more) was performed, with en bloc resection of the phlegmonous central compartment (including strap muscles). Whilst the right internal jugular vein (RIJV) had some residual flow, the left was fixed to the wall of the abscess. The vein was therefore partially resected with the abscess, the thrombus removed and the defect repaired. Swabs were sent for further microbiological analysis, and a thorough washout was performed. Complete haemostasis was achieved and the neck closed in layers. Both recurrent laryngeal nerves (RLN) were preserved and the patient was extubated in the intensive care department with a normal voice where she fared well for three days.

Three days later, she developed rapid neck swelling due to bleeding when her INR was above the superior measurable range, the aPTT >5 and thrombin time >180, and emergency re-intubation was required. All anticoagulation therapies (for her SLE-related prothrombotic state) were withdrawn. The episode was managed conservatively and repeat neck ultrasound again found a large RIJV thrombus with some blood flow, and normal flow in the right external jugular vein (REJV). The LIJV was occluded, but with flow in the left external jugular vein (LEJV). A further two days later, there was again an increase in neck size with very high skin tension within the neck and a decision was made to re-explore the wound. This revealed 200 ml partially clotted haematoma, which was removed, and no active bleeding. Again, both RLNs were preserved, and complete haemostasis achieved.

Pathologically, the thyroid gland was oedematous and showed interstitial and intrafollicular mixed infiltrate containing numerous neutrophils, several cystically dilated follicles and a cavity containing necrotic debris surrounded by inflamed granulation tissue (Figures 1 and 2). Interstitial siderophages suggestive of chronic haemorrhage were also noted. No cytopathic changes or viral inclusions were observed in epithelial or endothelial cells from the thyroid samples. Additional immunostaining, using DAKO anti-cytomegalovirus monoclonal cocktail (clones CCH2 & DDG9, 2 g/mL, developed with avidin-biotin complex and diaminobenzidine as chromogen), revealed no CMV antigens; appropriate positive and negative controls were run.

Soon after, there was further decline secondary to a new Gram negative septicaemia (identified as E. coli from blood culture bottles and line swabs) of unknown origin; antibiotics were adjusted according to sensitivities, with amikacin and meropenem commenced, but without improvement in her clinical condition. The neck stayed uncomplicated with no further collections or phlegmone. She subsequently developed disseminated intravascular coagulation and purpura fulminans as a consequence of the underlying sepsis.

She initially improved, but over the coming weeks ventilatory weaning proved difficult. CMV viraemia was found during the first week of her post-operative course and thereafter (most likely related to her long-standing immunosuppression for her SLE) with initial high titres of 89101 copies per ml. It was later responsive to ganciclovir. Due to the ongoing sepsis, with refractory hypotension, worsening leg skin necrosis and significant pain and distress, a decision was made in consultation with the patient herself, not to escalate care and referral was made to palliative care for ongoing symptom control. She subsequently died 46 days after admission to hospital. No post-mortem examination was performed. The cause of death was multiple organ failure due to sepsis. The source of sepsis did not pertain to the neck, which had in fact healed well about 3 weeks prior to her death without evidence of persistent infection.

**Figure 1:** Nodular thyroid gland reveals cystically dilated spaces with colloid and neutrophilic infiltrate that extends to the interstitium (a, hematoxylin-eosin 12.5x; b, hematoxylin-eosin 40x).

**Figure 2:** The inflammatory infiltrate is present in both the follicle lumen (active inflammation) and in the interstitium and it is associated with tissue destruction (abscess formation) and reactive regenerative changes in the follicular epithelium (a-c, hematoxylin-eosin 100x; d, hematoxylin-eosin, 200x).

**Discussion**

Although acute bacterial supplicative thyroiditis is a rare condition with only 224 cases existing in the literature between 1900 and 1980 [8,11] and totalled at 415 in 2010 [1], it is one that ought to be
considered in any patient with known thyroid abnormalities or disease who presents with non-specific symptoms and potential underlying sepsis [1]. Failure to recognise the condition at an early stage can have catastrophic consequences and can lead to significant morbidity or death.

The original source of infection is commonly unidentifiable, but several reports do exist that identify a specific source [12,13]. The most commonly reported causative organisms reported in the literature are Gram-positive organisms, in particular *Staphylococcus aureus* and *Streptococcus species* as reported since the early 20th century [14,15]. *Streptococcus pyogenes*, *Staphylococcus epidermidis* and *Streptococcus pneumoniae*, in descending order of frequency have all been identified. Similar proportions are seen in paediatric cases [16].

Numerous cases of other organisms are reported, in particular Gram-negative bacteria including *Klebsiella pneumoniae*, *Salmonella species*, *Pasteurella multocida*, *Brucella*, *Escherichia coli*, and *Haemophilus influenzae* amongst many others [11,13,17-20]. In immunocompromised individuals, there is an additional tendency for anaerobic infections including Pneumocystis jiroveci, and *Aspergillus* and *Candida species* [10,19], although fungal infections may indeed be present in immunocompetent individuals, e.g. *Blastomyces dermatitidis* [2,20]. Other causative groups of organisms are anaerobes, which make up a significant proportion, including *Bacteroides*, *Actinomyces species* and *Clostridium septicum* [1,8], mycobacteria, including *M. tuberculosis* and atypical mycobacteria [8,21], *Coccidioides immitis* and *Echinococcus species* [16]. The causative organisms and their estimated frequencies are summarised in Table 1 [1,8,16,19].

**Table 1: Summary of causative organisms and estimated frequency**

| Causative organism                                      | Estimated frequency |
|--------------------------------------------------------|---------------------|
| Gram-Positive Bacteria                                 | 35-40%              |
| Staphylococcus species (S. aureus, S. epidermidis)     |                     |
| Streptococcus species (S. pyogenes, S. pneumoniae)    |                     |
| Gram-Negative Bacteria                                | 25%                 |
| *Campylobacter jejuni*                                 |                     |
| *Klebsiella species*                                   |                     |
| *Haemophilus influenzae*                               |                     |
| *Salmonella species*                                   |                     |
| *Escherichia coli* (facultative anaerobe)              |                     |
| *Pseudomonas aeruginosa*                               |                     |
| Acinetobacter and many others                          |                     |
| Anaerobes (Gram-positive and -negative)                | 9-12% (Often polymicrobial culture) |
| Bacteroides species                                    |                     |
| *Actinomyces species*                                  |                     |
| *Clostridium septicum* among others                    |                     |
| Mycobacteria                                           | 9%                  |
| *Mycobacterium tuberculosis*                           |                     |
| Atypical mycobacteria (e.g. *Mycobacterium avium intracellulare*) |             |
| Fungal                                                 | Approx 15%          |
| *Pneumocystis jiroveci*                                |                     |
| *Aspergillus species*                                  |                     |
| *Candida species*                                      |                     |

Despite the large number of different reports regarding causative organisms, this is the first such report to isolate *Campylobacter jejuni* (only *Campylobacter fetus* has been reported as a cause of thyroid abscess) [22]. *C. jejuni* is a flagellated Gram-negative aerobic bacterium that is part of the normal flora of many wild and domestic birds and farm animals, and is primarily a cause of bacterial gastrointestinal disease; in industrialised countries it is thought to be the most common cause of this bacterial food-borne disease [23]. While it has been associated with infectious colitis, which can complicate inflammatory bowel disease and cause flare-up or relapse [24], and more commonly Guillain-Barré syndrome, no reports exist suggesting it as a cause of acute suppurative thyroiditis. An enteric origin with disruption of the intestinal barrier is the most likely origin of this infection that localized to the thyroid due to the underlying abnormalities related with a pre-existent nodular hyperplasia with cystic changes. CMV colitis, with its well-recognised effects on mucosal barrier function manifesting as erosion and ulceration, would be a predisposing condition in our patient. This hypothesis is further supported by the fact that *E. coli* sepsis of unknown origin supervened later in the course.

CMV disease is thought to be the pacemaker of progressive disease and death in this complex patient. It has been demonstrated that CMV-DNAemia is associated with CMV disease as opposed to infection in virtually all patients with CMV DNA levels of ≥500 copies/µg of total DNA in peripheral blood had clinical evidence of disease [25], but without evidence of any direct local contribution to the suppurative thyroiditis. CMV reactivation in critically ill patients is known to worsen prognosis and increase mortality [26-28].

Our case identifies the importance of early identification of acute suppurative thyroiditis and the severity and widespread illness that it may cause; prompt recognition is vital in optimising treatment. Furthermore, it adds to the growing number of known causative pathogens and highlights the need to identify the organism, in order to guide antimicrobial treatment accordingly.

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