Pain in the neck: a rare complication of carbimazole therapy

Introduction

Anti-thyroid drugs such as carbimazole and propylthiouracil are commonly used to treat thyrotoxicosis in the UK. Although mostly well tolerated they can cause various side effects, with agranulocytosis being potentially life-threatening. This article reports a case of carbimazole-induced agranulocytosis leading to the formation of bilateral deep neck abscesses in a clinically septic and thyrotoxic patient. This required acute surgical intervention under local anaesthetic and resulted in a good outcome. The authors believe this represents an unusual case of multiple deep neck space abscesses occurring secondary to carbimazole-induced agranulocytosis.

Discussion

Anti-thyroid drugs, e.g. carbimazole, are the usual first-line treatment for thyrotoxicosis. Side effects are usually minor, but a very small proportion will develop potentially life-threatening complications such as agranulocytosis, hepatotoxicity, vasculitis or even aplastic anaemia (Pearce, 2004).

Anti-thyroid drug-related agranulocytosis has a reported incidence of 0.03–0.18% (Kaufman et al, 1991). It is characterized by a decrease in peripheral neutrophil count to $<0.5 \times 10^9$/litre as a result of immunological or cytotoxic mechanisms (Pisciotta, 1990) and is commonly associated with sore throat and/or fever. A Medicine and Healthcare products Regulatory Agency report in 1993 found that anti-thyroid drugs had caused 7% of reported cases of agranulocytosis since 1963, and 27% of these were fatal. All patients started on anti-thyroid drugs should therefore be warned to seek medical attention and a full blood count check should they develop a sore throat or fever (Committee on Safety of Medicine, 1993). However, routine cell counts are not recommended as development of agranulocytosis is idiosyncratic. If any patient devel-

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Case Report

A 51-year-old Caucasian woman presented to the authors' hospital with a 1-week history of dysphagia and worsening sore throat. Three weeks earlier, she had presented to her GP with rapid weight loss and was confirmed to have thyrotoxicosis (thyroid-stimulating hormone <0.02 mIU/litre, normal range 0.45–4.5 mIU/litre; free T4 >50 pmol/litre, normal range 12–30 pmol/litre), for which she was started on carbimazole 40 mg once daily. She had a history of Graves' disease 11 years previously – this was treated with 3 months of carbimazole, which was stopped following pruritis, and 15 months of propylthiouracil, with subsequent remission. For 3 days before admission, she had been experiencing palpitations, muscle and joint aches, diarrhoea and vomiting, and was unable to keep anything down. She had also developed progressive odynophagia and pain on neck movement.

On examination she was febrile at 39.5°C, hypotensive and tachycardic at 135 bpm. Neck examination revealed palpable, tender cervical lymph nodes. There was no palpable goitre or evidence of thyroid eye disease. Visualization of the tonsils was limited by trismus, and flexible nasopharyngeal endoscopy showed oropharyngeal ulceration with moderate amounts of white/yellow mucus in the nose and throat. Fluid resuscitation with intravenous colloids was initiated, and intravenous vancomycin and gentamicin administered as per the hospital's neutropenic sepsis protocol. The results of initial baseline investigations are shown in *Table 1*. It is notable that blood cultures grew a sensitive pneumococcus.

Carbimazole-induced agranulocytosis with secondary septicaemia was diagnosed. The carbimazole was stopped, and propranolol was used to control her heart rate. She initially settled, but over the next 48 hours developed respiratory distress requiring intensive care monitoring (but not inotropic support). Treatment with granulocyte colony-stimulating factor was begun on the recommendation of the haematologist.

After a few days she stabilized haemodynamically, and the granulocyte colony-stimulating factor was stopped after 5 days as the white cell count had improved. Her sore throat improved and she was able to tolerate fluids orally. However, as her white cell count increased she developed painful, enlarging, bilateral cervical adenopathy (*Figures 1* and *2*). An ultrasound scan and computed tomography of the neck with contrast (*Figure 3*) revealed extensive bilateral parapharyngeal abscesses as well as enhancement of the thyroid gland as a result of uncontrolled thyrotoxicosis. The right-sided cervical abscess extended from the level of the angle of the mandible, between the deep portion of the parotid gland and the carotid sheath, down to the level of the upper pole of a markedly-enlarged but non-nodular thyroid gland. The left-sided cervical abscess extended from the level of the superficial lobe of the parotid gland down to just below the level of the cricoid cartilage.

The aforementioned blood cultures guided a change of antibiotic therapy to clarithromycin. After discussion with the endocrinologist, a neck exploration under general anaesthetic was deemed to be very high risk, so repeated bedside needle aspiration was performed. The left neck abscess was treated successfully, but the right neck abscess did not improve (*Figure 4*). She required neck exploration under local anaesthesia for the right parapharyngeal abscess, with a drain being left in-situ. This resulted in major clinical improvement, with removal of the drain after 3 days. The aspirate did not grow any micro-organisms and histology showed inflammatory tissue, consistent with tissues adjacent to an abscess cavity. Antibiotics were continued for a week postoperatively.

She subsequently underwent successful outpatient I^{131} radio-iodine treatment and is currently euthyroid on levothyroxine replacement. The neck swellings have resolved completely.

Table 1. Results of initial investigations

Investigation	Patient value (normal range)
White cell count	0.5 x10^9/litre (4–13 x10^9/litre)
Neutrophils	<0.1 x10^9/litre – undetectable on film (1.5–8.5 x10^9/litre)
Haemoglobin	12.8 g/dl (11.5–16.5 g/dl)
Platelets	154 x10^9/litre (150–500 x10^9/litre)
ESR	123 mm/hr (0–10 mm/hr)
Prothrombin time	16 seconds (10–13 seconds)
Sodium	134 mmol/litre (133–146 mmol/litre)
Potassium	3.7 mmol/litre (3.5–5.3 mmol/litre)
Creatinine	67 umol/litre (50–90 umol/litre)
Albumin	37 g/litre (35–50 g/litre)
Urine culture	No growth
Blood culture	*Streptococcus pneumoniae*, sensitive to penicillin and vancomycin
Chest X-ray	Nil focal parenchymal
Throat swab	No growth
Sputum culture (day 3)	*Haemophilus influenzae*
Pus culture	No growth

ESR = erythrocyte sedimentation rate

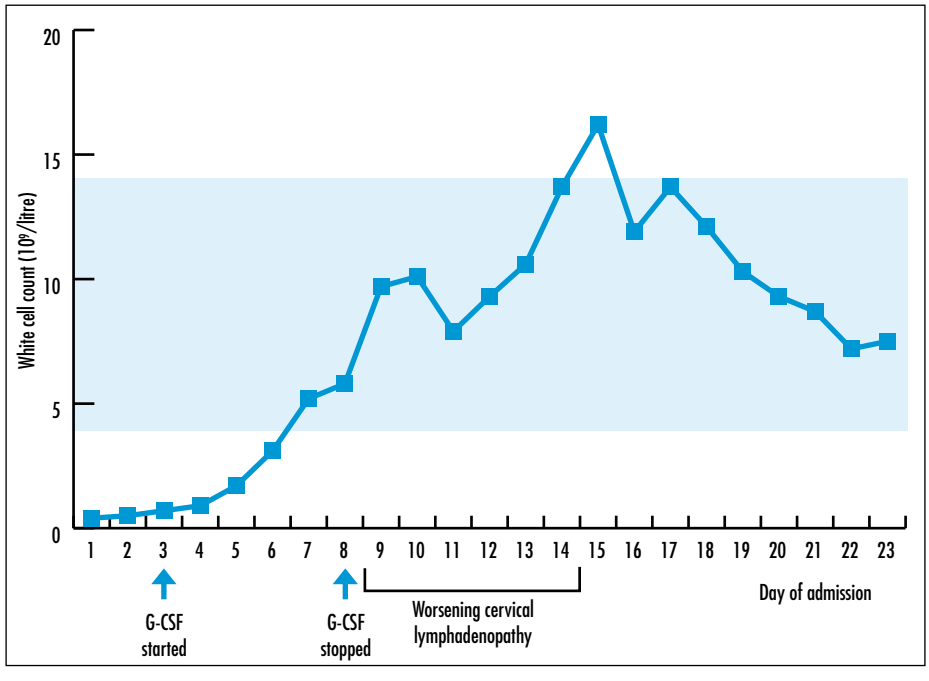
ops an unexplained fever, chills or sore throat after starting carbimazole, the physician should suspect agranulocytosis.

Cessation of the drug results in haematological recovery in 2–3 weeks (Andersohn et al, 2007), but occasionally the reaction can be severe and prolonged. Markers of poor prognosis include a neutrophil count of <0.1 x 10^9/litre at presentation, severe infections or septic shock, and renal insufficiency at diagnosis. As seen in this case, previous uncomplicated carbimazole use does not guarantee safety of future use (Pearce, 2004).

Although septicaemia is common in neutropenic patients, abscesses are rare. Anti-thyroid drug-induced agranulocytosis has been reported as causing retropharyngeal and peritonsillar abscesses (Sheng et al, 1999), as well as a perianal abscess (Aydn et al, 2009). Granulocyte colony-stimulating factor was apparently ineffective in those cases, in contrast with this patient.

Figure 1. Bilateral neck swelling outlined in the patient.

Figure 2. Graph of white cell count against day of admission. G-CSF = granulocyte colony stimulating factor.



Most neck space abscesses require drainage or repeated aspiration, especially if the patient is aged over 65 years, has underlying systemic disease, or fails to respond to antibiotics. If left untreated, life-threatening complications can ensue, such as haemorrhage as a result of involvement of great vessels, septic shock, mediastinitis and intrathoracic abscess (Zheng et al, 2005).

General anaesthesia in an uncontrolled thyrotoxic patient can cause significant morbidity (Diao et al, 1998), so local anaesthesia may be safest (Williams and Lo Gerfo, 2002). It led to a favourable outcome in this patient's case. **BJHM**

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Figure 3. Coronal computed tomography scan of neck (with contrast) showing bilateral neck abscesses.

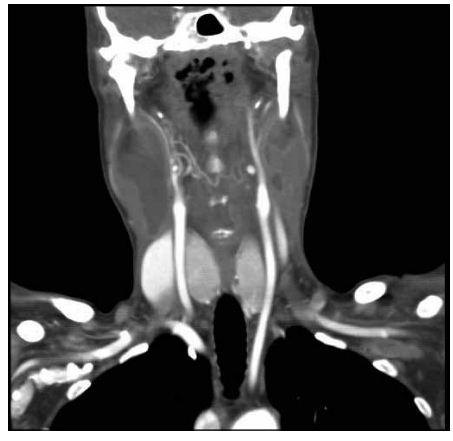

Figure 4. Lateral photograph of the patient showing right neck abscess (outlined).

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LEARNING POINTS

- Carbimazole is the most commonly prescribed anti-thyroid drug in the UK.
- Side effects of anti-thyroid drugs are uncommon and, when they do occur, are usually minor and transient.
- An extremely small proportion of patients will develop potentially life-threatening complications of agranulocytosis.
- General anaesthetics can be hazardous in an uncontrolled thyrotoxic patient recovering from neutropenic sepsis. Abscesses generally require drainage or repeated aspiration, and such cases can be successfully managed by local anaesthetic drainage.
- Patients started on anti-thyroid drugs should be advised to seek medical attention and have a full blood count performed should they develop a sore throat or fever. This should be part of routine endocrinological practice.