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Endocrinology Quiz – Case 8

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A 54-year-old man presented with severe neck pain and exhaustion for the preceding two weeks. He also had a fever up to 38 °C, occurring at approximately 6–8 pm in the preceding few days, associated with excessive sweating and flushing, as well as flu-like symptomatology. Review of systems revealed weight loss of 2 kg in the past month or so, which was, however, intentional. He had a history of gastro-esophageal reflux disease and hyperlipidemia, for which he was taking pantoprazole 20 mg and Liptruzet (ezetimibe/atorvastatin) 10/10 mg daily, respectively. There was no recent history of upper respiratory tract infection. He had never smoked; he was working in a beer brewery and consumed about 14 units of alcohol per week. There was no history of foreign travel.

On examination, he was alert, comfortable, and clinically euthyroid. Heart rate was 88 beats per minute with a regular rhythm, blood pressure 140/82 mmHg, aural temperature 36.9 °C, respiratory rate 16 breaths per minute and oxygen saturations of 97%. There was anterior neck tenderness on palpation centrally and in the lower half of the neck. Cardiovascular, respiratory, gastrointestinal and rheumatological examinations were unremarkable.

Investigations performed by his general practitioner revealed a normal chest x-ray; laboratory tests revealed a white cell count of 10.38×10^3/μL (normal range 4–10) with otherwise normal full blood counts, renal and liver function and bone profile. Of note his erythrocyte sedimentation rate (ESR) was raised at 65 mm per hour (<15) with a C-reactive protein (CRP) of 3.5 mg/dL (<0.5). TSH was 0.01 mIU/L (0.27–4.2) with a free T4 of 29.1 pmoL/L (12–22), indicating thyrotoxicosis. A neck ultrasound scan (USS) (esaote MyLabSeven, Italy; probe 3–13 MHz) performed as an extension of his physical examination revealed diffuse hypoechoic and heterogeneous appearances of the thyroid gland with reduced vascularity, but no (pseudo)nodular appearances; there were associated reactive lymph nodes (fig. 1). A nuclear medicine scan was deemed unnecessary for the diagnosis.

The diagnosis was established based on the clinical, biochemical and radiological picture described above. The patient was first commenced on ibuprofen 400 mg three times a day. Two days later, he felt no better with ongoing neck ache, fatigue, sweating and a nocturnal fever at 38 °C. He was therefore commenced on a reducing regime of prednisolone 30 mg daily. Within 24 hours of commencing glucocorticoids, he felt much better with resolution of both the neck ache and fever, and a return to his usual sense of general health and well-being.

He was reviewed again four weeks later and was asymptomatic with a normal ESR at 4 mm per hour and improved appearances on thyroid USS (not shown). He did however report an increased appetite. At roughly 10 weeks following glucocorticoid therapy initiation the neck ache recurred to an almost as severe intensity as the original pain and was associated with tiredness but no fever. This episode was correlated with a reduction of prednisolone from 10 mg to 5 mg daily. This was hence treated as a flare-up of subacute thyroiditis and necessitated a dose increment back to 10 mg of prednisolone daily. His prednisolone was once again gradually reduced, but at a lower rate. At six months following his original presentation the glucocorticoids were successfully withdrawn and the patient was euthyroid whilst not requiring any levothyroxine therapy. By this time there was resolution of the inflammation on the USS (fig. 1). The patient remained asymptomatic when he was reviewed again a month later.

Comment

Subacute thyroiditis (also known as painful or DeQuervain's thyroiditis) is a transient inflammatory condition of the thyroid of unknown etiology. It is reported to be commoner after an upper respiratory tract infection and clusters occurring in summer months have also been reported, potentially implicating a viral cause.

The patient as described above presented with the classical clinical picture for this condition. Typically, there is also a resolution of the symptomatology with glucocorticoid therapy initiation and as such can be utilized as a diagnostic criterion. Indeed, it is so rare for the patient to remain symptomatic after 24–48 hours' post-

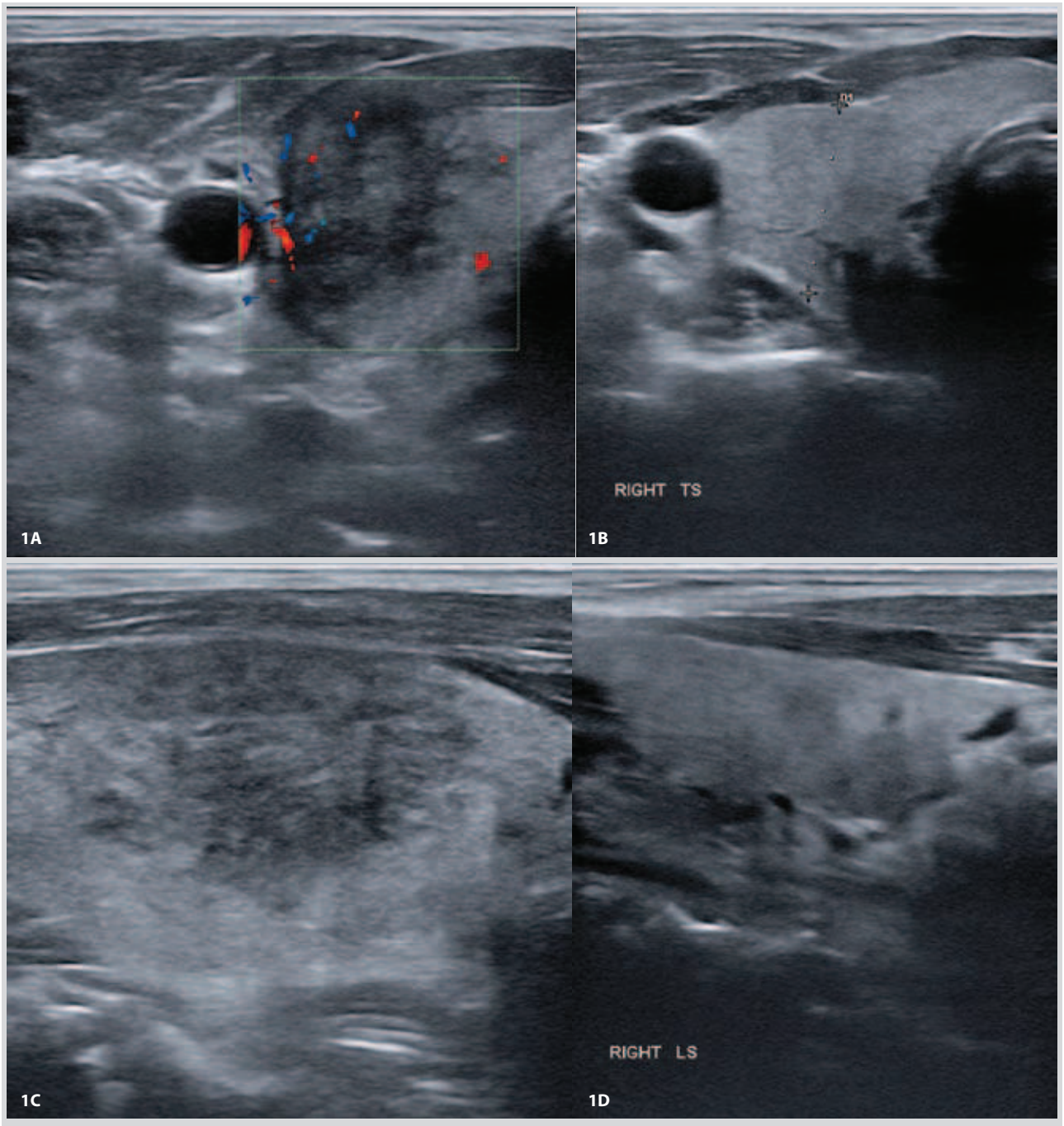

Figure 1. Figures 1A and 1C represent the transverse and longitudinal section sonographic images, respectively, of the right lobe of the thyroid gland, obtained during the original presentation of the patient. The thyroid gland was enlarged with an antero-posterior diameter at 25.2 mm and 20.5 mm on the right and left lobe (normal <20 mm), respectively. There was significant heterogeneity and non-specific hypoechogenicity affecting about two-thirds of the gland. No nodules were visible. Vascularity was overall reduced. The rest of neck had a few bilateral level 3 lymph nodes with normal hilum and vascularity (reactive lymph nodes). Figures 1B and 1D represent the transverse and longitudinal section images, respectively, of the right lobe, obtained six months after the original presentation of the patient and his treatment with glucocorticoids. They show normal homogeneous appearances of the thyroid gland and with normal vascularity; the AP diameters had also normalized at 17.8 and 13.6 mm on the right and left lobe, respectively. These changes were indicative of resolution of the inflammation.

glucocorticoid initiation that the treating endocrinologist should consider alternative diagnoses in such circumstances.

Biochemically, the commoner presentation is that of thyrotoxicosis (which may or may not be associated with clinical features of thyrotoxicosis), albeit the patient may occasionally be hypothyroid or even euthyroid. The thyrotoxicosis is classically followed by hypo-

thyroidism, which is in turn usually followed by a restoration of the euthyroid state. Subacute thyroiditis is among the few conditions that classically present with a raised ESR and a normal or, more modestly raised, CRP (the differential diagnosis of this biochemical pattern would include systemic lupus erythematous or multiple myeloma). The white cell count may be increased as well, but usually only mildly. Radiologically there are appearances of inflammation of the thyroid gland (as described in the aforementioned case) of varying severity; the inflammation may be diffuse or focal. Such appearances are indistinguishable between the various types of thyroiditis such as post-partum thyroiditis and other painless thyroiditis. In our experience an ultrasound scan is particularly useful in securing the diagnosis and excluding the differential diagnoses of acute neck pain with fever such as hemorrhage into a nodule or suppurative (acute infective) thyroiditis; it is especially useful in cases of diagnostic uncertainty, for instance when hyperthyroidism due to other causes such as Graves' disease is also considered. ^{99m}*Tc or* ^{123}*I scintigraphy usually shows reduced uptake in the thyroid gland. Scintigraphy is in our experience redundant when the clinical, biochemical and sonographic appearances are typical of subacute thyroiditis. Notwithstanding, it is an invaluable investigation in rare cases of thyrotoxicosis which have mixed features between subacute thyroiditis and Graves' disease, e.g. clinical thyrotoxicosis with mild/resolving neck pain, no fever, negative thyroid receptor antibodies, no pathognomonic features of Graves' disease on examination and inconclusive appearances on ultrasound scan.*

Treatment can follow three main pathways. Firstly, if the patient is minimally symptomatic or asymptomatic (e.g. if the patient presented in the recovery phase of the illness) a watch-and-wait conservative approach can be adopted. Secondly, if the patient is symptomatic then the option is between non-steroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids, with the latter considered if the symptomatology is moderate or severe. Traditionally, such medications administered in subacute thyroiditis were thought to function for pure symptomatic relief but there is some evidence that glucocorticoid utilization may reduce the overall disease duration and risk of eventual hypothyroidism. If NSAIDs are employed, then they should be switched to glucocorticoids if the patient remains symptomatic. There is currently no definitive evidence to guide clinicians as to the best choice of glucocorticoid or on the rate of reducing these medications. Most specialists use prednisolone 15–60 mg daily, with 40 mg being the most commonly cited dose. In a recent Japanese study, 15 mg of prednisolone was used as the initial dose in patients with subacute thyroiditis; 219 patients were followed-up every two weeks and their prednisolone reduced as needed; this regime was deemed successful by the authors. Nevertheless, the rate of recurrence was about 50% and 20% when the glucocorticoids were discontinued at six and eight weeks, respectively, and with 40% of the patients reporting pain or tenderness at the six-week follow-up appointment, suggesting that may be modestly higher initial dosage should be considered. Thirdly, treatment should be given directed for the thyroid status of the individual concerned; for the significantly symptomatic patients with thyrotoxicosis beta-blockers may be given (but avoid anti-thyroid drugs as are ineffective), and levothyroxine is given if the resultant hypothyroidism is symptomatic and/or permanent.

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