A RARE CASE OF NON-ISLET CELL TUMOUR HYPOGLYCAEMIA

Editor,

Non-islet cell tumour hypoglycaemia (NICTH) is a very rare paraneoplastic syndrome. The true incidence is unknown as many cases go undiagnosed. Only a few hundred cases are reported in English language medical literature since it was first described in 1929. The following describes a case of NICTH.

A 75-year-old undergoing chemotherapy for advanced endometrial carcinosarcoma; was admitted after routine blood tests revealed a severe acute kidney injury. Endometrial carcinosarcoma is a rare type of uterine malignancy that is classified as a mixed epithelial and mesenchymal tumour. Renal function normalised rapidly after bilateral nephrostomies were inserted.

However, during convalescence the patient developed hypoglycaemic symptoms with a low blood glucose of 1.1mmol/L. This was unresponsive to oral glucose, so intravenous glucose was administered. There was no history of any endocrine disorder or any previous hypoglycaemia. Hypoglycaemic attacks then became more frequent and an uninterrupted 10% glucose infusion was needed, however this did not prevent hypoglycaemic episodes (Fig 1).

DIFFERENTIAL DIAGNOSIS

There was negligible suspicion of alcohol or exogenous insulin use. Other hypoglycaemic agents were ruled out by a medication review. Critical illness such as sepsis or liver failure seemed unlikely as inflammatory markers and liver function were unremarkable. Malnutrition was considered, however a dietician assessment reported adequate calorie intake. Adrenal insufficiency was ruled out with a normal Synacthen response. Insulinoma was excluded by suppressed serum insulin and C-peptide in the setting of hypoglycaemia.

![Figure 1: Scatter plot of hypoglycaemic episodes. Arrow indicates initiation of uninterrupted glucose infusion.](image-url)
NICTH was considered once the above list of more common causes of hypoglycaemia had been excluded.

**TREATMENT & OUTCOME**

Calorie intake was optimised and steroid dosage was increased, but this had little effect in preventing hypoglycaemic episodes. The continuous glucose infusion was escalated to 20% glucose, however hypoglycaemia remained refractory. Interval imaging showed malignant disease progression and the options to treat her cancer with surgery, radiotherapy or chemotherapy had been exhausted. The patient died 22 days after the hypoglycaemic attacks began.

**DISCUSSION**

NICTH is a rare paraneoplastic condition that occurs due to tumoral over secretion of insulin-like growth factor 2 (IGF2). It occurs most commonly in patients with tumours of mesenchymal and epithelial origin. IGF2 binds to insulin receptors which increases glucose uptake by skeletal muscle and inhibits glucose release from the liver. IGF2 also acts on the pituitary gland and pancreas to suppress the secretion of growth hormone and glucagon.

In NICTH, the majority of overproduction is of ‘big’ IGF2 (a prohormone form of IGF2). This prohormone cannot easily be measured and only contributes a small fraction of the total IGF2 level. Therefore, total IGF2 may be reported as normal in NICTH. However, IGF1 is suppressed due to feedback inhibition and so the IGF2:IGF1 ratio is high. An IGF2:IGF1 ratio of greater than 10 confirms the diagnosis of NICTH.

Only half the cases of NICTH have a known tumour at the onset of hypoglycaemia. The remaining half present with hypoglycaemia and a tumour is diagnosed later.

Surgical removal of the tumour in NICTH is curative, however there is no consensus on the optimum strategy for managing inoperable patients. When surgical resection is not feasible, other antitumour therapies such as chemotherapy, radiotherapy or tumour embolization should be considered. In refractory cases, glucocorticoid steroids are the most commonly used medication used to treat NICTH.

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**DELAFLOXACIN, A NOVEL FLUOROQUINOLONE ANTIBIOTIC WITH ACTIVITY AGAINST HOSPITAL-, COMMUNITY- AND LIVESTOCK-ASSOCIATED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)**

**Editor,**

Delafloxacin is a new fluoroquinolone antibiotic, approved for treatment of acute bacterial skin and skin structure infections (ABSSSIs) caused by both Gram-positive and Gram-negative organisms. It recently received its regulatory licence from the European Medicines Agency in December 2019 (https://www.ema.europa.eu/en/medicines/human/EPAR/quofenix). For a seminal review on this background to this antibiotic, please see the recent seminal review by Mogle and colleagues.

As with any newly introduced antibiotic, it is important to evaluate a new antibiotic in the context of the local epidemiology and resistance rates, to aid physicians in the positioning of such a new antibiotic. To date, there have been no reports on the activity of delafloxacin against methicillin-sensitive (MSSA) and methicillin-resistant (MRSA) *Staphylococcus aureus*, within the Northern Ireland context, hence we wished to examine the *in vitro* susceptibility of MSSA and MRSA isolates to this new antibiotic.

*Staphylococcus aureus* (n=23) isolates [15 MSSA & 8 MRSA] were employed in this study, as detailed in Table 1. Isolates were obtained from the MicroARK Microbiology Culture Repository housed within the Northern Ireland Public Health Laboratory, Belfast City Hospital. Isolates within each category were selected at random for employment in this study. No other criteria were used in the selection of these organisms. Prior to use, all isolates were passaged twice by subculturing on Columbia Blood agar (Oxoid CM0031, Oxoid Ltd., Basingstoke, UK), supplemented with 5% (v/v) defibrinated horse blood for 24h at 37°C, under aerobic conditions. *In vitro* susceptibilities were examined on all 23 isolates, by employing Etest® gradient for delafloxacin (range:0.002-32 mg/L), as per manufacturer’s instructions (Biomerieux Ltd., France) and in accordance with EUCAST methodology and interpretive criteria. Susceptibility of...