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Diabetes insipidus as initial manifestation of extranodal NK/T cell lymphoma nasal type

Diabetes insípida como manifestación inicial de linfoma extraganglionar nasal de células T/NK

Central diabetes insipidus (CDI) is a disease caused by a decrease in or the absence of antidiuretic hormone (ADH) or arginine vasopressin (AVP), characterised by polydipsia and polyuria with hypotonic urine emission.¹ Possible causes include neoplasms, such as germinomas or craniopharyngiomas, accidental trauma or trauma secondary to intracranial surgery, midline malformations, diseases caused by accumulations such as sarcoidosis and autoimmune and/or infiltrative diseases such as Langerhans cell histiocytosis.² There are cases in which there are underlying genetic defects in AVP synthesis, while in others the cause is not fully understood and may be related to an autoimmune component.³ The diagnosis of CDI represents a major challenge in clinical practice, and the water deprivation test (WDT) or thirst test is the standard for diagnosis. However, the test is complex and the results are sometimes inaccurate, so new tools have been developed in recent years, such as measuring arginine- or hypertonic saline-stimulated copeptin.^{4,5}

Extranodal natural killer (NK)/T-cell lymphoma, nasal type (ENKL-NT) is a subtype of lymphoma whose aetiology is not fully understood. It is related to the Epstein–Barr virus (EBV), detection of which is a requirement for diagnosis. It is more common in Asia and America than in the West, it predominates in 40–80-year-old men and affects the nasal area in 80% of cases, presenting with symptoms of nasal obstruction. The definitive diagnosis is histopathological. The treatment of choice is radiotherapy (RT) combined with chemotherapy (CT) in different regimens. The disease has a poor short-to-medium-term prognosis.

We present the case of a 52-year-old male with no known allergies. He was a smoker, with a history of pneumothorax in 2001. One week before admission, he consulted for acute low-back pain, for which he was given an intramuscular injection of 40 mg of methylprednisolone. Three days later, he went to Accident and Emergency complaining of polydipsia and polyuria of seven litres a day, with intermittent paraesthesia on the right side of his face and bilateral nasal congestion. Chest X-ray showed no abnormal-

ities. He was admitted to endocrinology, where a WDT was consistent with the diagnosis of partial CDI (urinary osmolarity of 97 mOsm/kg, which increased after administration of desmopressin >100% up to 535 mOsm/kg), for which treatment was started with desmopressin, 60 mcg/day, at night. Magnetic resonance imaging (MRI) of the pituitary showed an increase in the stalk and the pituitary gland itself, with absence of physiological enhancement of the posterior pituitary on T1, and no evidence of tumour-type lesions. Computed tomography (CT) of neck and chest revealed no significant lymphadenopathy suspicious for sarcoidosis.

The patient's nasal congestion worsened, requiring assessment by Ear, Nose and Throat, who only observed bilateral mucosal thickening with a deviation of the nasal septum. During the first few days of his admission, his low-back pain worsened. A lumbar spine X-ray and lumbar MRI were performed without significant findings. Also performed were a bone series, showing no osteolytic lesions and a blood test for c-ANCA, p-ANCA, anti-cardiolipin Ab, ENA, ANA, anti-DNA Ab, which was negative. Angiotensin-converting enzyme, IgG4 immunoglobulin, alpha-foetoprotein, and human chorionic gonadotropin levels were all normal. The QuantiFERON® test for *M. tuberculosis* was negative, as were serology for human immunodeficiency virus and hepatitis C and B viruses, PCR for SARS-CoV-2, and the serological diagnoses of syphilis and Lyme disease. Urinary sediment was normal. While the patient was in hospital, several skin lesions appeared in the form of non-pruritic erythematous macule-papules, and Dermatology took a biopsy. The paraesthesia rapidly worsened, extending to the lower limbs with no clear metameric distribution. Neurology carried out a lumbar puncture (LP), with flow cytometry revealing a 66% infiltration of NK cells, findings consistent with the preliminary results of the skin biopsy. At that point the patient was transferred to Haematology.

PET/CT scan with 18-fluorodeoxyglucose (FDG) showed marked metabolic activity, both nodal and extranodal, with intense pituitary uptake suggestive of tumour invasion (SUVmax 10.1) (Fig. 1), as well as a large sinonasal hypermetabolic mass and intense activity in the left L3, bilateral L5 and right S1 nerve roots (SUVmax 3.1), consistent with the patient's symptoms of low-back pain. These results, in conjunction with those of the skin biopsy and LP, confirmed the diagnosis of stage IV ENKL-NT with skin and central nervous system involvement.

The patient suddenly developed severe dysphagia, which required treatment with high-dose intravenous dexam-

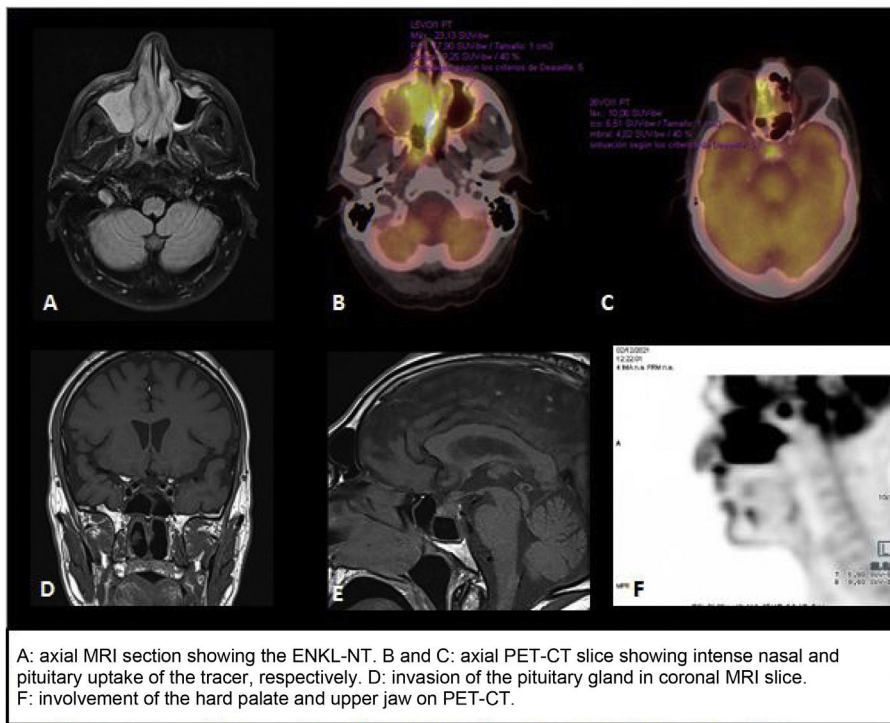


Figure 1 Involvement of the pituitary gland and adjacent structures by the ENKL-NT.

ethasone (8 mg/8 h) and total parenteral nutrition (TPN). Chemotherapy was started and several LP were performed to assess the treatment response, with a decrease in NK cell infiltration from 74.4% to 5.1% after 10 days, and progressive improvement in the patient's general condition. The EBV DNA result was positive, with 324,000 copies/ml. The patient required close follow-up by Endocrinology to adjust the desmopressin dose⁶ due to the high doses of corticosteroids received and the changes in fluid intake.

CDI is a complex disease often requiring extensive aetiological study. Although there have been several reported cases of lymphomas and other diseases with pituitary involvement,^{7,8} the first and only case of ENKL-NT with the initial manifestation secondary to invasion of the pituitary gland was described in 2007.⁹ In this case we ruled out underlying histiocytosis, autoimmune granulomatous diseases, a CNS germ cell tumour and various infections. The role of glucocorticoid therapy should be highlighted as, because cortisol is necessary for normal excretion of water, it can unmask incipient CDI.¹⁰ In this type of case, therefore, the participation of a multidisciplinary team is essential to guide the diagnostic process, with the aim of providing effective targeted treatment.

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Evaluation of the impact of the COVID-19 pandemic on gestational diabetes screening: DIABE-COVID Survey

Evaluación del impacto de la pandemia COVID-19 en el cribado de la diabetes gestacional: encuesta DIABE-COVID

Dear Editor,

Since the onset of the COVID-19 pandemic, pregnant women have been exposed to a higher risk of infection during health centre visits for reasons such as screening and/or diagnostic tests for gestational diabetes and its follow-up, if necessary. Prior to the COVID-19 pandemic, the Spanish Diabetes and Pregnancy Group (GEDE) (first page of Appendix 1) recommended two-stage screening, beginning with the O'Sullivan test (50 g of glucose) and followed by the 100-g oral glucose tolerance test if the O'Sullivan test was positive (≥ 140 mg/dl). However, during the COVID-19 pandemic and with a view to minimising pregnant women's risk of exposure during these tests, the GEDE, together with other scientific societies,^{1,2} published (version 1.0 in March 2020,³ version 1.1 in April 2020⁴) updated specific recommendations.⁵⁻⁷ These consisted of measuring HbA1c, basal plasma glucose or random plasma glucose if the usual diagnostic process could not be followed.

One year on, the GEDE sent out a survey to its members to assess the impact of the pandemic on gestational hyperglycaemia screening and diagnosis and whether any changes have been made in this regard.

This was a cross-sectional study in which all members of the GEDE were invited to take part. The GEDE has 31 members in total, both from the Spanish Diabetes Society [Sociedad Española de Diabetes, SED] as well as the Spanish Society of Gynaecology and Obstetrics [Sociedad Española de Ginecología y Obstetricia] and Family and Community Medicine [Sociedad Española de Medicina de Familia y Comunitaria], from several different autonomous communities (map by community) (Fig. 1). The group is a representation of gestational diabetes care provided in Spain (23 centres) and is made up of specialists in endocrinology and nutrition (18), obstetrics and gynaecology (12) and family and community medicine (1).

An electronic survey was developed (Google Forms®); the survey consisted of 16 questions about screening and diagnosis before and during the pandemic (Appendix 2).

The survey was designed by three of the authors (MG, MM and MV), initially reviewed by a further three authors (IV, RC and MC) and finally by the remaining members of the GEDE.

The survey was sent to the group members email distribution list by the secretary of the SED.

Statistical analysis: a descriptive analysis of the answers obtained was performed. The data were expressed as n (%).

The survey revealed a change in the screening/diagnosis method in seven of the 22 participating centres in the first quarter (31.8%), in six centres in the second quarter (27.3%) and in eight centres in the third quarter (36.4%), with changes being made by the same centres in all three quarters. These centres were located in the communities of Andalusia, the Canary Islands, Catalonia, Madrid and the Basque Country.

The results of the survey show that the onset of the COVID-19 pandemic forced a substantial number of centres belonging to the GEDE group to change their gestational hyperglycaemia screening and diagnosis procedure, reflecting the different realities experienced by each centre according to the epidemiological data.

Finding a balance between preventing the spread of COVID-19 and reducing the clinical risk of gestational hyperglycaemia is not easy to achieve. Recent recommendations promote diagnostic approaches that limit exposure in blood draws but result in more cases of undiagnosed gestational hyperglycaemia, which could potentially increase the risk of adverse pregnancy outcomes.

Options should be weighed up based on the epidemiological situation at each centre and progressively adapted as the pandemic progresses.

The gestational hyperglycaemia screening and diagnosis survey administered to GEDE members shows that 22%–27% of the centres (between six and eight out of 22 centres, depending on the quarter) adapted their procedures due to the COVID-19 pandemic in the autonomous communities where the epidemiological situation was most severe.

The complete survey can be viewed at: https://www.sediabetes.org/grupos_de_trabajo/diabetesy-embarazo/

Appendix A. The members of the Spanish Diabetes and Pregnancy Group (GEDE) are shown in the appendix

Appendix 1. Members of the GEDE

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