



ORIGINAL ARTICLE

Complexity of neuro-oncological in-hospital consultations: a multicentre study



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KEYWORDS

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Abstract

Introduction: Oncological patients may require evaluation by a neurologist when they are admitted to hospital. The aim of our study was to determine the frequency and characteristics of hospital interconsultations (IC) received by the neurology department concerning oncology patients admitted to the hospital.

Material and methods: A retrospective multicentre study analysing IC with neurology concerning onco-haematological patients admitted over 5 consecutive years (2016–2020) in 4 tertiary hospitals in Spain was carried out.

Results: A total of 2091 IC from 1710 patients were analysed, most of them male (55.5%; 969/2091) with a median age of 60.5 years (range 15–92). Most of the ICs came from the medical oncology (43.2%; 904/2091) and hematology (42.2%; 882/2091) departments. Neuro-oncological ICs accounted for approximately 17% (2091/12 242) of the total number of ICs performed in the neurology department during the 5 years included in this study. The most frequent reasons for consultation were limb motor deficit (18.3%; 381/2077), confusional syndrome (14.1%; 292/2077), epileptic seizures (12.2%; 254/2077), and headache (8.1%; 169/2077). The most frequent associated tumours were lung cancer (18.3%; 383/2089), leukaemia (19%; 396/2089),

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PALABRAS CLAVE

Cáncer;
Complicaciones
neurológicas;
Diagnóstico;
Interconsulta
hospitalaria;
Neurooncología;
Tratamiento

lymphoma (17.1%; 357/2089), and primary brain tumor (12.1%; 353/2089). The majority (69.9%; 1460/2089) of patients were undergoing active or recent cancer treatment. Final neurological diagnoses included metabolic encephalopathy (11.2%; 234/2091), tumor progression (11%; 231/2091), cerebral vascular complications (10.1%; 212/2091), metastases (9.1%; 191/2091), and leptomeningeal dissemination (8.9%; 186/2091). A total of 15.4% (323/2091) of the ICs were closed with an undetermined diagnosis. The median time that the ICs were open was 3 days (range, 1–152).

Conclusions: ICs concerning onco-haematological patients are heterogeneous, with an increasing incidence and complexity, requiring management by neurologists with experience in neuro-oncological patients.

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Complejidad de las interconsultas hospitalarias neuro-oncológicas: Estudio multicéntrico

Resumen

Introducción: El paciente oncológico puede requerir la valoración por el neurólogo durante el ingreso hospitalario. El objetivo de nuestro estudio es conocer la frecuencia y las características de las interconsultas hospitalarias (ICH) solicitadas al servicio de neurología de pacientes oncológicos ingresados en el hospital.

Material y métodos: Se realizó un estudio multicéntrico retrospectivo de revisión de las ICH solicitadas al servicio de neurología de pacientes onco-hematológicos durante 5 años consecutivos (2016–2020) en cuatro hospitales terciarios en España.

Resultados: Se analizaron un total de 2.091 ICH de 1.710 pacientes, la mayoría hombres (55,5%; 969/2.091) con una mediana de edad de 60,5 años (rango 15–92). La mayoría de las ICH provenían de los servicios de oncología médica (43,2%; 904/2.091) y hematología (42,2%; 882/2.091). Las ICH neuro-oncológicas representaron aproximadamente un 17% (2.091/12.242) del total de ICH realizadas al servicio de Neurología durante los cinco años incluidos en el estudio. Los motivos de consulta más frecuentes fueron: déficit motor de extremidades (18,3%; 381/2.077), síndrome confusional (14,1%; 292/2.077), crisis epilépticas (12,2%; 254/2.077) y cefalea (8,1%; 169/2.077). Los tumores asociados más frecuentes fueron el cáncer de pulmón (18,3%; 383/2.089), la leucemia (19%; 396/2.089), el linfoma (17,1%; 357/2.089) y el tumor cerebral primario (12,1%; 353/2.089). La mayoría de los pacientes (69,9%; 1.460/2.089) estaban en tratamiento oncológico activo o reciente. Los diagnósticos neurológicos finales incluyeron encefalopatía metabólica (11,2%; 234/2.091), progresión tumoral (11%; 231/2.091), complicaciones vasculares cerebrales (10,1%; 212/2.091), metástasis (9,1%; 191/2.091) y diseminación leptomeningea (8,9%; 186/2.091). Un 15,4% (323/2.091) de las ICH se cerraron con diagnóstico indeterminado. La mediana de tiempo que la ICH requirió estar abierta fue de 3 días (rango 1–152).

Conclusiones: Las ICH de pacientes onco-hematológicos a los servicios de neurología son heterogéneas, con una incidencia y complejidad creciente, por lo que requieren de un manejo por neurólogos familiarizados con el paciente neuro-oncológico.

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Introduction

Cancer is one of the main causes of morbidity and mortality worldwide.¹ In Spain, cancer is the second leading cause of death after cardio- and cerebrovascular diseases. A report presented by the Spanish Society of Medical Oncology (SEOM, for its Spanish initials) in collaboration with the Spanish Network of Cancer Registries estimates that cancer incidence will reach 341 new cases per 100 000 person-years in Spain by the year 2040.²

Between 15% and 20% of patients with cancer present some type of neurological complication during the course of the disease.³ Twenty-five percent of patients with cancer develop cerebral metastases, especially in cases of lung or breast cancer, and melanoma.⁴ Again, SEOM estimates that 4630 primary tumours of the nervous system will be diagnosed in Spain in 2025.² Advances in the development of cancer diagnostic tests and treatments have led to increased survival of oncological patients and, therefore, a potential increase in neurological complications in these patients.^{5,6}

In addition to the direct tumour involvement of the nervous system as metastasis or meningeal carcinomatosis, patients with cancer may develop infectious, metabolic, vascular, or paraneoplastic/dysimmune neurological complications.⁷ Furthermore, due to the increasing implementation in clinical practice of new treatments against cancer, it is essential to be aware of neurotoxicity mechanisms and to recognise the clinical syndromes associated with new oncological therapies.^{8,9} Therefore, diagnosing neurological complications may be difficult in patients with cancer.

Several studies have shown that correct assessment by neurologists with knowledge and experience in hospital-admitted patients leads to more accurate diagnosis and treatment of neurological complications and, therefore, to better clinical outcomes and more efficient use of resources.^{10–12} Furthermore, several national and international series published in recent years have described a significant increase in demand for neurological consultations in hospitalised patients.^{13–15} However, there are no studies specifically analysing the characteristics of in-hospital oncology and haematology consultations (IC).

The aim of this study is to analyse the frequency and to describe the characteristics of ICs with the neurology department for onco-haematological patients admitted to 4 tertiary hospitals in Spain over a period of 5 years.

Material and methods

This is a retrospective, observational, cross-sectional, multicentre study of all ICs with the neurology departments of 4 Spanish tertiary hospitals: Instituto Catalán de Oncología l'Hospitalet–Hospital Universitario de Bellvitge (ICO-HUB), with an assigned population of 201 192; Hospital Universitario y Politécnico de La Fe (HUPLF), with an assigned population of 295 785; Hospital Universitario Son Espases

(HSE), with an assigned population of 338 852; and Hospital Universitario de Navarra (HUN), with an assigned population of 501 180. All 4 hospitals are reference centres for health-care districts with populations of approximately 1 000 000, with the exception of ICO-HUB, whose district has a population of more than 2 000 000. This study covered the period between 1 January 2016 and 31 December 2020.

All 4 participating centres belong to the Spanish public healthcare system. ICO-HUB has 997 beds, HUPLF has 1000 beds, HSE has 1020 beds, and HUN has 1100 beds. All centres perform haematopoietic stem cell transplantation (HSCT), but CAR T-cell therapy was only performed at ICO-HUB and HUPLF during the study period.

We designed a specific data collection form and a database including 14 variables: age, sex, date of IC request, department requesting the IC, type of primary tumour, date of cancer diagnosis, active or recent (past 3 months) treatment, type of treatment, reason for consultation, complementary examinations performed, neurological diagnosis, time to resolution of the IC, and date of death. Demographic and clinical data were collected retrospectively. Each form was anonymised and sent to the centre coordinating the study (HUN). Queries and inconsistencies were resolved through consultation with the hospital researchers before recording data in the digital database. The study was approved by the ethics committee of the coordinating centre and subsequently by the ethics committees of each participating centre.

Statistical analysis was performed using the SPSS software, version 25.0. Results from the descriptive analysis are shown as percentage (number of cases), mean (standard deviation [SD]), or median (range), according to the distribution of each variable. Continuous quantitative variables were compared using the *t* test and discrete quantitative variables with the Kruskal-Wallis test. The level of statistical significance was set at $< .05$.

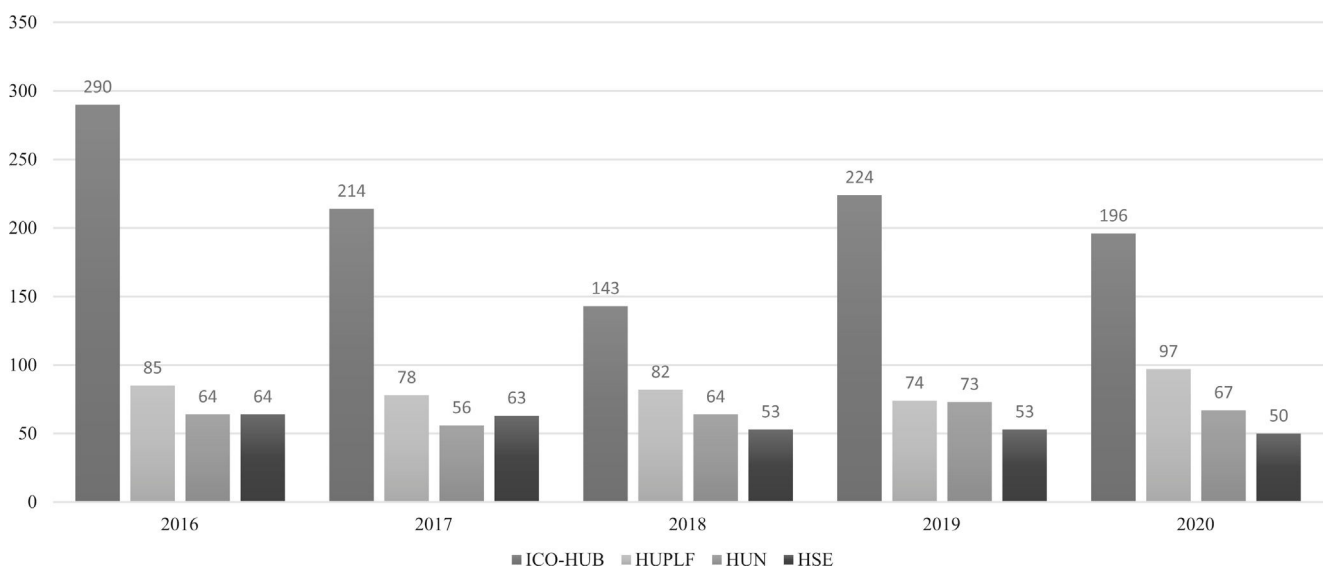


Figure 1 Distribution of in-hospital consultations by hospital and year. ICO-HUB: Instituto Catalán de Oncología l'Hospitalet–Hospital Universitario de Bellvitge; HSE: Hospital Universitari Son Espases; HUN: Hospital Universitario de Navarra; HUPLF: Hospital Universitario y Politécnico de La Fe.

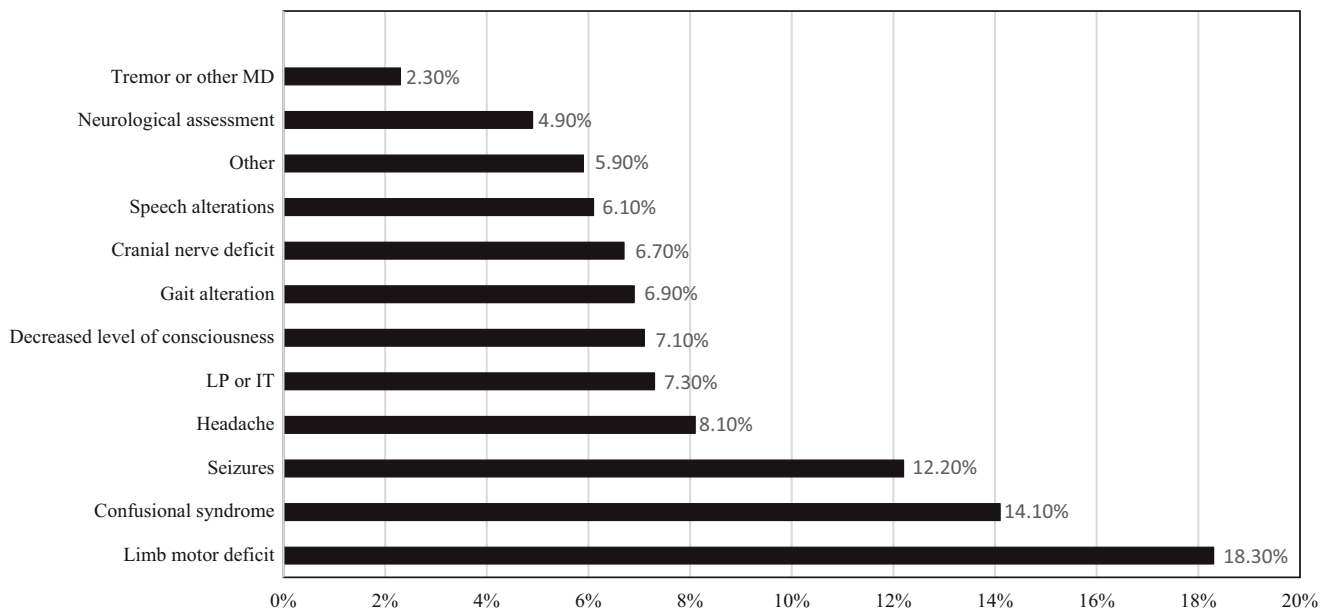


Figure 2 Reasons for consultation. IT: intrathecal therapy; LP: lumbar puncture; MD: movement disorder.

Results

We included a total of 2091 neuro-oncological ICs; the distribution between hospitals is shown in Fig. 1. More than half of ICs (51%; 1067/2091) were requested at ICO-HUB; 19.9% (417/2091) at HUPLF; 15.5% (324/2091) at HUN; and 13.5% (283/2091) at HSE. Regarding the total number of ICs with the neurology department at each centre during the 5-year study period, neuro-oncological ICs represented 37.4% (1067/2856) at ICO-HUB, 11.3% (417/-3698) at HUPLF, 11.1% (324/2913) at HUN, and 10.2% (283/2775) at HSE. The number of neuro-oncological ICs remained stable over the years, with a total number of 503 ICs received in 2016, 411 ICs in 2017, 342 ICs in 2018, 424 ICs in 2019, and 410 ICs in 2020 (Fig. 1).

In-hospital consultations with the neurology department were most frequently requested by the medical oncology department (43.2%; 904/2091), haematology department (42.2%; 882/2091), and emergency department (4.5%; 94), with the remaining 10% (211/2091) being requested by the neurosurgery, radiotherapeutic oncology, and palliative care departments, intensive care unit, and other services. A total of 1710 patients were the subject of the 2091 ICs; most were men (56.7%; 969/1710), and the median age was 60.5 years (range, 15–92).

The most frequent reasons for consultation were limb motor deficit (18.3%; 381/2077), confusional syndrome (14.1%; 292/2077), seizures (12.2%; 254/2077), headache (8.1%; 169/2077), lumbar puncture (LP) or intrathecal therapy (IT) (7.3%; 151/2077), decreased level of consciousness (7.1%; 148/2077), gait alterations (6.9%; 144/2077), cranial nerve deficit (6.7%; 139/2077), speech alterations (6.1%; 127/2077), and neurological assessment associated with CAR T-cell therapy (4.9%; 102/2077). Tremor and other movement disorders, as well as other less frequent reasons for consultation, are also summarised in Fig. 2.

The most frequent neoplasms were lung cancer (18.3%; 383/2089), leukaemia (19%; 396/2089), lymphoma (17.1%; 357/2089), primary brain tumour (12.1%; 353/2089), myeloma (6.2%; 129/2089), and breast cancer (5.8%; 121/2089). Other less frequent primary tumours are summarised in Fig. 3.

Most of the patients included (58.1%; 1213/2089) were under active oncological treatment at the time of the IC. A total of 11.8% (247/2089) had received treatment recently and 30.1% (629/2089) had received no previous treatment at the time of the IC. Of the patients with active or recent treatment, 61.6% (897/1455) had only received chemotherapy; 12.3% (179/1455) a combination of several treatments: immunotherapy in 11.1% (161/1455), HSCT in 6.6% (96/1455), radiotherapy in 5.6% (82/1455), and surgery in 2.7% (40/1455).

Several complementary examinations were requested in almost half of ICs (45.8%; 956/2087). Of these ICs, the highest percentage corresponds to patients attended due to cranial nerve deficit (61.2%; 85/937). Complementary examination was considered unnecessary in only 14.9% (311/2087) of ICs. The examinations requested mostly consisted of brain neuroimaging studies (23%; 480/2087), LP (8%; 168/2087), neurophysiological study (5.3%; 111/2087), spinal cord MRI (2.8%; 59/2087), and brain biopsy (0.1%; 2/2087). Among patients for whom a single examination was requested, the most frequent were brain MRI (12.9%; 270/2087) and head CT (10.1%; 210/2087).

The most frequent neurological diagnoses were metabolic encephalopathy (11.2%; 234/2091), tumour progression (11%; 231/2091), cerebrovascular complications (10.1%; 212/2091), metastasis (9.1%; 191/2091), and leptomeningeal dissemination (8.9%; 186/2091) (Fig. 4). Of the patients with metastasis, 8.4% (16/191) presented epidural metastasis, and the remaining patients (91.6%; 175/191) presented brain metastasis. The main reasons for consultation for patients with brain metastasis were

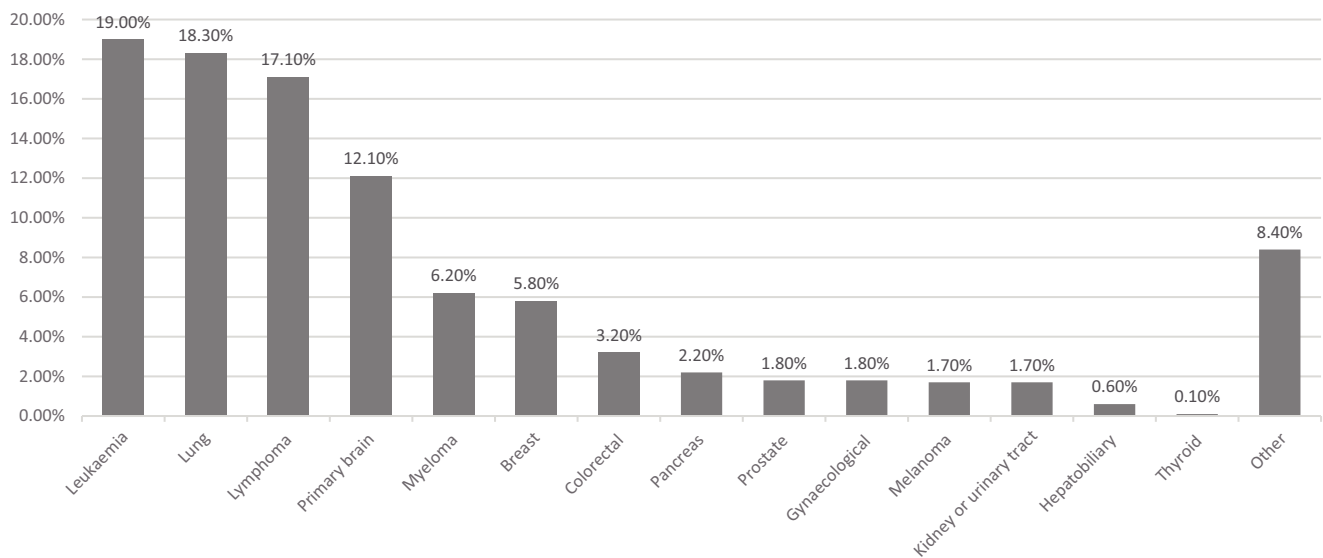


Figure 3 Types of primary cancer.

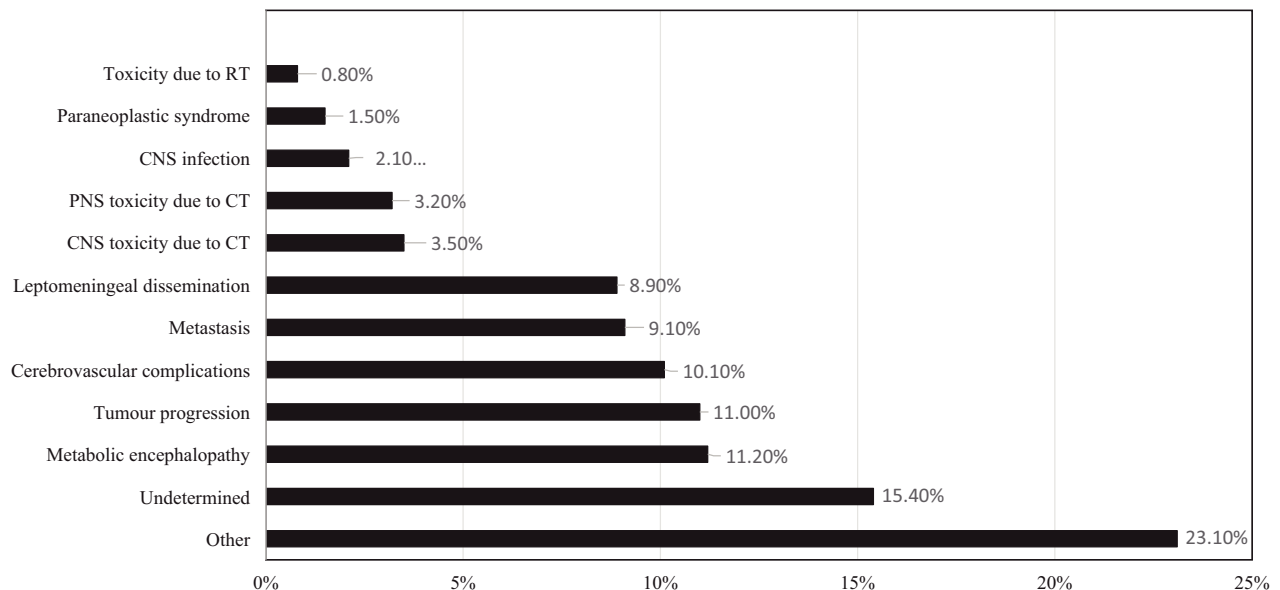


Figure 4 Neurological diagnoses. CNS: central nervous system; CT: chemotherapy; PNS: peripheral nervous system; RT: radiotherapy.

seizures (24.7%; 43/174), limb motor deficit (24%; 43/174), cranial nerve deficit (10.3%; 18/174), and headache (9.8%; 17/174). Among patients diagnosed with epidural metastasis, the reason for consultation was limb motor deficit in 75% (12/16) of cases and spinal pain (grouped under "other reasons") in the remaining 25% (4/16). Central or peripheral nervous system toxicity due to chemotherapy or radiotherapy, central nervous system infections, and paraneoplastic syndromes were less frequent. No determined diagnosis was reached in 15.4% (323/2091) of ICs. Other diagnoses were reached in 23.1% (484/2091) of patients, including ICs for assessment to start treatment or for assessment of patients with neurological disease who were unable to attend consultations because they were hospitalised, and other miscellaneous cases.

In patients with brain tumour (253/2089), the most frequent neurological diagnosis was tumour progression (37.9%; 96/253). In patients with lung cancer (383/2089), the most frequent diagnoses were metastasis (21.7%; 83/383), cerebrovascular complications (15.4%; 59/383), leptomeningeal dissemination (13.3%; 51/383), and tumour progression (11.2%; 43/383). In patients with leukaemia (396/2089), the most frequent neurological diagnoses were metabolic encephalopathy (12.4%; 49/396) and cerebrovascular complications (12.1%; 48/396); in patients with lymphoma (357/2089), leptomeningeal dissemination (10.9%; 39/357) and tumour progression (8.4%; 30/357) were the most frequent diagnoses.

Whereas 42% (875/2082) of ICs were resolved in one day, 58% (1207/2082) needed longer follow-up (median of 3 days;

range, 1–152). We observed statistically significant differences in follow-up time between departments requesting the IC, with longer times for the group of other departments (median of 5 days; range, 1–44), and shorter times for the emergency department (median of 1 day; range, 1–33) ($P < .001$). Follow-up time in the group of patients with cranial nerve deficit was significantly longer (median of 5 days; range, 1–118) than in those whose reason for consultation was assessment to start oncological treatment (median of 1 day; range, 1–110), in patients with tremor or other movement disorders (median of 1 day; range, 1–42), and those undergoing LP or IT (median of 1 day; range, 1–69) ($P < .001$). Regarding neurological diagnoses, follow-up time was longer in patients with paraneoplastic syndromes (median of 13 days; range, 1–64) than in the group of patients with other diagnoses (median of 1 day; range, 1–113) ($P < .001$). However, we observed no statistically significant association between follow-up time of the IC and age, sex, being under active treatment, or type of treatment.

The median time from tumour diagnosis to the date of the IC amounted to 9.2 months (range, 1–444.4). At the time of the study, 63% (1318/2091) of the patients were deceased. The median time from tumour diagnosis to death amounted to 14.8 months (range, 0–432.3). The median survival time after the IC was 1.9 months (range, 1–73.5).

Discussion

This study represents the first article specifically analysing ICs with the neurology department for onco-haematological patients in Spain. According to our findings, neuro-oncological ICs are a frequent source of consultation, representing almost 20% of the total ICs received by neurology departments, even reaching one-third of the total in centres including an exclusively oncological hospital, as is the case of ICO-HUB, with more than twice the number of ICs recorded at the remaining centres. Although the number of neuro-oncological ICs remained stable throughout the study period, we should bear in mind that the findings from year 2020 may have been underestimated due to the COVID-19 pandemic. It is likely that, in the coming years, we may observe an increase in this activity due to the new oncological treatments and the increased survival time of patients, which may also exacerbate their potential neurological complications in the short and in the long term.^{16–18} Such other advanced therapies as CAR T-cell therapy, whose implementation is becoming increasingly widespread in Spain, may cause neurological complications; patients receiving this treatment need neurological monitoring and follow-up before and during administration of the therapy, which may contribute to a greater number of ICs.^{19,20} In this regard, we should mention that the hospitals accredited for administration of CAR T-cell therapy (ICO-HUB and HUPLF) received a considerable number of ICs for this reason.

Among the scarce published studies on ICs with neurology departments over the past 20 years in Spain, ICs requested by oncology departments consistently represent below 10% of these consultations,^{21–24} or are not considered among the IC received,¹⁵ probably due to their minimal representation in the total volume. International studies do not make men-

tion of the origin of ICs from oncology departments, with the exception of a British study published in 1996,²⁵ which reports that these account for 8.7% of the total.

In our literature search, we only identified one study that analysed the characteristics of ICs with neurology departments for oncological patients: the study by Porta-Etessam and Dalmau,¹² published in 1999 and performed over a period of 3 months at the Memorial Sloan Kettering Cancer Center, an oncological hospital in New York. In this study, the most frequent reasons for consultation were pain, focal deficits, and altered level of consciousness. We included headache as reason for consultation, but we did not include other pain locations as a variable. In the study by Porta-Etessam and Dalmau,¹² the most frequent diagnoses were brain or epidural metastasis, toxic or metabolic encephalopathies, and cerebrovascular disease; this is consistent with the findings of our study. The most frequent types of neoplasms were lung cancer, haematological neoplasms, and brain tumours, in line with previous studies and with our findings.^{5,12}

The rate of paraneoplastic syndromes in our study amounted to 1.5%. We believe that this percentage is consistent with the incidence of paraneoplastic syndromes in recently published studies, which amounts to approximately 1 case in every 334 patients with cancer.²⁶ We should not forget that the ICs analysed are related to patients with an existing cancer diagnosis and that the majority of paraneoplastic syndromes precede the diagnosis of cancer.²⁷

Several complementary examinations were requested for the majority of patients; in more than half of cases, the IC could not be resolved within one day and required follow-up. We should underscore the fact that the follow-up times of ICs for patients diagnosed with paraneoplastic syndrome were significantly longer than in the remaining cases, which reflects the complexity of establishing this diagnosis. Patients whose reason for consultation was “cranial nerve deficit” required longer follow-up times, as they needed more complementary examinations. Furthermore, although an aetiological diagnosis was reached in the majority of ICs, diagnosis was undetermined in 15.4% of cases, probably due to incomplete studies in very severe patients or due to the copresence of several diagnoses; this reflects the complexity of neuro-oncological patients, which probably differentiates them from other types of IC. Finally, we observed a median survival time shorter than 2 months after reception of the IC, which may be attributed to the greater presence of neurological complications in patients with advanced cancer or, alternatively, poorer prognosis inherent to this type of complications.²⁸

The performance of LP, with or without IT, or the assessment of patients eligible for CAR T-cell therapy accounted for significant activity in our study (12.2%), which underscores the need for consideration of these procedures in healthcare planning in order to better organise neurology departments.

The main limitation of this study is its retrospective design. One of its advantages is its multicentre design, including 4 hospitals that are similar in terms of structure, complexity, and size (approximately 1000 beds), which enabled us to include a large number of cases. Although the inclusion of data from the year 2020, marked by the COVID-19 pandemic, may represent a limitation in our study, the

possibility of analysing a 5-year period for all centres enables us to establish the real situation of this type of healthcare activity in neurology departments. However, analysis of the trend over time is likely to require longer studies or the comparison of different time periods before and after the introduction of advanced oncological therapies and the neurotoxicity associated with these new treatments. In our opinion, studies like ours are needed to understand the characteristics of this type of care and in order to organise human resources. They also underscore the relevance of neurologists in multidisciplinary neuro-oncology teams. Several studies have reached the conclusion that neurologists involved in IC should be motivated and trained, and have shown that these professionals contribute to healthcare quality and efficiency, providing clear financial and healthcare benefits.²⁹ In this respect, it has recently been shown that the participation of neurologists with experience in immunotherapy-related complications in multidisciplinary teams specialised in the management of these patients is associated with better patient outcomes and lower healthcare costs.³⁰

In conclusion, neuro-oncological ICs represent an essential healthcare activity within neurology departments. Due to the volume of these consultations and the fact that some ICs could not be resolved in one day, requiring several complementary examinations and a follow-up period, the response to these ICs should be provided by physicians working in IC and familiarised with the complexity of neuro-oncological patients, with specialised experience and knowledge.

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Declaration of competing interest

The authors have no conflicts of interest to declare.

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