HISTIO UK

No-one should die of Histiocytosis

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Contents

LANGERHANS CELL HISTIOCYTOSIS

A 15-MONTH- OLD CHILD PRESENTING WITH HIGHLY AGGRESSIVE BRAF+ MULTISYSTEM LCH WITH CNS INVOLVEMENT: IMMUNE CELL AND CYTOKINE PROFILES

ZDENKA KRENOVA **PRESENTING**

A 1.5 yearold boy with Langerhans cell histiocytosis (LCH) with massive infiltration of the cerebellar middle fossa was given monthly pulses of low dose cytarabine plus BRAF inhibitor. Despite the premedication (indomethacin, corticosteroids) we had to terminate the cytarabine completely after 4th cycle (initially meant to last 12 months) due to cytokine storm accompanied with high CRP and very high presepsin. We analysed monocyte subsets and their maturation markers within peripheral blood mononuclear cells isolated from whole blood, as well as cytokines by multiplex cytokine array in plasma and liquor samples. We found a high degree of fluctuation in monocyte subset frequencies in peripheral blood across multiple timepoints in patient with severe LCH after initiation of treatment when compared to two patients in remission. We observed that innate immune parameters including monocytes maturation, phagocytic capacity increased by cytarabine treatment initiation, whilefrequency to phagocytes remained stable after 7 months post treatment initiation resemblingthe level of patients in remission. However, the amount of phagocyted material remained lower compared to patients in remission. Cytokine analysis revealed, that the treatment with BRAF/MEK inhibitors decreased the amount of many pro- and anti-inflammatory cytokines present in plasma. Results highlight the fluctuation of monocyte and cytokine production profiles during the therapy. Observed strong increase of presepsin (sCD14) levels after cytarabine administration will be further analysed in the context of changes in innate immune markers. The patient achieved complete resolution of LCH lesions at 4 months evaluation. Positivity of BRAF-V600E in the bone marrow is lasting.

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LANGERHANS CELL HISTIOCYTOSIS

INCIDENCE AND SURVIVAL OF LANGERHANS CELL HISTIOCYTOSIS: A NATIONAL REGISTRY STUDY IN ENGLAND, 2013-2018

HANHUA LIU **PRESENTING**

Introduction Langerhans cell histiocytosis (LCH) is a rare disorder characterised by accumulation of dendritic- or monocyte-derived cells in organs, ranging from self- healing lesions to life-threatening multi-system disease. A delay in the full recognition of LCH as a common malignant process is reflected in the paucity of population-based information on the incidence and outcome of LCH.

Aims This paper reports the first population-based study of incidence and survival forall ICD-O-3 coded LCH without age restriction, covering the whole of England.

Method The study population was identified in the National Cancer Registration Dataset using ICD-O-3 morphologies 9751-9754 for malignancies diagnosed in 2013- 2018 (inclusive). Crude and age-standardised incidence rate per million person years (ASR) were calculated. Overall survival estimates were calculated. For patients aged ≥15 years, relative survival and the proportional hazards of death were also estimated.

Results We identified 528 patients with LCH diagnosed in 2013 -2018, of whom 269 were children aged 0-14 years. The ASR of LCH in England was 1.50 (95%CI:1.37 -1.63)per million person years, with 1.80 (95%CI:1.57-2.04) in the most deprived areas, compared to 1.37 (95%CI:1.17-1.58) in the least deprived. Children had a 5-year survival of 99% (95%CI:96%-99%) versus 71% (63%-78%) in ≥15s, decreased with increasing age to 33% for ≥65s.

Conclusions This study confirms that incidence is increasing, and that younger age, male sex and deprivation are associated with LCH incidence. Survival is excellent in children, but it decreases markedly with increasing age and opportunities to improve outcome in older age groups need to be pursued.

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LANGERHANS CELL HISTIOCYTOSIS

GREEK PAEDIATRIC LCH NATIONAL REGISTRY RESULTS OVER THE LAST TWO DECADES

VASSILIOS PAPADAKIS PRESENTING

Introduction/Aims To describe characteristics, treatment and outcome of Greek paediatric LCH patients.

Methods Between 2000-2018, 169 patients(62.72% males) were retrospectively registered, with mean diagnosis age 5.59 years (range:0.01-20.51), 52<2years.

Results One-hundred-thirty-three(78.7%) patients had SS-disease, bones:110(82.71%), skin:11(8.27%), hypothalamus/pituitary:3(2.26%), other:3(2.26%). Forty-six(34.6%) patients had CNS-Risk+ lesions, 4 patients had diabetes insipidus (DI). Initially, 66(49,6%) were observed only, 5(7.5%) relapsed. All patients are alive in CR (OS:100%, EFS:92.5%, median-time of follow-up (MTFup) 4.2 years (range, 0.1-19.7). Systemic chemotherapy received 71(53.4%) SS-disease children, all Prednisolone/Vinblastine. Thirty (22.6%) patients had CNS-Risk+ lesions and 4 developed DI. Two patients died,OS:98.5%. Thirteen patients relapsed, EFS:85.7%, MTFup:6.51 years (range:0.3-19.7).

Thirty-six patients (21.3%) presented with MS-disease. Median-age 1.7 years (range:0.35-10.33/ 21<2 years, 58.3%), with 2-5 system involvement and hematopoietic/liver/spleen involvement in 6/9/6 patients, respectively. Twenty-seven patients had bone localization (CNS-Risk+21). Risk-Organ+ had 22 patients(59.5%). Ten patients (27.0%) developed DI. The majority received Prednisolon/Vinblastine, 3 Prednisolon/Vinblastine/Etoposide and 1 Prednisolone-only, for median treatment duration: 12 months (range:1-43). First relapse/resistant disease was observed in 9 patients (24.3%):EFS:75.0%, second/third relapse in 6/3 patients. One patient succumbed, OS:97.3%.

Overall, 27/51(52.94%) evaluated patients were BRAF-V600E+, 21/39 SS and 6/12 MS. Five SS BRAF-V600E+ patients relapsed, 6/6 MS BRAF-V600E- patients in CR1 and 3/6 BRAF-V600E+ have relapse/resistant disease.

Conclusions These retrospective results of Greek children with LCH are comparable with international and are the basis for our participation to LCH-IV Protocol, supported by Artemis Association.

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LANGERHANS CELL HISTIOCYTOSIS

PREVALENCE OF THE *BRAF*^{V600E} MUTATION IN GREEK ADULTS WITH LANGERHANS CELL HISTIOCYTOSIS

DIMITRA STATHI **PRESENTING**

Introduction Langerhans cell histiocytosis (LCH) is a rare inflammatory myeloid neoplasia with a broad spectrum of clinical manifestations. The activation of the MAP kinase pathway plays an integral role in the pathogenesis with genetic alterations found in the majority of cases, most frequently a somatic mutation that produces the oncogenic *BRAF*^{V600E} variant.

Aims In this study we investigated the prevalence of the *BRAF*^{V600E} mutation and its clinical relevance among patients of our LCH adult clinic.

Methods Real-time PCR was used to detect the *BRAF*^{V600E} mutation in paraffin- embedded tissue samples from 31 adults with LCH. Clinical data was retrieved from the clinic's database for retrospective analysis. The study was approved by the Medical Ethical Committee of 251 Hellenic Air Force & VA General Hospital.

Results The *BRAF*^{V600E} mutation was identified in 12 patients of our cohort (38.71%), while 13 patients (41.94%) did not carry the mutation. Six patients had inconclusive results (19.35%). The presence of the mutation did not correlate with age at diagnosis, organ involvement, disease extent, response to initial treatment, development of diabetes insipidus and relapse risk. A gender difference was observed as the mutation was more common in females.

Conclusions Our results support that an up to 50% prevalence of *BRAF*^{V600E} mutation could be expected among adults, which in our series is at the lower range of the relative percentage found in children. Further studies with a larger number of adults are needed to identify the exact prevalence of mutations in the RAS-RAF-MEK-ERK pathway and their role on clinical parameters and disease outcome.

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ROSAI-DORFMAN-DESTOMBES

A RELAPSING DISEASE DESCRIPTION

ROSAI-DORFMAN-DESTOMBES DISEASE (RDD) IS A RARE NON-LANGERHANS CELL HISTIOCYTIC DISORDER CHARACTERISED BY THE PROLIFERATION AND ACCUMULATION OF HISTIOCYTES; CLASSIFIED INTO CUTANEOUS, FAMILIAL OR SPORADIC. SPORADIC RDD IS THE MOST COMMON ENTITY AND ENCOMPASSES CLASSICAL, EXTRA-NODAL, MALIGNANCY-ASSOCIATED AND AUTOIMMUNE-ASSOCIATED FORMS.

SAMIR PATEL **PRESENTING**

CASE DESCRIPTION

A 55-year-old woman presented with a nasal nodular rash and lethargy. She was previously diagnosed with RDD on skin biopsy which showed an inflammatory infiltrate comprising of lymphocytes, numerous plasma cells and histiocytes (S100, CD68, CD163 positive) with occasional emperipolesis. She was previously treated with intralesional corticosteroids, laser, radiotherapy and resection. Blood tests were unremarkable (ESR 21mm/h, CRP <1mg/L) and excluded an autoimmune rheumatic disease. A PET-CT scan showed increased FDG uptake in the nostrils, right eyelid and bilateral cervical nodes. She was treated with a weaning course of oral prednisolone (20mg) and methotrexate (10mg weekly). Her symptoms resolved within 3 months and methotrexate was discontinued (nausea). She remained in remission whilst under surveillance.

DISCUSSION

EXTRA-NODAL DISEASE OCCURS IN ROUGHLY 43% OF PATIENTS, AFFECTING THE SKIN IN 10% AND NASAL CAVITY IN 11% OF PATIENTS. TREATMENT IS INDIVIDUALISED WITH NO EVIDENCE-BASED STRATEGIES DUE TO THE RARITY OF RDD. 20-50% OF CASES WITH NODAL AND CUTANEOUS DISEASE SPONTANEOUSLY RESOLVE. STUDIES HAVE SHOWN VARYING RESPONSES TO A RANGE OF AGENTS INCLUDING: CORTICOSTEROIDS, THALIDOMIDE, VINCRISTINE AND RITUXIMAB. OUR PATIENT HAD RECURRENT DISEASE CONFIRMED ON PET-CT DESPITE MEDICAL AND SURGICAL THERAPY WHICH RESPONDED WELL TO A 3-MONTH WEANING COURSE OF ORAL PREDNISOLONE AT A MODEST DOSE (~0.33MG/KG).

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