reached for the histopathological diagnosis of eosinophilic colitis. The most widely accepted definition is an eosinophil count exceeding 20–30 per high power field on biopsy [2]. Biopsies usually demonstrate eosinophilic infiltration of the colonic mucosa especially involving the lamina propria with occasional infiltration of the crypts. Patients usually present with persistent, diarrhea, nausea, vomiting and abdominal bloating. The most frequent secondary causes of eosinophilic colitis include food allergy, parasitic infection and drugs such as non-steroidal anti-inflammatory drugs, rifampicin and tacrolimus. Eosinophilic colitis has a bimodal age of distribution. It is frequently seen in infants and young children where milkprotein allergy and parasitic infections can predominate. In adult population, it usually presents in the late 30's-40's. Secondary causes of eosinophilia which can be seen in adult population include inflammatory bowel disease. There have been reports describing eosinophilic colitis which later progressed into ulcerative colitis after several months [3]. Other rare causes of eosinophilic colitis include leukemia, lymphoma, and vasculitis such as Churg Strauss syndrome and Polyaretritis Nodosa [3]. The association between lymphoid malignancy and eosinophilia has been recognized for more than 50 years [4]. Several secondary causes of eosinophilic colitis have been associated with lymphoid malignancies. The predominant interleukin that can cause the associated blood eosinophilia include Interleukin-5 secreted by T helper-2 cells. As was seen with our patient, the hypereosinophilia can be seen in a spectrum from myeloproliferative disorders including hypereosinophilic syndrome and eosinophilic leukemia to lymphocytic variant- hypereosinophilia. Multiple previous reports have been described where lymphocytic varianthypereosinophilia having progressed to T-cell lymphoma especially angioimmunoblastic T-cell lymphoma. An interesting finding for our patient was she was diagnosed with T-cell lymphoma from excisional lymph node biopsy and later developed blood eosinophilia likely secondary to cytokines from the lymphoma. Cases of eosinophilic colitis in association with T-cell lymphoma are extremely rare. A report by Wu et al. described a 56 year old male who presented with diarrhea and cervical lymphadenopathy [5]. Colonic biopsy demonstrated eosinophilia and later lymph node excisional biopsy showed T cell lymphoma. In our patient, the management of eosinophilic colitis was limited as during her hospital course, she developed malignant pleural effusion from her lymphoma and later decided to undergo palliative and hospice care. Given her recent immigration from Mexico, further workup for other parasitic causes of eosinophilia including pinworms and hookworms was limited as patient opted for palliative care.

Strongyloides infection has also been associated with eosinophilic colitis [6]. In most case of strongyloides infection, histologic evaluation reveals nematode larvae in the submucosa, along with eosinophils in the colon [7,8]. Although strongyloides anti-body was equivocal in our case, no nematodes, larvae or signs of strongyloides infection were seen on histological examination of colon biopsies, suggesting a primary eosinophilic colitis.

Treatment options for eosinophilic colitis are limited. Steroids appear to be the corner stone for treatment of primary eosinophilic colitis. It is essential to rule out infectious etiology prior to making a diagnosis of primary eosinophilic colitis, since subsequent steroid treatment could lead to disseminated infection. Systemic steroids as well as budesonide have been successfully used in some cases [9,10].

Our cases highlight the fact that eosinophilic colitis could be more common than we think. It is important for gastroenterologists to know about this rare entity and its associations with various systemic conditions, so early diagnosis can be made. This would avoid the cost of repetitive testing to establish the diagnosis, and prompt treatment can be initiated.

# **Conflict of interest**

None declared.

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Between reality and the guidelines: A survey on perception, diagnosis and management of hepatic encephalopathy in 201 Italian specialist centres



Dear Editor,

An evidence-based guideline for the diagnosis and management of hepatic encephalopathy (HE) was published jointly by the European and the American Association for the Study of Liver Diseases (EASL/AASLD) in 2014 [1]. The document is innovative in terms of: (i) disease definition and nomenclature, (ii) provision of strict criteria for diagnosis/differential diagnosis of overt HE, and (iii) provision of well-defined, stepwise treatment schemas [2]. The impact of guidelines on practice is acknowledged to be more modest than commonly perceived [3]. In addition, guidelines are the end-result of a consensus procedure, based on available and sometimes patchy

evidence, thus they are not necessarily user-friendly or easily applicable. The aim of this survey was to check access, perception and adherence to HE guidelines on a large, representative sample of physicians with a specialist interest in liver disease working in hospital or academic medical units within the Italian National Health System.

In the Spring of 2016, 295 Italian centres were identified as having a specialist interest in liver disease since they had been registered by AIFA (Agenzia Italiana del Farmaco) as providers of care for chronic viral hepatitis. Physicians responsible for each centre were contacted, and 201 (68.1%) agreed to participate in a telephone interview on HE, or to provide contact with a physician at the same centre for the interview. Seventy-two centres (36%) were located in the North, 48 (24%) in the Centre and 81 (40%) in the South of Italy. Amongst doctors interviewed, 108 (54%) were specialists in Internal Medicine, 62 (31%) in Gastroenterology/Hepatology, 24 (12%) in Infectious Diseases, 4 (2%) were surgeons, and one each (0.5%) were specialists in Nephrology, Geriatrics and Endocrinology. Each doctor was asked 21 questions, the first three of which required open answers and the remaining 18 required yes/no or multiple choice answers. Open questions were summarized by content analysis and closed questions by descriptive statistics.

Seventy percent of the doctors interview had not yet had an opportunity to read the EASL-AASLD joint guidelines on HE [1], some two years after publication. They estimated that 30% of patients with liver disease referring to their centres had cirrhosis, for a total of approximately 50,000 individuals. The aetiology of cirrhosis was reported to be most commonly HCV (66%), followed by alcohol (27%), autoimmune (3%), NASH (2%) and HBV/other (1% each). The doctors knew and/or estimated that 42% of their patients with cirrhosis had or had had some degree of HE in the course of their disease history. Thus, 96% felt HE were a relevant clinical issue and 94% stated they would be prepared to screen for minimal/covert HE should slim, user-friendly tools become available. When asked if they usually try to identify precipitants of an episode of overt HE, 99% confirmed they do. Precipitants were reported to be most commonly infection (30%), followed by dehydration (27%), constipation (20%), gastrointestinal bleeding (15%), electrolyte disorders (6%) and unidentified (2%). Considering that no distinction was made between episodic and recurrent HE, the distribution of precipitants is reasonably coherent with the available literature, only the unidentified precipitant episodes being significantly lower than expected [1,4]. Despite constipation being identified as a precipitant only in 20% of cases, 81% of doctors declared they prescribe an enema as a first step in case of overt HE. In our experience, this is indeed common practice and may contribute to temporary worsening of the condition, especially when the precipitant is dehydration. Of note, dehydration was reported to be a more common precipitant than constipation (27 vs. 21%) in the present series. Both the 2002 [5] and the 2014 [1] guidelines seem clear on how an identified precipitant should be managed but the advice has obviously not penetrated routine practice. Seventy-four percent of doctors reported using blood ammonia measurement for purposes of differential diagnosis, which is reassuringly in line with the 2014 guidelines [1]. In terms of treatment, 85% of doctors declared using non-absorbable disaccharides, 86% non-absorbable antibiotics (rifaximin in 80% of cases; 7 other compounds were listed, 3 of which are actually systemic antibiotics) and 80% reported using a combination of non-absorbable disaccharides and antibiotics; 75% reported using intravenous branched chain amino acids (BCAA) in case of overt HE. Intravenous BCAA are an Italian tradition that

still lacks strong evidence-based proof but is supported by both pathophysiological studies [6] and series of small trials [7]. Almost half of the doctors interviewed (44%) felt there is solid literature to support the replacement of animal with vegetable and dairy protein in patients with HE [8]. It is also our experience that dietary suggestions are provided freely, and not necessarily confined to very selected cases, as suggested by the ISHEN guidelines on nutrition in HE [9]. While no specific questions were asked on this, we are also under the impression that the role of malnutrition/sarcopenia as a risk factor for HE, and the negative impact of inappropriate, unsupervised dietary advice remain as inadequately perceived as they were in 1999 according to a UK-based survey [10]. Finally, 67% of doctors declared that they are often asked or they spontaneously provide advice on driving.

In conclusion, it would seem reasonable to enhance the circulation of the 2014 guidelines, at least in centres with an interest in the care of liver patients, and to highlight the guidelines position in relation to treatment of the precipitant of an episode of overt HE, and on the provision of dietary advice and advice on driving. While in recent years HE has received considerably more attention than it used to, unless the liver community perceives it as requiring strict diagnostic and management criteria, it probably will not make it from Cinderella to superstar.

## **Conflict of interest**

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