NYU Long Island School of Medicine

DEPARTMENT OF PATHOLOGY

Short Report in Pathology

Organ system: Stomach

Prepared by: Ning Li, MD, PhD, Jianhong Zhou, MD

Department of Pathology, NYU Long Island School of Medicine, Mineola, New York.

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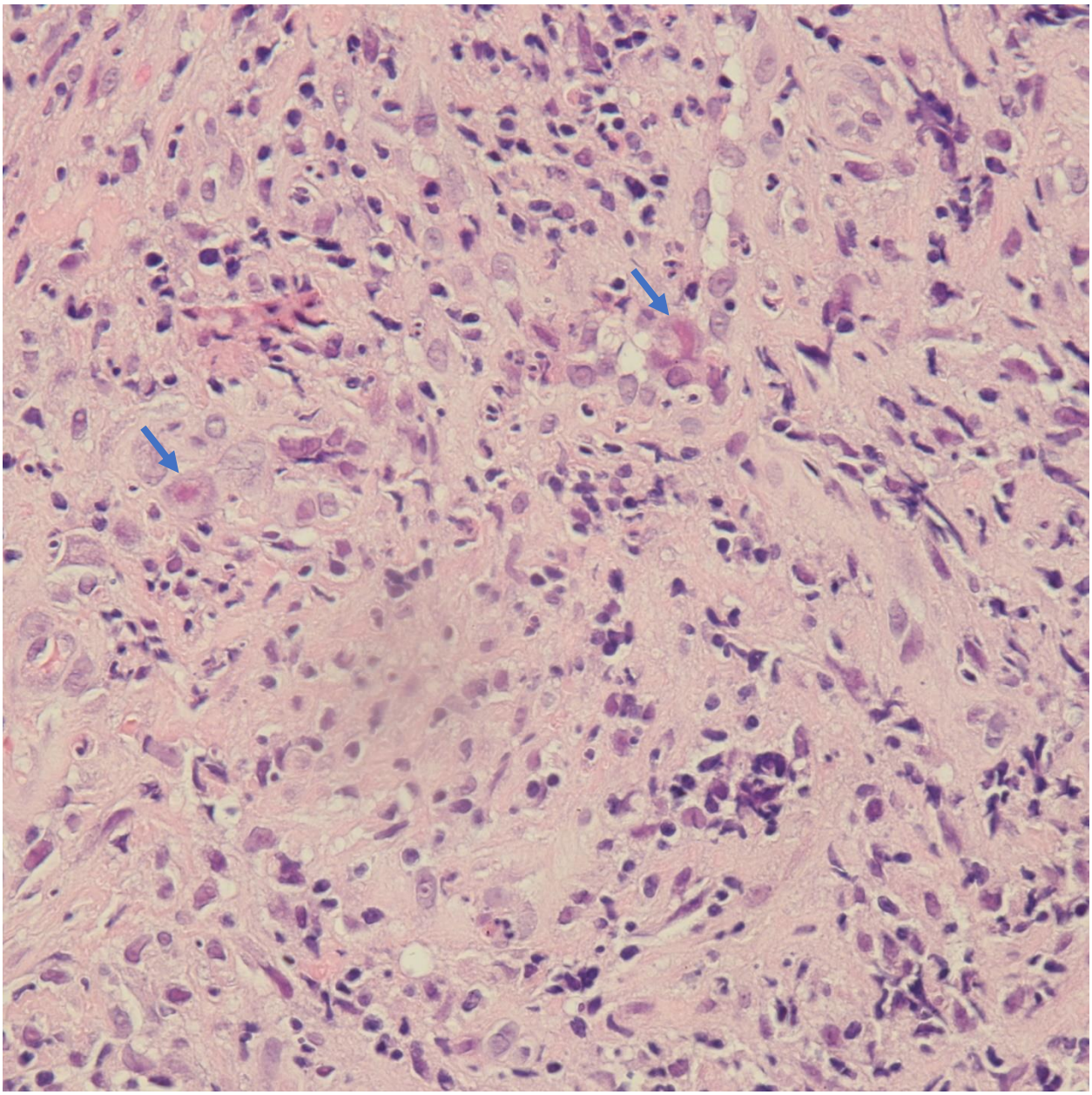
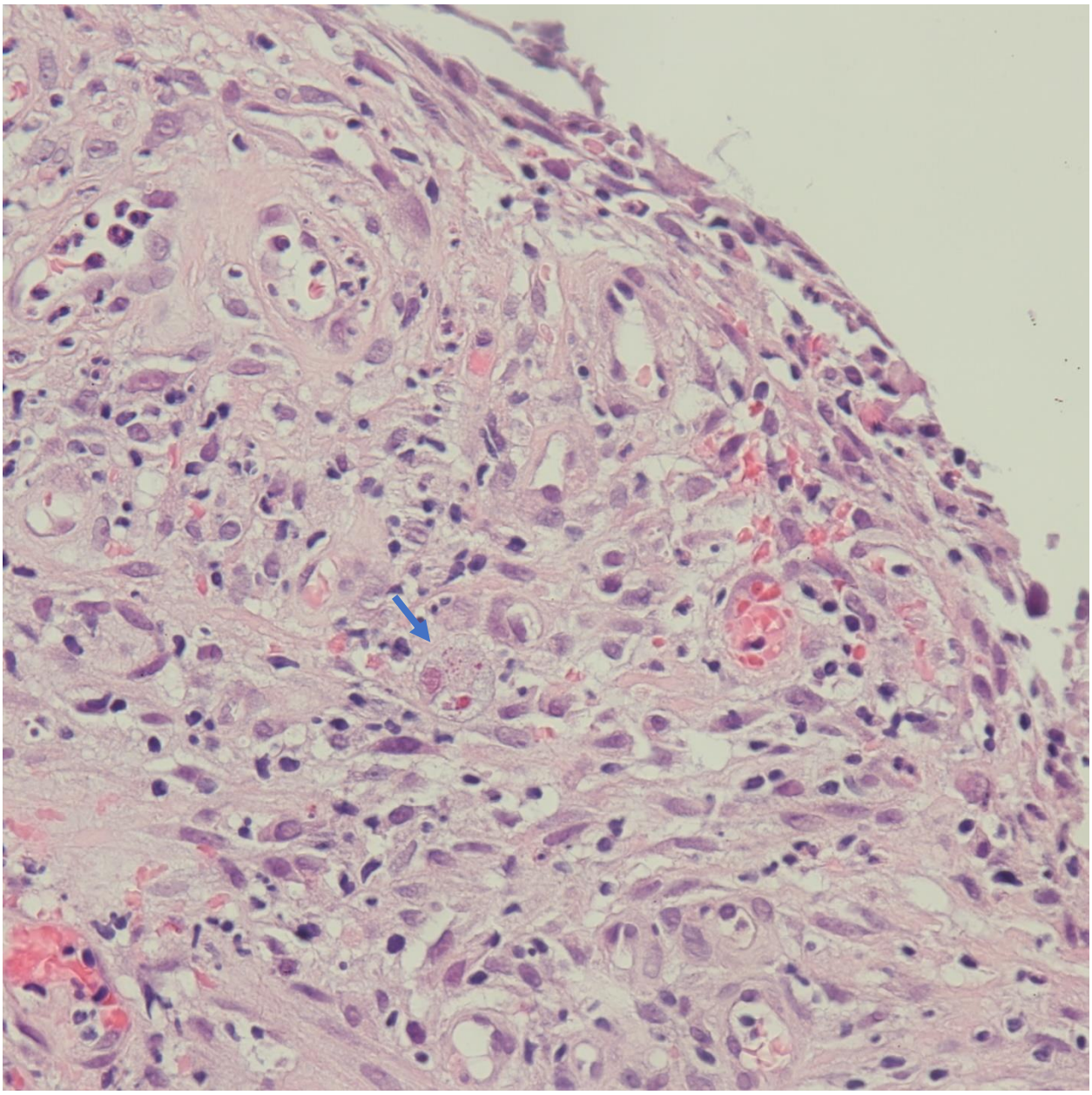
History:

A 78-year-old woman with a past medical history of follicular lymphoma presented with melena and hematemesis. Her Esophagogastroduodenoscopy (EGD) one month before was positive for malignant gastric ulcer suspicious for stage IV follicular lymphoma transformed Diffuse large B cell lymphoma (DLBCL), for which she received mini CHOP therapy. Additionally, radiation therapy was initiated. The patient underwent an EGD in the ICU due to active GI bleeding. Biopsies taken during EGD revealed Cytomegalovirus (CMV) gastritis, for which the patient was treated with valganciclovir.

Microscopic Images:

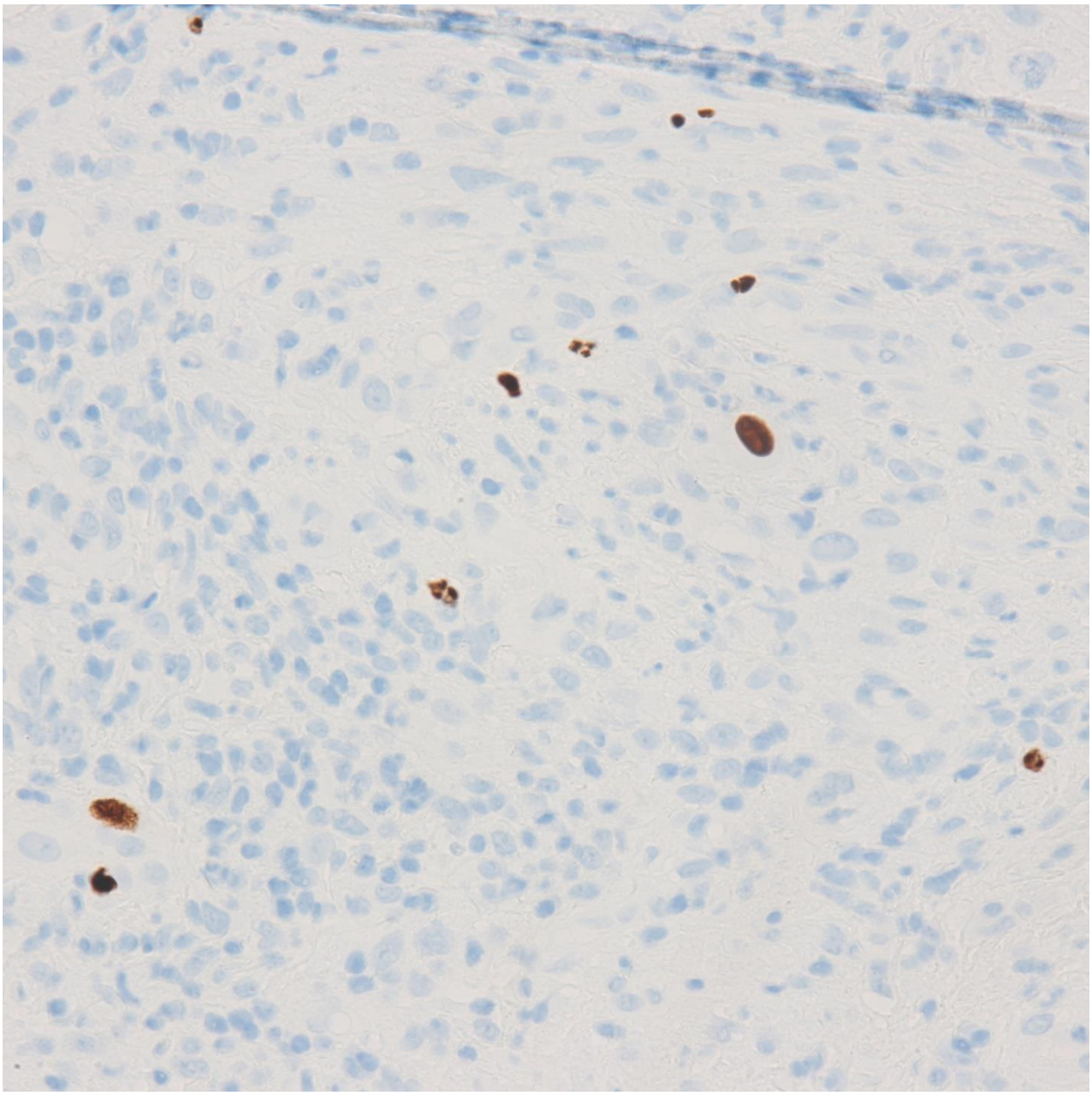


Histopathologic examination of ulcer base reveals granulation tissue with scattered enlarged stromal cells (arrows) with eosinophilic nuclear inclusion body surrounded by a clear halo (H&E, 400x).



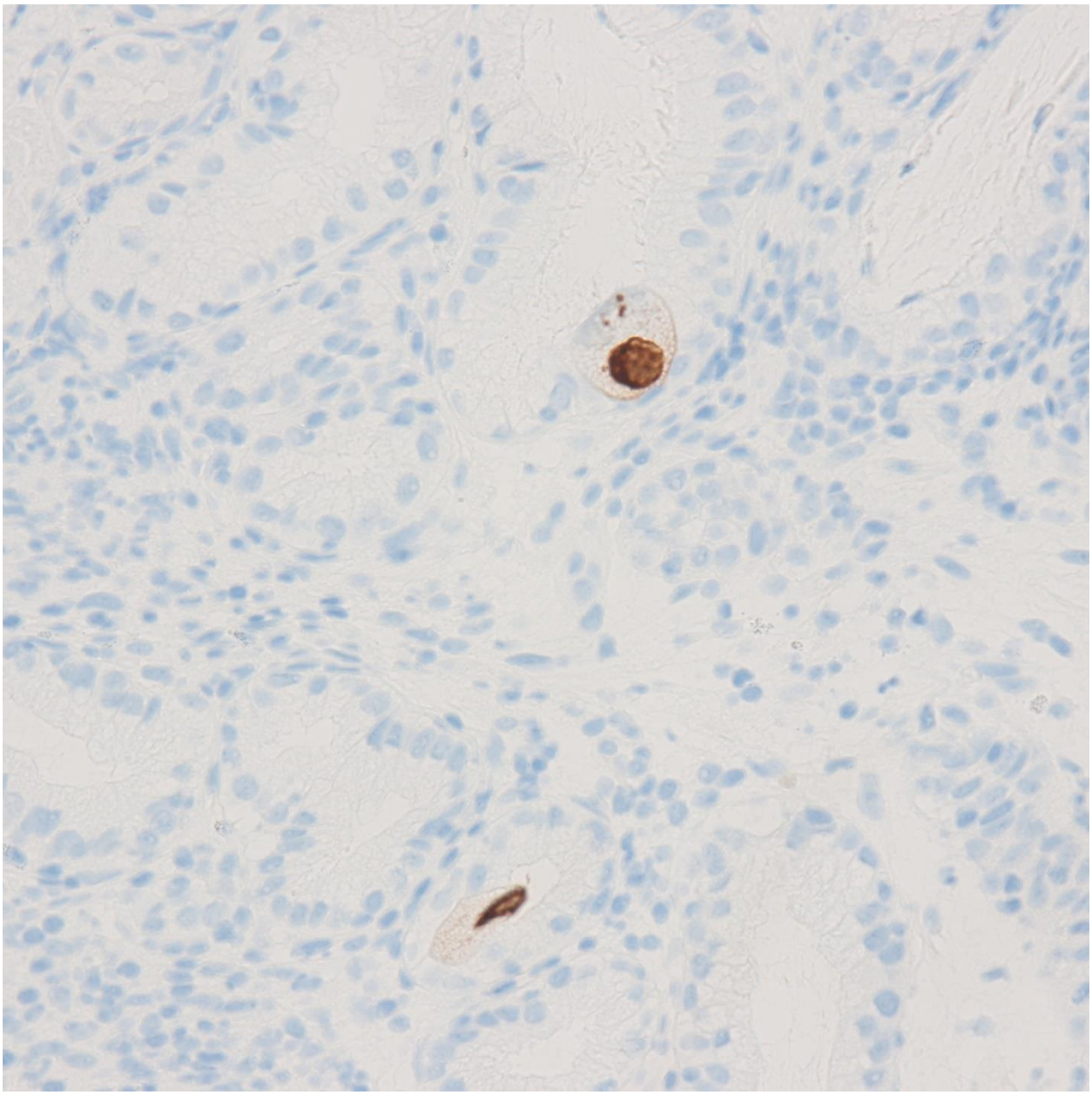
Histopathologic examination of ulcer base granulation tissue showing (arrow) eosinophilic nuclear and cytoplasmic inclusion bodies in a cytomegalic endothelial cell (H&E, 400x).

Immunohistochemistry:



Immunostaining of cytomegalovirus (CMV) antigens indicating scattered CMV positive cells (endothelial or stromal cells) in granulation tissue (CMV, 400x).

Cytokeratin CK7 and AE1/AE3 negative in ulcer base granulation tissue to rule out infiltrative malignant cells



Immunostaining of cytomegalovirus (CMV) antigens, of note, both nuclear and cytoplasmic CMV inclusions in cytomegalic cells possible epithelial (CMV, 400x).

Diagnosis:

Cytomegalovirus (CMV) gastritis

Differential diagnoses:

1. Chemotherapy effect

2. Gastric dysplasia or adenocarcinoma

3. Herpes simplex virus gastritis

Discussion:

Cytomegalovirus (CMV) gastritis is a rare and under-diagnosed disease generally seen in patients with acquired immunodeficiency syndrome, malignant lymphoma, organ and bone marrow transplantation, or other immunocompromised states (1, 2, 3). It may manifest as a standalone condition or be part of a more widespread disseminated CMV infection. It is worth noting that CMV infection has been linked to Menetrier's disease in the pediatric population (4). Clinical symptoms are nonspecific, encompassing epigastric pain, fever, nausea, and bleeding. Endoscopically, ulceration appears to be the most common manifestation, displaying variations in number, depth, and morphology, ranging from single or multiple, superficial to deep. Other observed endoscopic features encompass normal mucosa, diffuse erythema, nodules, pseudotumor, and erosions (1, 2, 3). CMV inclusions are commonly located at the bases of ulcers rather than at the edges or superficial mucosa, underscoring the significance of considering the depth of endoscopic biopsy. Most CMV gastritis responds well to ganciclovir.

The hallmark of CMV infection is the characteristic "owl's eye" amphophilic intranuclear inclusion body surrounded by a clear halo. Variable eosinophilic granular cytoplasmic inclusions may also be present, found in vascular endothelial cells, connective tissue stromal cells, and less frequently in mucosal epithelial cells. It is imperative to differentiate CMV gastritis from chemotherapy effects, where hyperchromatic nuclei resembling viral inclusions are present, but the classic CMV inclusions are absent. Attenuated dilated crypts and apoptotic debris are typically observed in chemotherapy effects. Immunohistochemical staining of CMV antigens is essential for confirming the diagnosis. CMV-positive "cytomegalic" cells with nucleomegaly may mimic infiltrative malignant epithelial cells, requiring exclusion through immunohistochemical staining with epithelial cell markers like AE1/AE3. Herpes simplex virus (HSV) infection is another opportunistic disease in immunocompromised patients, presenting with multiple small shallow punch-out ulcers or confluent map-like lesions. In contrast to CMV, which predominantly infects endothelial cells and mesenchymal/stromal cells over epithelial cells, HSV primarily targets epithelial cells and the HSV acidophilic inclusions (with surrounding halo) are exclusively nuclear (Cowdry type A inclusions). Additional distinctive features of HSV infection include multinucleation, nuclear molding, and periphery margination of chromatin (ground-glass Cowdry type B inclusions). HSV infection is typically observed at the edges of ulcers, unlike CMV, which is more likely to be found at the ulcer bases. In cases where histopathologic and immunohistochemical analyses are inconclusive, molecular biology analysis, polymerase chain reaction (PCR), serves as an additional diagnostic method for both CMV and HSV infections.

References:

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2. Cytomegalovirus infection in the gastrointestinal tract. Chetty R, Roskell DE. J Clin Pathol. 1994 Nov;47(11):968-72. doi: 10.1136/jcp.47.11.968.
3. The differential diagnosis of Helicobacter pylori negative gastritis. El-Zimaity H, Choi WT, Lauwers GY, Riddell R. Virchows Arch. 2018 Nov;473(5):533-550. doi: 10.1007/s00428-018-2454-6.
4. Menetrier disease and Cytomegalovirus infection in paediatric age: report of three cases and a review of the literature. Barbati F, Marrani E, Indolfi G, Lionetti P, Trapani S. Eur J Pediatr. 2021 Mar;180(3):679-688. doi: 10.1007/s00431-020-03782-6.