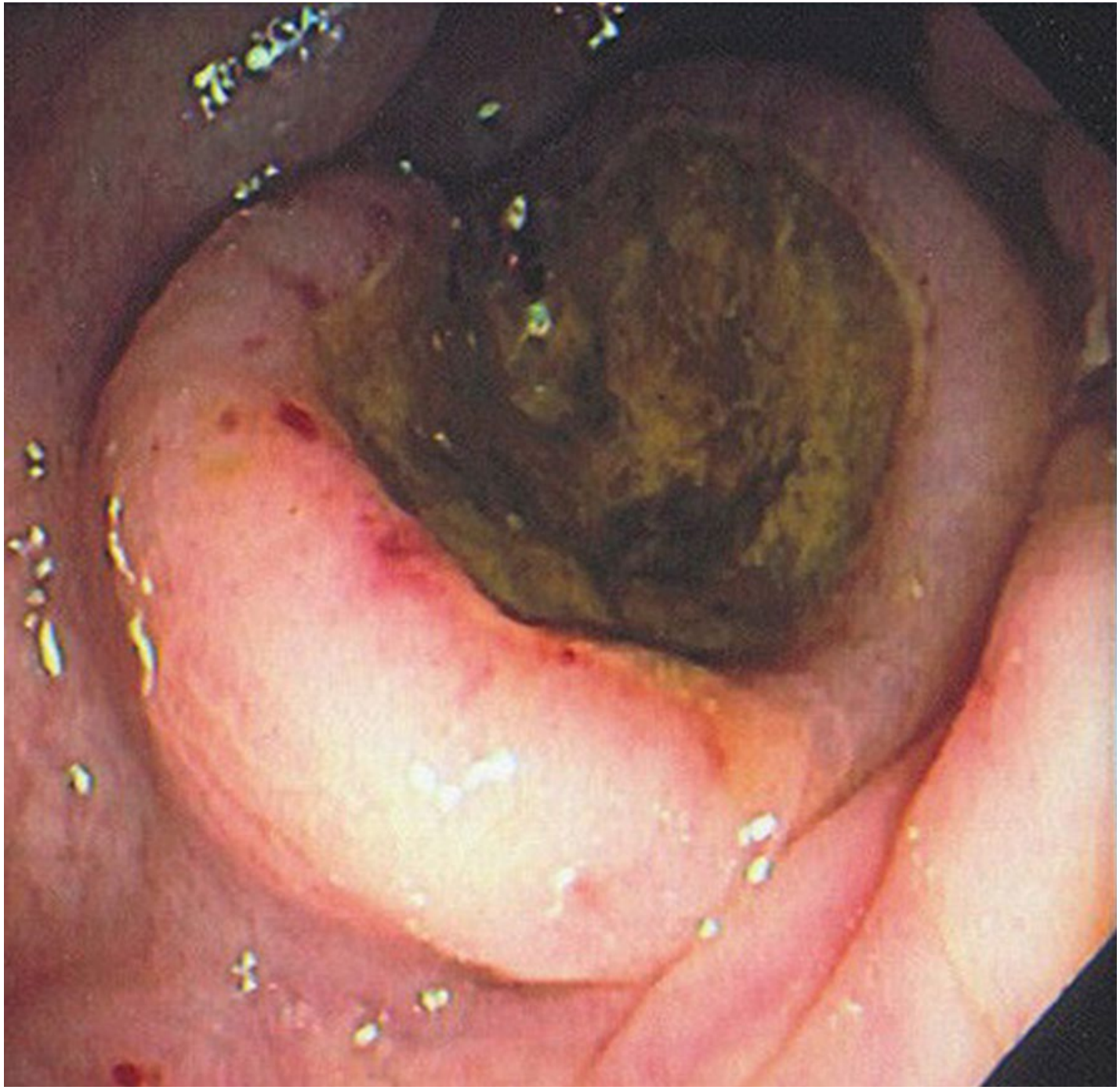
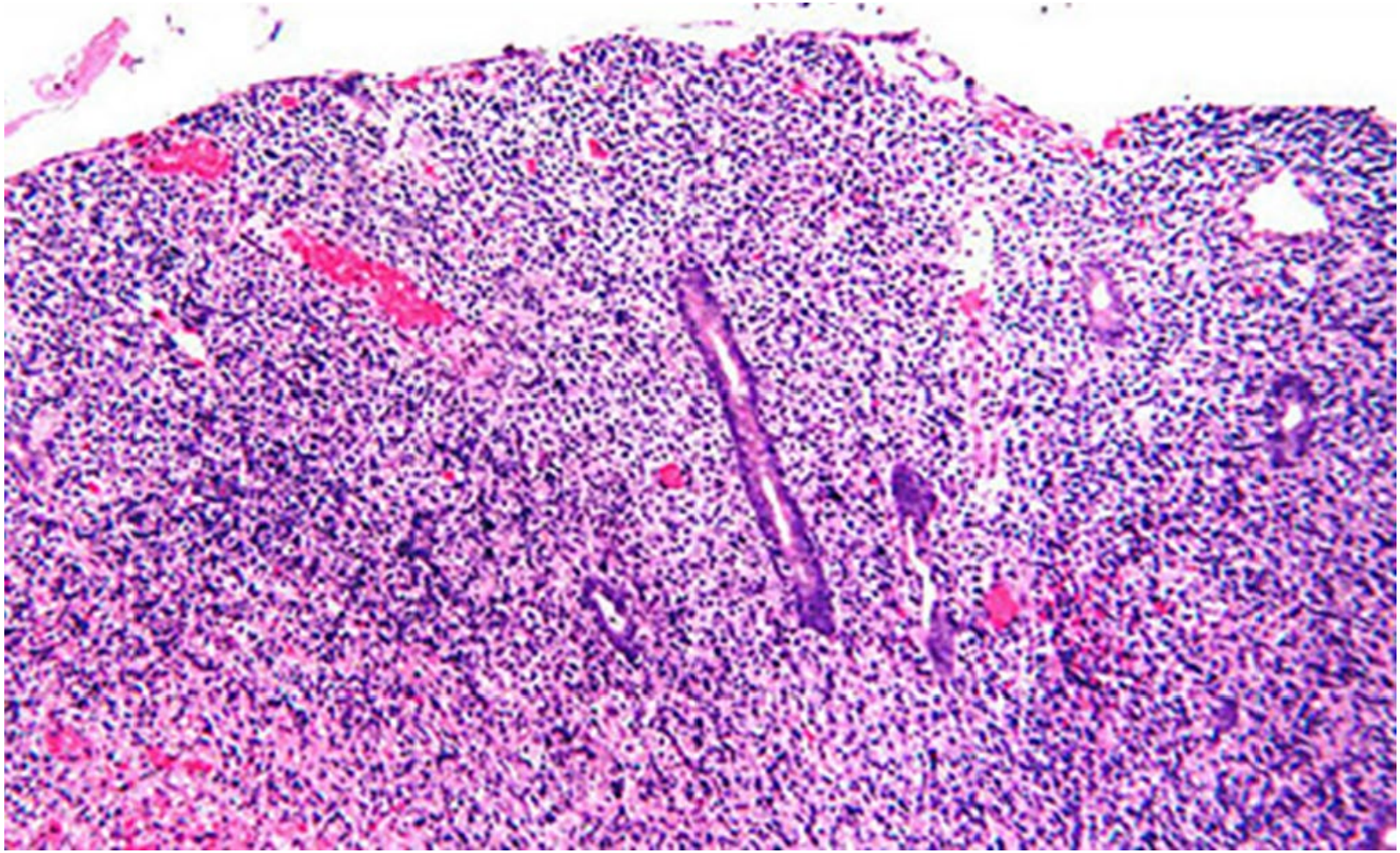
- A 53-year-old woman who had undergone a liver transplant 1 year ago was admitted with fatigue, dyspnea on exertion, and watery diarrhea.
- Prior to transplantation she was cytomegalovirus (CMV)-negative and Epstein-Barr virus (EBV)-positive, whereas the donor was CMV-positive.

- CT scan performed at 1 year was done because of SOB revealed multiple new right lung nodules.
- Fine-needle aspiration was negative for tumor or infection.
- Her immunosuppressive regimen included prednisone 15 mg per day, mycophenolate mofetil 1000 mg twice daily, and tacrolimus 5 mg twice daily.

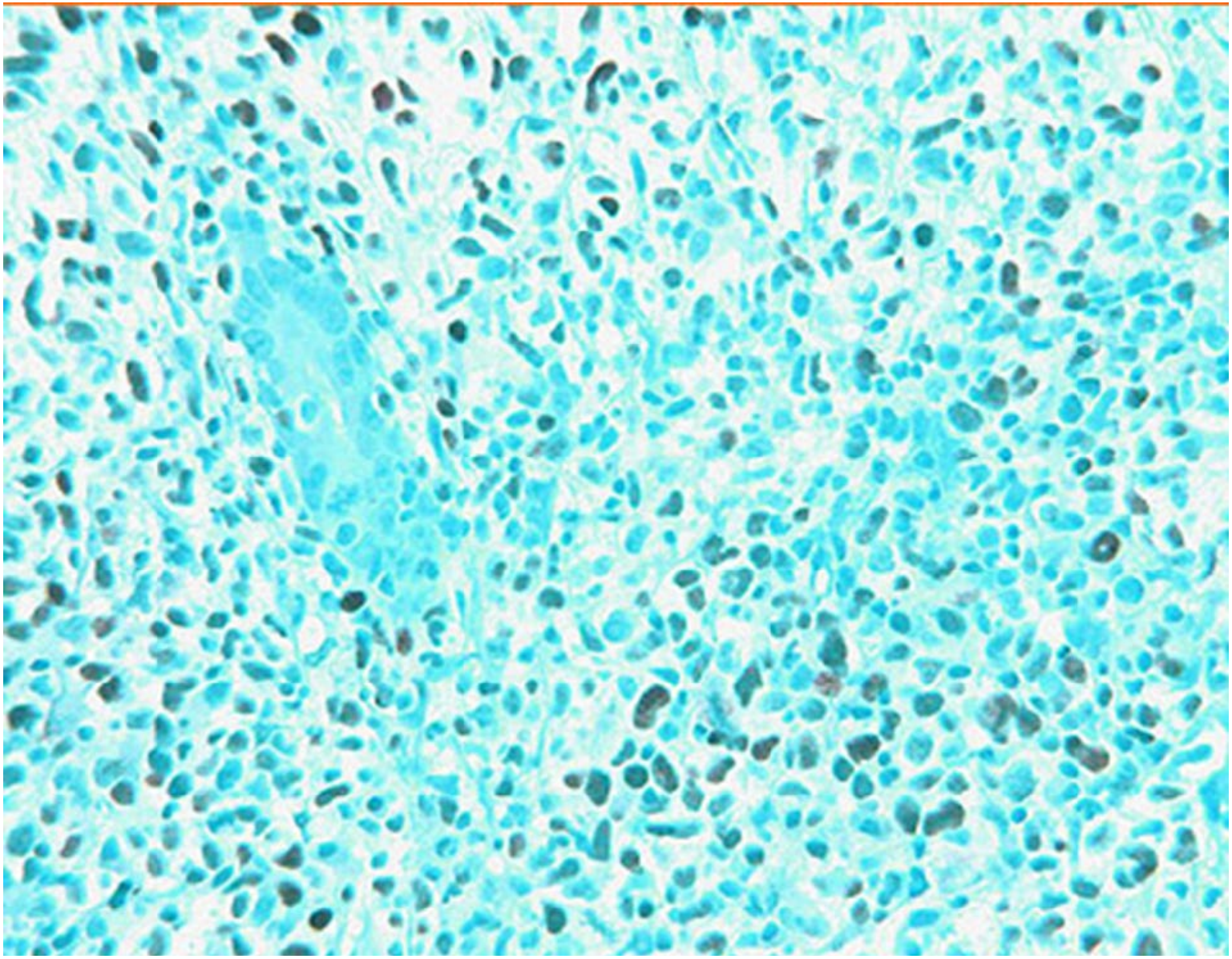
- Bronchoalveolar lavage on admission revealed CMV for which the patient was started on valganciclovir.
- Abdominal CT scan showed thickened cecum with regional lymphadenopathy, a 2-cm left para-aortic lymph node, and 3 masses in the right lobe of the liver, the largest of which was 1.8 cm.
- Colonoscopy : multiple ulcers with regular borders and heaped-up edges with variable size throughout the entire colon, more in the proximal colon







Diffusely positive CD20 (B-cell marker) immunostain.



- Biopsies were consistent with a large, B-cell-type non-Hodgkin's lymphoma that was EBV-positive by in situ hybridization.

PTLD

- Overall incidence of PTLD after solid organ transplantation : 5%
- The highest incidence in pretransplant EBV-seronegative patients and in the more severely immunosuppressed patients, with rates as high as 30% to 50%.
- PTLD is associated with a high mortality rate during the first year after diagnosis.

Other risk factors for PTLD:

- Primary EBV infection post- transplant
- CMV mismatch between donor and recipient
- CMV disease
- Use of OKT3 (anti-CD3 monoclonal antibody)
- Type of transplanted allograft

Renal transplants have the lowest risk of developing PTLD (1%), whereas the risk from lung transplants is highest (1.8% to 10%)

PTLD , types

- **Predominantly of B-cell origin** (T-cell lymphomas occur rarely)
- **Almost universally associated with EBV** (but EBV-negative PTLD occur)
- **Heterogeneous group of disorders**
  - **b**enign polyclonal hyperplasia
  - Polyclonal B-cell proliferation with evidence of early malignant transformation
  - Monoclonal malignant lymphoma

Clinical presentation

- Ranges from a fulminant course with widespread, multiorgan disease early after transplant, to an infectious mononucleosis-type presentation typically associated with benign polyclonal hyperplasia
- PTLD that presents > 1 year after transplantation tends to have a *more indolent* course with *fewer systemic symptoms* and more *extranodal or visceral disease*

Most common sites of involvement include:

- Extranodal (83%)
- Gastrointestinal (32%)
- Liver (32%)
- Bone marrow (25%)

Graft involvement

- Late-onset PTLD : 15%
- Early-onset PTLD : 57%

- EBV-negative patients usually present later, with malignant lymphomas with more limited disease.

Endoscopy

- Characteristic lesion : raised, rubbery, and erythematous, with central ulceration ranging in size from 5-15 mm in diameter.
- Typically in the stomach or colon

Treatment

- Reduction of immunosuppression : remission in 0% to 25% of cases (usually with polyclonal B-cell populations)
- Surgical resection or radiation (In anatomically limited cases).
- Anti-B-cell antibodies, specifically anti-human CD20 antibody (rituximab): 65% response rates in solid organ transplants.
- Chemotherapy : the last resort in management, high mortality rate(70%) due to complications of therapy.