CASE REPORT

Histopathological features of an incidental case of cytomegalovirus salpingitis in a patient with inflammatory bowel disease

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Abstract

Ovarian and fallopian tube cytomegalovirus (CMV) infection is a rare finding, reported mostly in autopsy studies of immunocompromised patients. We report here a case of CMV salpingitis in a 22-year-old female, with Crohn's disease and on immunosuppressive drugs. The fallopian tube involvement by CMV infection was an incidental finding during resection of a large, matted mass involving the appendix, right ovary and right fallopian tube with bowel perforation and abscess formation. Review of literature revealed that most cases of CMV involving the fallopian tube have concurrent CMV oophoritis in pre- and post-menopausal women having pelvic inflammatory disease (PID). We concluded that fallopian tube can be involved by CMV infection in an immunocompromised patient.

Keywords: Cytomegalovirus, Salpingitis, Inflammatory bowel disease.

Introduction

Cytomegalovirus (CMV) infection has been described in female genital tract in a few case reports. Friedmann et al[1] have described disseminated CMV infection of female genital tract involving the vulva, vagina and cervix in immunocompromised patients. CMV inclusion bodies have been described in recurrent ulcerative vaginal lesions. Cases of CMV endometritis and cervicitis have also been reported.[1-4] Involvement of ovaries has also been reported by several authors.[5-7] To date, more than 10 cases of CMV oophoritis have been reported in the literature. Review of literature revealed that most CMV salpingitis cases have concurrent CMV oophoritis in pre- and post-menopausal women having pelvic inflammatory disease (PID). While age-related vasculopathy was thought to be a causative mechanism for CMV oophoritis, observation of inflammation mediated microthrombosis provides an evidence of age-independent mechanism, suggesting that restrictive and obstructive vascular changes can be involved in the pathogenesis of CMV infection.

Myerson et al[8] studied widespread presence of histologically occult CMV in situ hybridization (ISH) in formalin-fixed paraffin-embedded tissue sections and detected occult infection in normal appearing cells like cardiac myocytes, hepatocytes, spleen, lymph node reticular cells, endometrial stromal, glandular cells, breast stromal cells, cells of renal glomerulus, tubule and interstitium, adrenal cortex and medulla, fallopian tube submucosa, myometrium and anterior pituitary.

There have been increasing number of case reports on inflammatory bowel disease (IBD) complicated by CMV. The role of CMV in the pathogenesis of IBD is debatable. Most studies suggest a role for a latent or active CMV infection in causing exacerbations of IBD, particularly in association with severe or refractory cases under corticosteroid and/ or immunosuppressive therapy. CMV can be found in both blood and intestines of patients with IBD. The role of CMV in steroid refractoriness remains unknown. Studies also suggest that CMV infection exacerbates IBD refractory to immunosuppressive therapies. It is imperative that concurrent CMV infection be considered in IBD patients with active colitis, especially in an immunosuppressed host.

Case Presentation

A 22-year-old Saudi female presented with right abdominal pain for the last two months, with history of anorexia and weight loss. The patient was a known case of Crohn's disease for two years, treated with steroids and eight cycles of infliximab. Clinical examination showed that the right flank mass was suspected to be malignant. Computerized tomography was done which showed a right adnexal mass. The patient underwent right salpingo-oophorectomy and an appendectomy. On gross examination, the specimen consisted of an irregular, tan coloured, matted mass measuring 11.0 x 6.0 x 3.0 cm. Outer surface showed congestion and marked adhesions. On sectioning, it was solid and cystic

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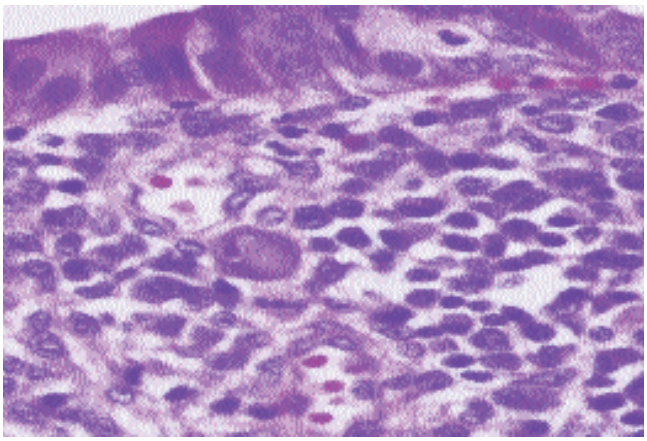

Figure-1: Fallopian tube connective tissue having blood vessels containing CMV-infected endothelial cells. (Original magnification, haematoxylin & eosin, 200 x).

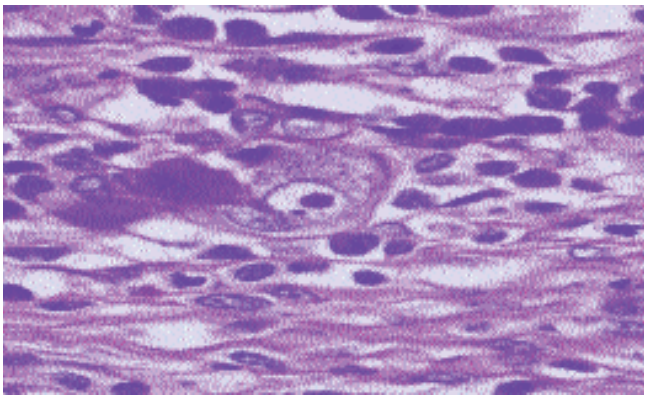

Figure-2: High power magnification of cytoplasmic and nuclear inclusions. (Original magnification, haematoxylin & eosin, 200 x).

with extensive areas of haemorrhage and necrosis. The adherent fallopian tube was markedly oedematous and thickened. Microscopic examination revealed ovarian parenchyma with extensive oedema, and prominent cortical necrosis, haemorrhage and foreign body giant cell reaction to faecal/vegetable material indicating bowel perforation or leakage with mixed inflammatory cell infiltration. The fallopian tube showed marked oedema, muscular hypertrophy, and dense acute and chronic inflammatory cell infiltration. Vasculitis and fibrin microthrombi were noted. Numerous blood vessels were seen with CMV infected endothelial cells (Figures-1). Both intranuclear and intracytoplasmic inclusions were present (Figures-2). Inclusions showed immunohistochemical positivity for anti-CMV protein (Dako anti-CMV primary antibody #M854) (Figure-3).[9] Sections showed colonic mucosa with evidence of active colitis. Appendix showed similar changes. No

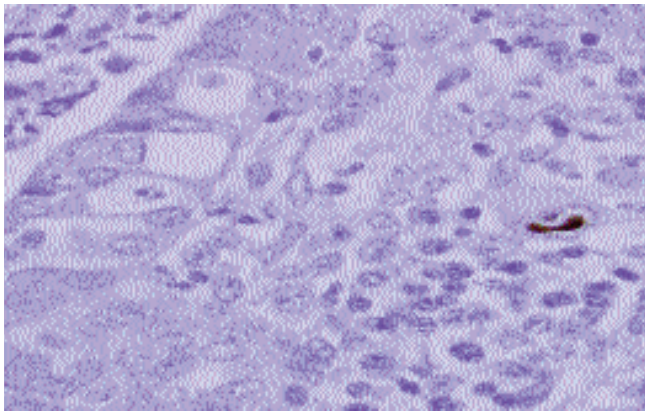

Figure-3: Immunohistochemical stain for anti-CMV protein (400 x).

CMV inclusions were identified in appendix and colon despite extensive sampling. Upon discovery of CMV inclusions in tissue sections, blood CMV, PCR and CMV Ig M and Ig G antibodies were requested. The result was 518 copies/ml (analytical measurement range 10-10,000 copies/ml).

Serologic investigations were requested which showed:

CMV, Ig M was in the interval range; CMV, Ig A 20.2 U (0-34.9); and CMV, Ig G 93.1 U (0-34.9).

The CMV nucleic acid quantification and detection by Polymerase chain reaction (PCR) was done using an automated extraction system (BioRobotEZ1: virus kit, virus card, QIAGEN).[10] The CMV DNA detection and quantification was performed using Artus® CMV TM PCR kit which is based on amplification of a 105 bp region of CMV genome by RT-PCR technology in the ABI PRISM 7000 instrument. An internal control was included in the assay to monitor any possible amplification inhibitors.

Acyclovir was started with reduction of immunosuppressive therapy. The patient had an uneventful post-operative recovery. Her appetite and weight improved after treatment. Previous histopathology reports and slides of colonic biopsies were reviewed and diagnosis of Crohn's disease (CD) was concurred. The patient was asymptomatic for CD at this time. Raised serum levels of Ig G anti-Saccharomyces cerevisiae antibodies (ASCA) were identified by ELISA (IMMCO Diagnostics, Inc. USA/Canada). The patient was discharged and remained symptom-free during the 4 month followup period.

Discussion

CMV infection involving the female genital tract is a

rare condition. It is usually reported as an incidental finding or in immunocompromised patients either as part of disseminated infection or as an isolated infection.

Bilateral CMV oophoritis is a rare pathological finding associated with a systemic infection.[7] An underlying malignancy or immunosuppression status is present and steroid therapy has been shown to be a strong risk factor for CMV reactivation in both groups. Sharma et al[6] reported a case of 50-year-old woman with metastatic breast carcinoma refractory to chemotherapy who died of candidal septicaemia after an autologous bone marrow transplantation. Histological evidence of CMV oophoritis was found on autopsy. The DNA in situ hybridization (ISH) revealed CMV infection in one fallopian tube and in adrenal glands.

The age distribution has some implications with regards to pathogenesis. The predilection of CMV for endothelial cells is thought to be important in its pathogenesis. Initially, an explanation of the predilection of CMV oophoritis towards the postmenopausal age was that the obstruction of blood flow secondary to age-related restrictive vascular changes were seen in postmenopausal women and was a critical factor for localising the infection to ovary, thus allowing progression of the disease. Histopathological findings described by Jing Yu et al[5] in a case of bilateral CMV oophoritis were extensive coagulative necrosis with vasculitis, microthrombosis along with numerous intranuclear and variable intracytoplasmic CMV inclusions in endothelial cells. Prominent postmenopausal restrictive vascular changes were also seen in surrounding ovarian parenchyma. Colonic mucosa also showed CMV inclusions. They suggested that the inflammatory response and secondary vasculitis also perpetuates the vascular restriction, and fibrin microthrombosis may have been a contributing factor in CMV oophoritis in pre- and postmenopausal women. Vascular changes, both native (restrictive) and virally-induced (obstructive), represent viable pathogenetic mechanisms.

McGalie et al[4] described the morphological features in five biopsies from four immunocompetent patients with CMV infection of the female genital tract. The CMV inclusions were occasional to abundant, intracytoplasmic and eosinophilic, mainly located in endocervical glandular epithelial cells and in endothelial and mesenchymal cells. Associated histopathological findings were fibrin thrombi, dense active inflammatory infiltrates largely composed of neutrophils, lymphoid follicles, vacuolation of glandular epithelial cells and reactive changes in glandular epithelial cells. The inclusions stained positive with anti-CMV antibody. The CMV endometritis reported by Wenckebach et al[2] was associated with lymphoplasmacytic infiltrate with germinal centre formation within the endometrium. Granulomatous inflammation is also described in histologically occult CMV in a healthy patient.[3] These pathological features should alert the pathologist to look closely for the CMV inclusion bodies.

Although, there have been an increasing number of case reports on IBD complicated by CMV infection, few reports have described its prevalence. Takahashi et al[11] studied prevalence of CMV in IBD patients. They found CMV infection in 1 of 55 biopsy specimens and in 8 of 39 surgical specimens obtained from the patients with ulcerative colitis (UC). None of the 49 biopsy specimens and 30 surgical specimens showed CMV infection taken from patients with CD. Twenty percent of the surgical specimens taken from patients with UC showed CMV inclusions. They suggested that the possibility of CMV infection should always be taken into account in patients with UC who are steroid resistant.

CMV is a herpes virus that infects 40-100% of adult population by their fourth decade of life.[12] Human CMV infection is usually asymptomatic and sub-clinical and can remain latent lifelong. It is an opportunistic infection seen in patients following renal and bone marrow transplantation, AIDS, haematological malignancies, or those on steroids and immunosuppressive therapies. The clinical course was more severe when patients have associated co-morbid e.g. malignancies, older patients and neonates. The prevalence of CMV complicated colitis in patients with IBD is 0.53%-4% and in patients with steroid refractive CD it is 11-36%.[12]

Regarding our case, the patient was young (22 years) with a history of CD and the possible explanation of isolated CMV salpingitis as a complication. CD can involve the appendix as part of course of disease which shows prominent vasculitis, and accordingly this will compromise blood supply causing partial ischaemia. The ischaemia can involve the fallopian tube with evidence of inflammation fibrosis and adhesion leading to amalgamation of the appendix with fallopian tube and ovary as a matted mass mimicking malignancy.

Conclusion

Isolated fallopian tube involvement by CMV can be seen

in an immunocompromised patient.

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