CASE REPORT

Klebsiella endophthalmitis as the herald of occult colorectal cancerChun Yue Mak,^{1,2} Helena Pui-yee Sin,^{1,2} Vesta Cheuk-ki Chan,¹ Alvin Young^{1,2}¹Department of Ophthalmology and Visual Sciences, Chinese University of Hong Kong, Hong Kong, China²Department of Ophthalmology & Visual Sciences, Prince of Wales Hospital, Hong Kong, China

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SUMMARY

A 67-year-old Chinese man presented with acute loss of vision and pain in the left eye with hypopyon in the anterior chamber. The patient was afebrile with no systemic symptoms at presentation. Diagnosis of endogenous endophthalmitis was made with vitreous tap yielding *Klebsiella pneumoniae*. Pars plana vitrectomy was performed twice to clear the infection. Thorough investigations showed no septic foci. Whole body positron emission tomography CT revealed a rectal tumour and biopsy showed adenocarcinoma. He was treated with neoadjuvant chemoradiation followed by surgery to resect the tumour. Vision in the left eye was hand movement at 12 months postoperatively. This case illustrates *Klebsiella* endogenous endophthalmitis might be a herald of occult colorectal cancer. Bacteria might gain access into bloodstream via mucosal defect in the tumour.

BACKGROUND

Endogenous bacterial endophthalmitis is a sight-threatening condition. Reports from South-east Asia demonstrated high incidence of *Klebsiella* endophthalmitis in patients with *Klebsiella* liver abscess. Reports have also shown relationship between *Klebsiella* liver abscess and occult colorectal cancer.

Herein, we report a case of *Klebsiella* endophthalmitis without clinically evident liver abscess. Imaging incidentally discovered occult colorectal malignancy. We speculate that mucosal defects in colorectal cancer provided a route of bloodstream entry for *Klebsiella*, which then seeded in the eye causing endophthalmitis. The case also highlights the importance of thorough search of septic source in the management of endogenous endophthalmitis.

CASE PRESENTATION

A 67-year-old Chinese man with a history of type 2 diabetes mellitus and essential hypertension on oral medications, presented with acute loss of vision and pain in the left eye for 1 day.

There was no recent history of trauma or surgery. Systemic inquiry revealed no respiratory, urinary, bowel or constitutional symptoms.

His presenting vision was hand movement in the left eye and 6/9 in the right eye. There was intense injection and chemosis in the left eye. Fibrin and 0.5 mm hypopyon were noted in the anterior chamber (figure 1). There was also severe vitritis in the left eye preventing fundal examination. Right

eye examination was unremarkable except mild non-proliferative diabetic retinopathy. He was afebrile and systemically well.

INVESTIGATIONS

Clinical diagnosis of left eye endophthalmitis was made and vitreous tapping was performed together with intravitreal injection of amikacin and vancomycin. Gram-negative bacilli were seen in urgent Gram-stain microscopy of the vitreous sample. Culture of the vitreous yielded *Klebsiella pneumoniae*.

Blood work showed normal liver and renal function. C reactive protein was elevated at 60.4 mg/L. Mild leucocytosis of $9.8 \times 10^9/L$ with neutrophilia was noted.

Systemic workup was performed to look for the source of *Klebsiella*. Abdominal ultrasound revealed no liver abscess or any other abdominal pathology. Sputum, urine and repeated blood cultures were negative.

Whole body positron emission tomography CT (PET-CT) was performed in search of occult septic source, which showed an area of focal rectal wall thickening with increased tracer uptake (figure 2). Findings were suggestive of rectal malignancy. Therefore, colorectal surgeons were consulted and colonoscopy was performed. A circumferential lesion was seen at midrectum with stool obstructing further advancement of the endoscope. Biopsy of the lesion confirmed adenocarcinoma. Carcinoembryonic antigen level was normal at 3.9 µg/L. On retrospective questioning, patient had non-specific abdominal complaints of intermittent loose stool for the past 6 months.

Subsequent MRI revealed a tumour at upper and middle thirds of rectum. Another annular lesion was noted at distal sigmoid colon 4 cm proximal to the rectal tumour, likely representing a synchronous tumour. Flexible sigmoidoscopy with biopsy confirmed the presence of synchronous adenocarcinoma. CT of the thorax and abdomen showed no distant metastases.

DIFFERENTIAL DIAGNOSIS

Acute onset of hypopyon and vitritis can be infective or non-infective in nature. Infective causes include bacterial and fungal endophthalmitis. Fungal endophthalmitis is usually seen in immunocompromised or very ill individuals. Viral retinitis such as acute retinal necrosis caused by herpetic viruses can sometimes present similarly.

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Figure 1 Slit-lamp photo of the left eye showing conjunctival injection, chemosis and hypopyon.

Non-infective causes include severe anterior uveitis and intermediate uveitis. These uveitides may be primary or secondary to systemic diseases such as Behçet and HLA-B27 spondyloarthropathies. Finally, masquerade syndromes such as intraocular lymphoma and metastases should also be considered.

Ruling out infection is the first priority in an endophthalmitis picture, therefore the first investigation that we performed was vitreous tapping, followed by intravitreal injection of antibiotics. As urgent microscopy of the vitreous sample already showed Gram-negative bacilli, the diagnosis of endogenous bacterial endophthalmitis was made immediately.

TREATMENT

Patient was started on topical fortified tobramycin and ceftazidime after vitreous tapping and intravitreal injection of amikacin and vancomycin. He was also given intravenous ciprofloxacin. His left eye vision further deteriorated to light perception despite the use of local and systemic antibiotics. Pars plana vitrectomy, anterior chamber washout and intravitreal injection of amikacin and ceftazidime were performed on day 2. Intraoperative finding was a poor retinal view with severe vitritis.

Patient later developed left eye hydrated cataract with persistent fibrin in the anterior chamber (figure 3). Staged operation in the form of phacoemulsification and anterior chamber washout was performed on day 7, followed by pars plana vitrectomy for residual vitritis on day 12.

Intraoperatively, severe fibrinous reaction was evident in the vitreous cavity. The retina appeared necrotic with generalised non-perfusion. Iatrogenic retinal break was created as a result of poor fundal view and necrotic retina. Surgeon decided to go for permanent silicone oil tamponade.

Figure 3 Persistent fibrinous reaction in the anterior chamber with increase in hypopyon.

As for the colorectal cancer, a transverse colostomy was performed due to impending bowel obstruction. A course of neoadjuvant chemoradiation was given followed by laparoscopic low anterior resection with transanal total mesorectal excision. Pathological examination of the specimen showed stage ypT3N0 adenocarcinoma of the rectum, with synchronous adenocarcinoma of the sigmoid colon invading into submucosa.

OUTCOME AND FOLLOW-UP

His right eye remained unaffected. Vision on the left eye was hand movement at 12 months after first vitrectomy with no signs of infection.

DISCUSSION

Endogenous bacterial endophthalmitis is a rare but sight-threatening condition. Over 40% of cases are left with visual acuity worse than 6/60.¹ Typical presentation is blurring of vision and pain. Clinical signs include hypopyon and vitritis, often with absence of fundal view. Diagnosis should be made clinically and empirical systemic or intravitreal antibiotics should be given promptly before microbiological proof is available.

Unlike postcataract surgery endophthalmitis, for which specific clinical indications of pars plana vitrectomy has been established by multicentre randomised clinical trial,² the optimal treatment of endogenous endophthalmitis remains unclear due to its rarity and heterogeneity. In the management of our case, ophthalmologists relied heavily on the degree of inflammation to make surgical decisions.

Bacteriology of endogenous endophthalmitis is diverse with regional variation. Gram-positive organisms are more common in the West, accounting for 60% of endogenous endophthalmitis

Figure 2 Positron emission tomography CT of the pelvis showed focal rectal wall thickening with increased tracer uptake.

in North America.¹ On the other hand, Gram-negative organisms predominate in Southeast Asia, particularly for *K. pneumoniae*, which on its own accounts for 54%–61% of all endogenous endophthalmitis in Southeast Asian studies.^{3–5}

Another report from Southeast Asia points out that 3.8% of patients with *Klebsiella* bacteraemia develop endophthalmitis,⁶ which is a relatively high incidence. *Klebsiella* serotype K1 is known to cause metastatic infections such as endophthalmitis.⁷ At the same time, significantly high proportion of *Klebsiella* that colonised gastrointestinal tract of healthy adults in Hong Kong belongs to serotype K1, amounting to 10%.⁸ Despite the testing for serotype of *Klebsiella* is not a commonplace, it is a routine practice here in our tertiary hospital to consult ophthalmologist for screening of endophthalmitis whenever blood culture yields *K. pneumoniae*.

On the other hand, *Klebsiella* liver abscesses in Southeast Asia have increasingly been associated with occult colorectal cancer.⁹ Colonic mucosal defects are speculated as route of bacterial invasion into portal system in a Southeast Asian series of cryptogenic liver abscesses.¹⁰ In the series, diabetes and *Klebsiella* are proposed risk factors of underlying colorectal cancer for patient with cryptogenic liver abscesses.

However in our case, despite thorough investigations including culture of various bodily fluid, hepatobiliary ultrasound and whole body PET-CT, no definite septic source can be identified. The vitreous is normally a sterile environment and therefore, the *Klebsiella* bacteria that cause endophthalmitis in our patient must come from an endogenous site. From our understanding that *Klebsiella* endophthalmitis has strong association with *Klebsiella* liver abscess in our locality, also the fact that *Klebsiella* abscess is associated with occult colorectal cancer, it is reasonable to speculate association exists between the *Klebsiella* endophthalmitis and the seemingly incidental colorectal cancer in our patient. In fact, previous case report had demonstrated the association of colorectal cancer with *Klebsiella* endophthalmitis and concomitant disseminated *Klebsiella* lung, liver and brain abscesses.¹¹ In comparison, the missing link in our case would be the absence of *Klebsiella* liver abscess.

We believe the finding of the colorectal cancer on whole body PET-CT is not merely incidental. Mucosal defects on the tumour provide a route for *Klebsiella* bacteria entering the bloodstream. Background diabetes mellitus might have further compromised patient immunity by impairing leucocyte functions and allow for propagation of the bacteria.¹² Location of the tumour at the rectum might explain why *Klebsiella* liver abscess is not detected, as part of the venous drainage of the rectum goes through rectal venous plexus into internal iliac vein, therefore bypasses portal venous system.

The proposition that the colorectal cancer is not incidental is supported by past reports of similar cases of endogenous endophthalmitis leading to the discovery of colorectal malignancy. The reported inciting organisms include *Streptococcus bovis* and *Clostridium septicum*.^{13–14} The authors of the above reports proposed a similar mechanism of bacterial entry. Interestingly, bacteraemia of the two organisms, similar to *Klebsiella*, have long been recognised to be associated with colorectal malignancy.^{15–16}

This case is, to our knowledge, the first report of isolated *Klebsiella* endogenous endophthalmitis as herald of occult colorectal cancer. As illustrated by this case, the search of septic source of *Klebsiella* endogenous endophthalmitis in Southeast Asia should not be limited to the usual blood, urine and sputum cultures or hepatobiliary imaging. When the above investigations were

negative, whole body PET-CT or colonoscopy should be considered as occult colorectal cancer might be a cause.

Learning points

- *Klebsiella* endophthalmitis might be a herald of occult colorectal cancer
- Strong associations exist between *Klebsiella* endophthalmitis, *Klebsiella* liver abscess and colorectal cancer in Southeast Asia.
- Thorough search of septic source is mandatory for endogenous endophthalmitis
- Prognosis of endogenous endophthalmitis is guarded and surgical indications of pars plana vitrectomy remain unclear.

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