An unusual case of a gallbladder polyp

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Abstract

A 63-year old female patient with a medical history of hypereosinophilic syndrome with neurological and pulmonary involvement presented for a routine follow-up. The patient was asymptomatic but a routine scheduled ultrasound showed a gallbladder polyp of 19mm. One month later this polyp had grown to 36 mm. On magnetic resonance imaging of the liver there was a suspicion of gallbladder cancer and for this reason cholecystectomy was performed. Pathology however showed eosinophilic infiltration. Serum analysis showed an increase in her eosinophil count. The diagnosis of hypereosinophilic syndrome with eosinophilic infiltration of the gallbladder was made. The dose of corticosteroids was augmented and she recovered completely post-operatively with no residual flares of other organ damage during follow up. (Acta gastroenterol. belg., **2021,** 84**, 675-677**).

Keywords: hypereosinophilic syndrome; eosinophilic cholangiopathy; eosinophilic cholecystitis; eosinophilia; gallbladder polyp; gallbladder cancer.

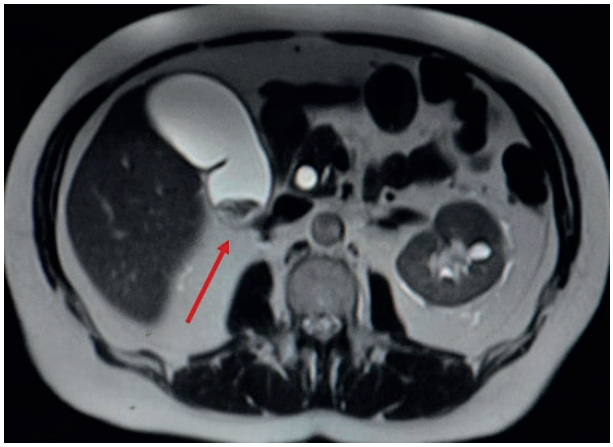

Figure 1. — Magnetic resonance imaging showing a mass in the fundus (red arrow) with a heterogenous signal and with a diameter of 25 mm x 27 mm suspect for early carcinoma.

Introduction

Hypereosinophilic syndrome (HES) is a rare disease and gastro intestinal involvement and especially involvement of the bile duct system is a rare manifestation of this disease. One could suspect this disease by measuring an elevated serum eosinophil count (EC) but the definitive diagnosis is made by biopsy and tissue analysis that shows infiltration of the tissue with predominantly eosinophilic granulocytes (1,2).

This patient already had two organ involvements consisting of pulmonary and neurologic manifestations. This was the third organ involvement.

Some case reports of HES presenting with acute cholecystitis have been published. This patient however was asymptomatic and presented with an incidental finding of a rapid growing gallbladder polyp where gallbladder cancer was suspected on imaging, which makes it a unique presentation of this disease. To our knowledge, this is the first case published with this clinical manifestation of HES.

Case report

A 63-year old female patient presented at the outpatient clinic for a routine consultation.

She had a medical history of hydradenitis suppurativa, polyposis nasi, penicillin allergy, asthma and diabetes type 2. Sixteen years ago the diagnosis of HES was made with a neurological presentation of polyradiculoneuropathy in which the nerve biopsies showed eosinophilic infiltration with raised serum eosinophilic counts. At that time she was treated with corticosteroids (CS) with a loading dose and then tapered to a chronic dose of prednisolone 6mg in association with calcium tablets. In 2007 she developed a second organ involvement with shortness of breath, cough and multiple ground glass opacities, bilateral consolidations and interstitial manifestations on her chest CT scan. Biopsies were not taken at this time but she was treated with IV CS. After the initial phase, the CS were tapered and azathioprine 100mg was associated because she had a second organ involvement. Ten years later she presented herself for her yearly routine consultation with a routine ultrasound (US) of the abdomen. On this US a gallbladder polyp of 19 mm was seen with typical non shadowing and immobile aspect. At that time she was asymptomatic but because this polyp was larger than 10 mm in diameter, cholecystectomy was advised, but the patient however preferred to wait. A new consultation was planned with a new US after 4 weeks. The US showed an increase in size of the polyp from 19mm to 36 mm. Because of the rapid increase in size, an urgent MRI was performed. This showed a mass

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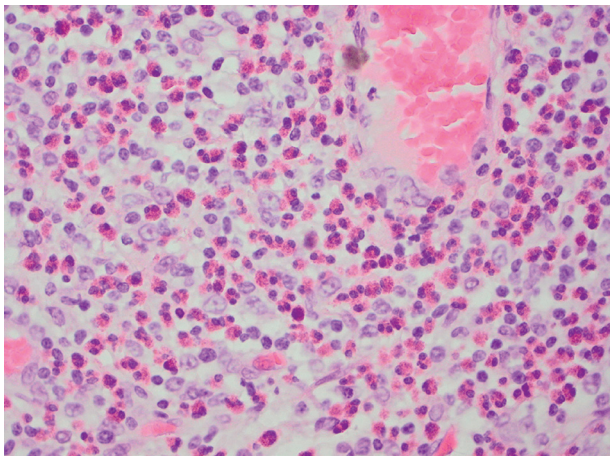

Figure 2. — At high magnification the inflammatory infiltrate mainly consists of numerous eosinophilic granulocytes (haematoxylin and eosin, x40).

in the fundus of the gallbladder (25mm x 27mm) with a heterogenous signal (Fig. 1). Because of its size and rapid growth, gallbladder cancer was suspected. The tumour marker CA 19.9 (kU/L) was not elevated (ref < 37.0 kU/L). Her serum EC were routinely measured and this showed a significant increase from 480 to 1170 eosinophils/µL (ref: 28-273/µL). Other liver tests were within normale range. The patient gave her consent for a laparoscopic cholecystectomy and postoperatively she had no complications. Pathology examination of the gallbladder showed no sign of malignancy but showed edema, inflammation and polypoid thickening with acute inflammation with predominantly eosinophilic granulocytes expanding to the mucosa, submucosa and muscularis propria (Fig. 2). There were also signs of chronic gallbladder inflammation and no bile stones were observed. The initial differential diagnosis in this case was carcinoma of the gallbladder, gallbladder polyp, bile stones, parasites and medication induced eosinophilia. Eosinophilic cholecystitis was not suspected given the fact that she had no symptoms and the MRI and US did not show a thickened gallbladder wall.

Primary eosinophilic gastro enteritis (EGE) was not suspected given the fact that she already had two other non-gastrointestinal related organ involvements.

Malignancy was excluded via pathology and we did not find any bile stones on imaging. We had no arguments for medication induced eosinophilia and an additional focused look by the pathologist showed no arguments for parasitic infection. Given the patient's history of HES a diagnosis of a HES- associated gallbladder involvement was made. Given the fact that there was also a flare-up of her EC and that this was a third organ involvement, the dose of CS was raised to 40 mg prednisolone daily and was tapered very slowly over the following months. During follow-up (2 years) she did not develop an additional flare-up of her HES.

Discussion

HES is rare and the true prevalence is unknown. In one study, the estimated prevalence was between 0.36 to 6.3 cases per 100,000 persons (3). Most patients are between 20 and 50 years of age at the time of diagnosis. HES is a group of disorders marked by the sustained overproduction of eosinophils, in which eosinophilic infiltration and mediator release cause damage to multiple organs. HES is defined by the following: 1) persistently elevated EC for at least six months, 2) eosinophilia with no recognizable causes such as parasite infection, cancer, or allergic disease, and 3) symptoms of eosinophilia-mediated organ dysfunction (4).

GI involvement is the third most commonly reported (38%) clinical manifestation in patients with HES (5). This disease is often confused with eosinophilic gastroenteritis (EGE), also a rare disease, which affects the entire GI tract. EGE most importantly has no involvement of multiple organs outside the GI tract. In contrast to EGE, HES also involves multiple organs outside the GI tract. This case is quite exceptional because she presented with gallbladder involvement. Eosinophilic cholangiopathy refers to a rare condition, which is characterized by the eosinophilic infiltration of the biliary tract but in most cases there is involvement of the common bile duct (6). Gallbladder involvement in HES is more frequently described in the literature as an eosinophilic cholecystitis. The clinical presentation is similar to that of a typical cholecystitis, with right upper quadrant pain and with pathology reporting infiltration of eosinophils (7). This case is quite unique and to our knowledge this is the first case of HES presenting with an asymptomatic gallbladder polyp mimicking gallbladder cancer.

In this case rapid MRI and surgery was the chosen strategy because of the size of the polyp.

Retrospectively, one could however argue about the chosen approach because surgery is invasive. An alternative to this approach could have been to perform an endoscopic ultrasound (EUS) with biopsy puncture of the lesion first and to await pathology report, given the fact that she already had two other organ manifestations of HES. In a case report about a patient with EGE and secondary HES, Crapé et al. described EUS-guided fine needle biopsy (FNB) of the bulboduodenal wall with a succesfull pathological diagnosis, avoiding unnecessary surgical biopsies (2). In our case however, FNB was required of a galbladder polyp. Sung Hoon Kang et al. described one of the first case reports of succesfull EUS-guided FNB for galbladder polyps (8). So retrospectively this could have been a less invasive approach, because if the FNB had ruled out malignancy and confirmed eosinophilic infiltration, cholecystectomy could have been avoided and medical treatment with higher dose of CS would have been the better and less invasive option here in combination with regular ultrasound follow-up of this polyp.

Management

Before starting treatment one should always rule out secondary causes of hypereosinophilia including: allergy, drug hypersensitivity, helminth, protozoic or fungal infections, HIV, etc.

If these conditions are excluded, tissue biopsy of an affected organ (in our case the gallbladder) should confirm eosinophilic infiltration. Tissue damage is generally thought to be more likely to occur when the EC exceeds 1500/mL but also occurs at lower thresholds.

However, there does not appear to be a direct correlation between the level of peripheral eosinophilia and the presence of clinical disease, as the degree of eosinophilia does not accurately predict the risk of end-organ damage (9). Treatment in patients with idiopathic HES frequently relies on CS as mainstay because of the inhibition of chemotaxis. Tapering typically needs to be prolonged over months and inability to reduce eosinophilia or development of a worsening clinical picture is a likely indication to add another agent. In this case azathioprine was chosen but one could also use hydroxyurea, IFN-α, methotrexate, cyclosporine or imatinib (9). The primary goal of treatment is to prevent further damage to major organs. Surgery is normally reserved for patients who are refractory to medical treatment. In this case however it was the mainstay of therapy since there was a suspicion of malignancy. EUS guided FNB can be an alternative and a less invasive option but needs further research. There are however no evidence based treatment algorithms for gallbladder involvement in HES, so this could be a topic for further research in the future.

Conflict of interest statement

None

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