

## HPV papilloma in the lung in a Crohn's disease patient treated with Infliximab

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### To the editor,

A 74 year old male patient was admitted to the emergency room with a gastrointestinal obstruction. His medical history revealed multiple abdominal surgeries with a Hartmann's resection for perforated diverticulitis, transabdominal prostatectomy, cholecystectomy and correction of an umbilical hernia.

Giving his medical history of multiple abdominal surgeries a tentative diagnosis of gastrointestinal obstruction due to adhesions was made. Our patient underwent a laparotomy and multiple adhesions were treated with adhesiolysis. During the laparotomy a subobstructive terminal ileum was seen with a macroscopic appearance of Crohn's disease with creeping fat and active inflammation. A stricturoplasty was performed and biopsies showed the presence of granulomas. An oral treatment with budesonide 9 mg/day, tapering with 3 mg every month, was started.

Three months later, a colonoscopy showed active terminal ileitis with ulcers. On magnetic resonance enterography there was persistent inflammation of the terminal ileum with substenosis, prestenotic dilatation of the small intestine and skip areas. At that time 6-mercaptopurine was started.

After two months 6-mercaptopurine had to be stopped due to hepatotoxicity and Infliximab was started. Due to a positive tuberculosis skin test, start of Infliximab was postponed for 6 weeks and prophylactic treatment with Nicotibine was started.

On year later, colonoscopy showed complete mucosal healing. Biopsies were normal. Patient had no abdominal complaints, but he suffered from a cough with yellow expectorations. A new chest X-ray did not show any abnormalities. After 2 months, the cough was still present and chest X-ray now showed a consolidation in the right upper lobe (Fig. 1). Bronchoscopy revealed 2 papillomatous tumors in the larynx and a stenosis of the right upper bronchial branch. Pathology showed a squamous papilloma. We promptly stopped our treatment with infliximab and by only doing this we saw a complete resolution of the cough and consolidation over a 2 months period (Fig 2). Our patient is now doing fine under treatment with mesalazine 2g per day.

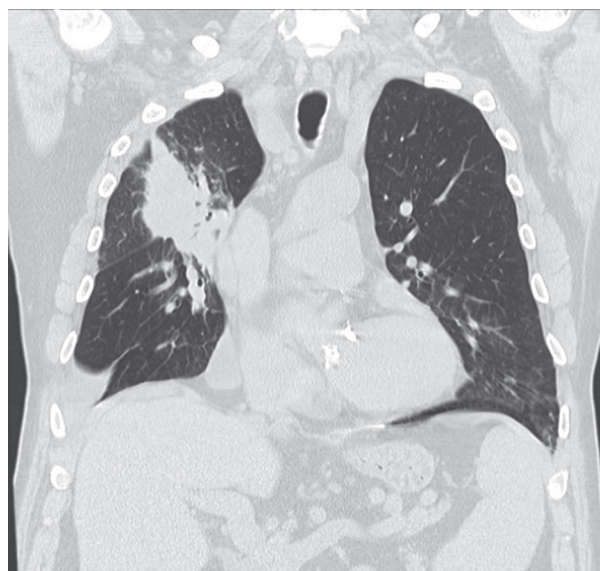


Fig. 1.

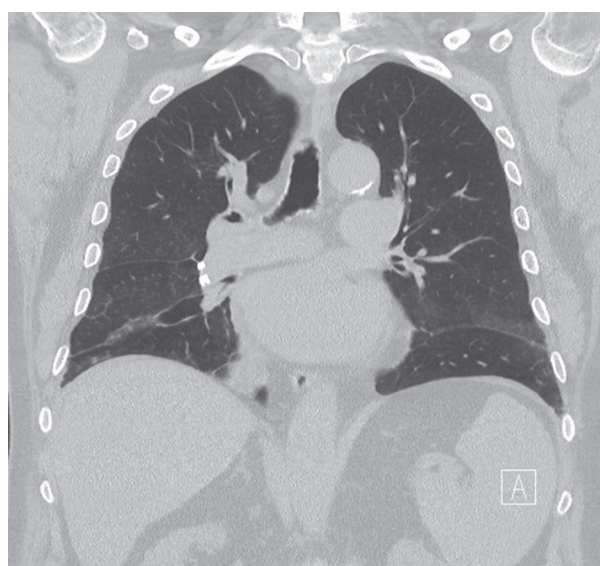


Fig. 2.

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Laryngo-bronchial papilloma, caused by Human Papilloma Virus (HPV) is a very rare disease with a prevalence of 2/100.000 in adults and 4.5/100.000 in children. There are more than 100 subtypes of HPV and laryngeal papillomatosis is mostly caused by subtypes 6 and 11 (1). The overall prevalence of HPV carrying state was evaluated in a cross-sectional study of 5579 women and men who provided an oral sample for HPV DNA sampling. The overall prevalence of HPV DNA was about 10 percent in man and 3.1 percent in women (2).

Since tumor necrosis factor alpha (TNF- $\alpha$ ) plays a role in the immune system, treatment with TNF- $\alpha$  blocking agents results in a higher risk for bacterial, fungal and viral infections. A meta-analysis demonstrated a 2 fold increased risk of opportunistic infections with anti-TNF therapy (3). There are several reports of reactivation of HPV due to immunomodulator therapy (4,5).

To date there are no antiviral agents known to be effective in treating or eradicating HPV. In our case we tried to restore the immune system back to a non-compromised state by stopping infliximab. By only doing this, the patient's immune system managed to control the virus and the papillomatous tumor disappeared.

To our knowledge, there are no other cases reported of laryngobronchial papillomatosis due to infliximab

therapy. There are some data of HPV reactivation in association with anti-TNF therapy, resulting in anorectal or skin warts, but data are very scarce. A specific effect of anti-TNF in reactivation of HPV remains unknown. There are only a few case reports suggesting an increased risk (6).

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