Magnetic resonance imaging monitoring of post-treatment changes to Crohn's disease–related anal fistula in patients prescribed infliximab

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The incidence of inflammatory bowel disease, particularly Crohn's disease, is rising in Hong Kong.[1] The age-adjusted incidence of Crohn's disease increased from 0.01 per 100 000 population in 1985 to 1.46 per 100 000 population in 2014.[1] Crohn's disease is a multisystem disorder with specific radiological features such as transmural inflammation, fistulation, and skip lesions. Perianal fistulas often complicate Crohn's disease, affecting up to 36% of patients.[2]

Infliximab, a monoclonal antibody against tumour necrosis factor-α, has revolutionised the treatment of Crohn's disease–related anal fistula. Current evidence shows encouraging results for closure of perianal fistulas. According to a local consensus statement, biologics are advocated in patients with active fistulising Crohn's disease, particularly those with complex perianal fistulising disease.[3]

Response to monoclonal antibody therapy needs to be monitored. This pictorial review illustrates the post-treatment changes on magnetic resonance imaging (MRI) of anal fistula in patients prescribed infliximab.

Patients with a known history of Crohn's disease complicated by perianal fistula and prescribed infliximab between 2012 and 2016 were reviewed. The treatment regimen at our centre comprises an intravenous loading dose of infliximab 5 mg/kg, followed by the same dose at week 2 and week 6. Thereafter a maintenance dose of 5 mg/kg is given every 8 weeks.

Magnetic resonance images were acquired with the 1.5T Siemens Magnetom Avanto system (Erlangen, Germany). The pelvic MRI protocol for perianal fistula evaluation consists of T1-weighted and high-spatial-resolution T2-weighted imaging sequences without fat saturation to delineate the muscle groups, fat planes, and fistula tract. T2-weighted imaging with fat suppression is used to assess oedema and fluid-containing tracts and cavities, whereas fat-suppressed T1-weighted unenhanced and contrast-enhanced sequences are used to assess the presence and degree of inflammation (Table). Diffusion-weighted imaging is not routinely performed in view of the need for an extended examination time. Information about the presence of fluid, oedema, cavities, and inflammation can be obtained through these sequences. Anal fistulae are classified according to the Parks' classification system (Fig 1).[4]

Three patients (two men, one woman) were reviewed and all received infliximab. At least one pre-treatment and one post-treatment MRI were performed.

Patient A was a 34-year-old woman with a history of systemic lupus erythematosus, retinitis,

TABLE. Pelvic MRI protocol for evaluation of anal fistula*

Sequences and slice orientation	No. of signal averages	Matrix (phase x frequency)	Slice thickness (mm)	TR / TE (ms)	Flip angle
T2-TRUFI coronal (localiser)	1	448 × 448	4	1182/1.5	64
T2-TRUFI sagittal (localiser)	1	448 × 448	4	1182/1.5	75
T2-TRUFI axial (localiser)	1	448 × 448	5	1182/1.5	64
T1-TSE axial	3	320 × 320	3	583/15	150
T2-TSE axial with fat suppression	1	256 × 256	3	6900/119	180
T2-TSE axial	1	320 × 320	3	5040/121	180
T1-TSE coronal	2	320 × 320	3	497/16	150
T2-TSE coronal with fat suppression	1	256 × 256	3	4700/119	180
T1-TSE axial with contrast and fat suppression	1	256 × 256	3	672/9.8	150
T1-TSE coronal with contrast and fat suppression	2	256 × 256	3	570/15	150

Abbreviations: MRI = magnetic resonance imaging; TR/TE = repetition time/echo time; TRUFI = true fast imaging with steady-state free precession; TSE = turbo spin echo

* Examinations were performed by Siemens Magnetom Avanto 1.5T MRI (Erlangen, Germany)

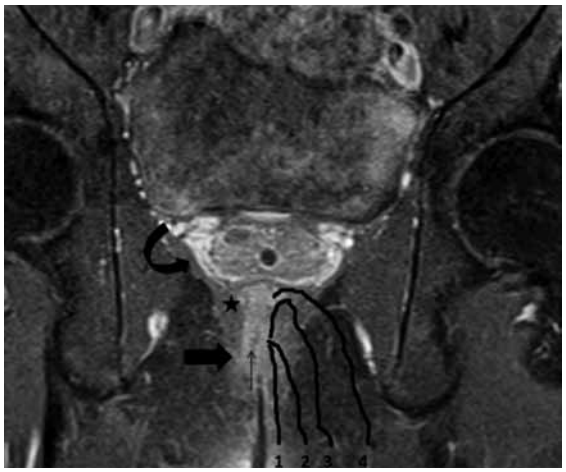

FIG 1. Schematic diagram demonstrating different types of perianal fistula according to Parks' classification. Internal sphincter (thin arrow); external sphincter (thick arrow); puborectalis (asterisk); and levator ani (curved arrow). Intersphincteric fistula tracks between internal and external sphincter (1); trans-sphincteric fistula pierces through the external sphincter (2); suprasphincteric fistula tracks superior to the puborectalis (3); and extrasphincteric fistula penetrates the levator ani (4)

and neuropsychiatric lupus. She had had recurrent ischiorectal abscess and perianal fistula since 2002. Rectal biopsy confirmed Crohn's disease. Despite treatment with azathioprine, the perianal fistula failed to close. She was scheduled to initially receive three doses of infliximab. Close monitoring was essential in view of the potential to develop lupus-like disease. Progress MRI after the third dose of infliximab showed slight interval improvement in her perianal fistula. Biologics were continued in view of the residual disease. After the seventh dose of infliximab, progress MRI revealed a largely quiescent perianal fistula (Fig 2). In view of the radiologically healed fistula, clinical improvement and potential risk of lupus-like disease, the decision was taken to stop the infliximab infusion but continue close clinical and radiological monitoring.

Patient B was a 24-year-old man with a history of perianal fistula since 2015 and an episode of perianal abscess that required incision and drainage. Crohn's disease was confirmed on rectal biopsy. He had previously developed azathioprine-induced pancytopenia. Subsequent infusion of infliximab infusion resulted in responsive disease, evident on

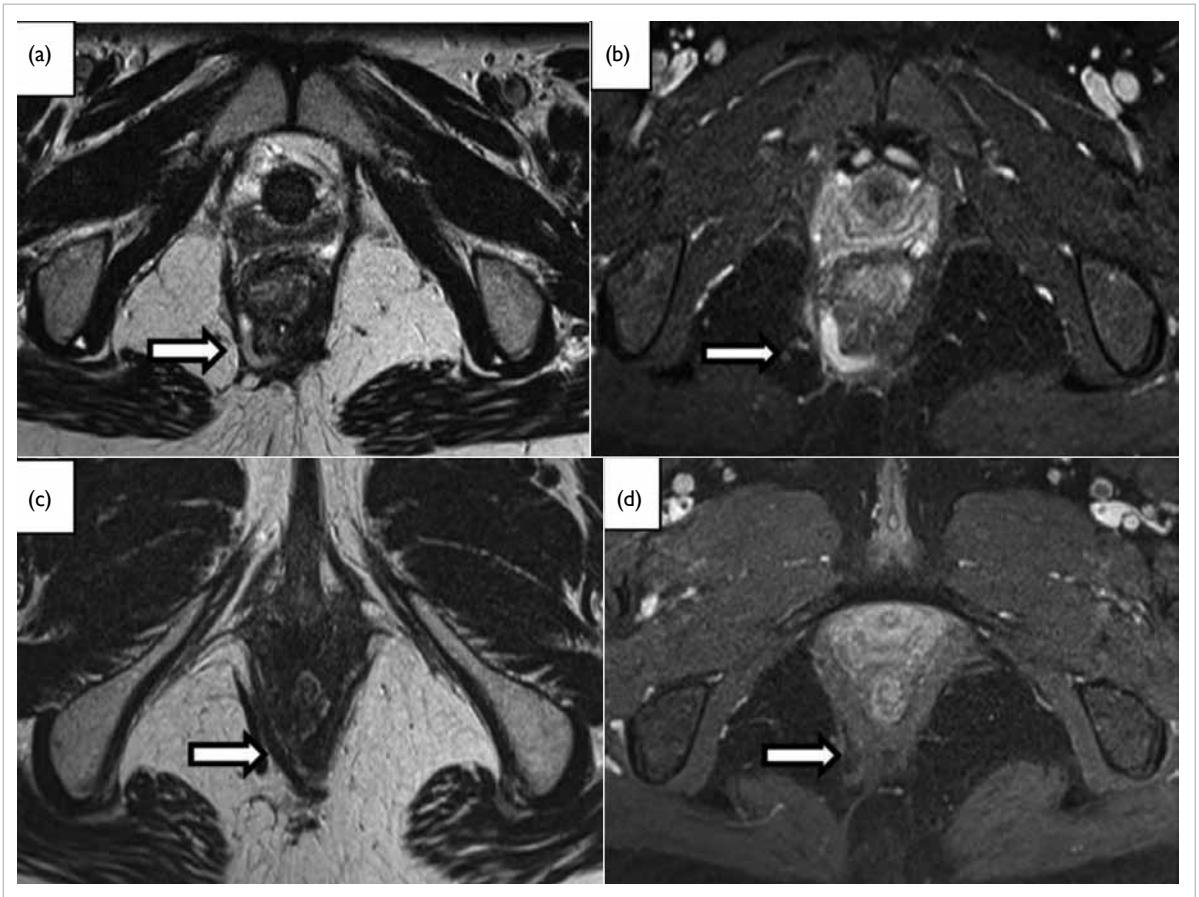

FIG 2. Patient A. (a and b) T2-weighted axial and T1-weighted post-contrast fat suppression axial magnetic resonance images showing an active trans-sphincteric tract at the 8 o'clock position with T2-weighted hyperintense signal and contrast enhancement (arrows). (c and d) One-year post-treatment. Loss of T2-weighted hyperintense signal and contrast enhancement suggested quiescent disease (arrows)

MRI (Fig 3). Clinical and radiological monitoring (progress MRI) at 6-month intervals was carried out to determine progress of the perianal fistula. Infliximab would be stopped when there was evidence of healed tract and clinical improvement.

Patient C, a 42-year-old man had a history of ileocolic Crohn's disease since 2008, with episodes of perianal abscess and fistula refractory to steroid and azathioprine treatment. Magnetic resonance imaging showed progressive perianal fistula (Fig 4) after the second maintenance dose of infliximab. Previous infliximab dose/frequency was continued and progress MRI planned for the purpose of reassessment and consideration of alternative treatment if there was persistent progression.

Crohn's disease–related anal fistulae are frequently encountered in radiologic practice due to their complexity and propensity for incomplete treatment response and relapse.

Magnetic resonance imaging is a well-established diagnostic tool for anal fistula. Its inherent high spatial and contrast resolution allows precise anatomical delineation.[5] Magnetic resonance imaging plays a critical role in helping determine the appropriate treatment that should be individualised according to the type of perianal fistula and the degree of involvement of surrounding pelvic structures. Clinical examination can often be difficult because of induration and inflammation in patients with anal sepsis. At MRI, identification and localisation of the entire fistula, including the external opening, the primary track, secondary tracks, abscesses, and the internal opening, are essential for fistula classification and treatment. Inadequate assessment may result in progression of a simple fistula to a complex fistula, and failure to recognise secondary extensions can result in recurrent sepsis. Anti–tumour necrosis factor antibodies (infliximab) have been introduced with good clinical results. Magnetic resonance imaging also plays an important role in evaluation of the response to medical therapy. Magnetic resonance imaging does not have field of view limitations and offers excellent views of the supralevator, retrorectal and anteroanal spaces, where occult sepsis may

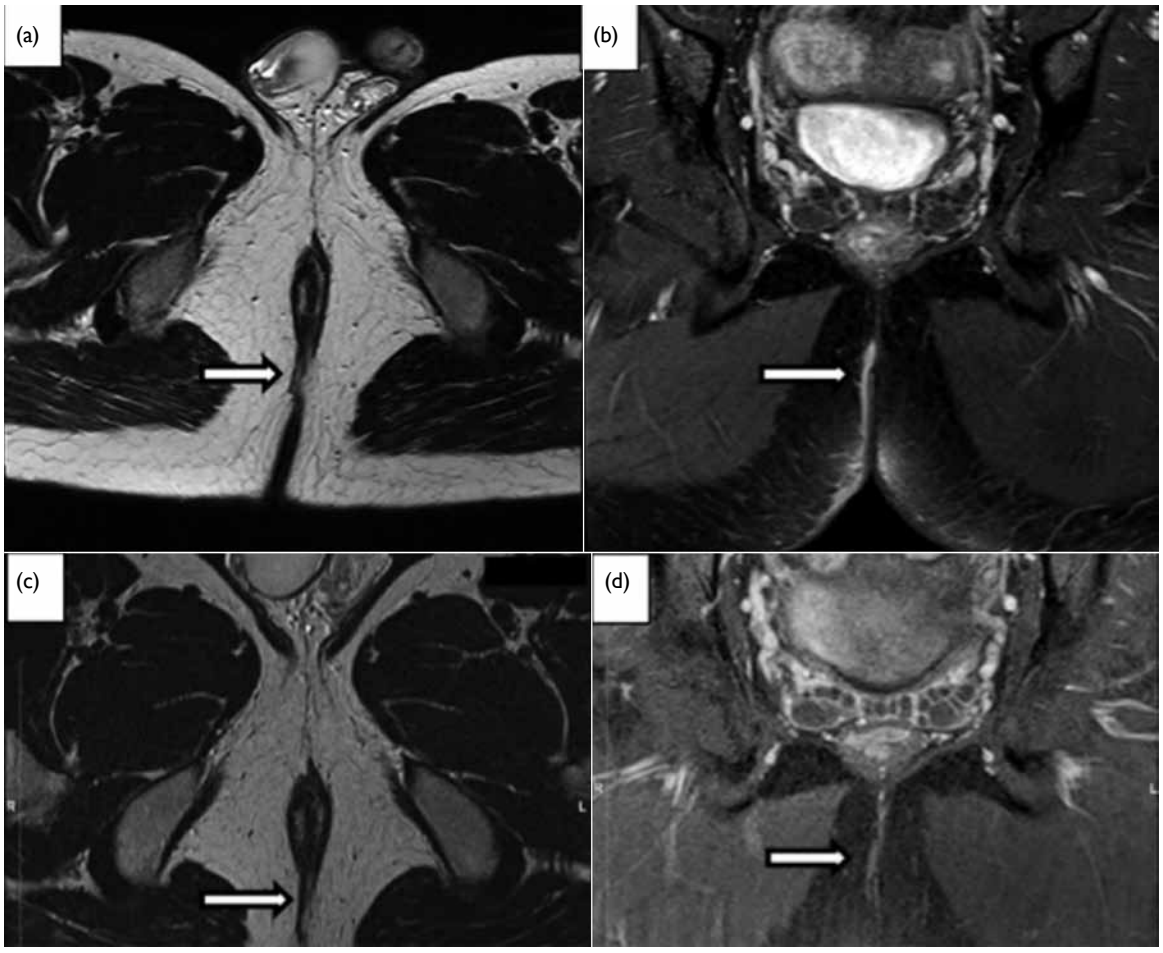

FIG 3. Patient B. (a and b) T2-weighted axial and T1-weighted post-contrast fat suppression coronal magnetic resonance images showing an active intersphincteric tract at the right-sided natal cleft with T2-weighted hyperintense signal and contrast enhancement (arrows). (c and d) Six months post-treatment. Loss of T2-weighted hyperintense signal and contrast enhancement suggested quiescent disease (arrows)

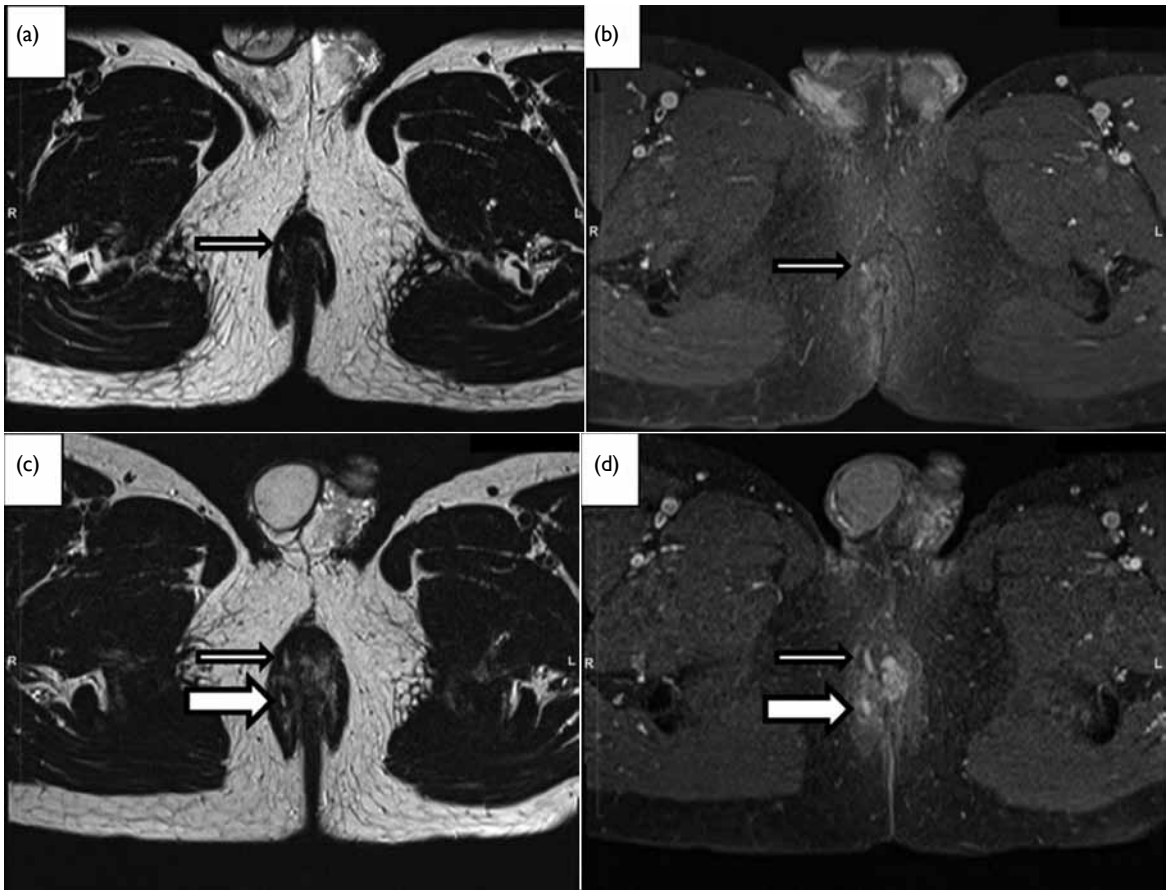

FIG 4. Patient C. (a and b) T2-weighted axial and T1-weighted post-contrast with fat suppression axial magnetic resonance images showing a T2-weighted hyperintense-enhancing active trans-sphincteric tract (arrows) passing through the external sphincter at the 11 o'clock position. (c and d) Five months post-treatment. Interval progression of the 11 o'clock trans-sphincteric tract (arrows) and a new T2-weighted hyperintense-enhancing active intersphincteric tract over the 7-8 o'clock position (thick arrows)

be missed clinically due to extensive scarring or a remote location.[6]

This pictorial review demonstrates the ability of MRI to monitor the response to therapy of anal fistula in Crohn's disease patients receiving infliximab.

Author contributions

KY Man is responsible for the design, acquisition and interpretation of data, and drafting of the article. EMF Wong, FKY Cho, and CM Leung are responsible for critical revision for important intellectual content.

Declaration

All authors have disclosed no conflicts of interest. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

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