Author's response to reviews

Title: Occurrence of bladder metastasis 10 years after surgical removal of a primary gastric cancer. Case presentation and review of the literature.

Authors:

Csilla Andras (andrascilla@yahoo.com)
Laszlo Toth (tothlasz@dote.hu)
Janos Posan (posanjanos@freemail.hu)
Emese Csiki (emesecsiki@yahoo.com)
Miklos Tanyi (mtanyi@hotmail.com)
Zoltan Csiki (csikiz@gmail.com)
Zoltan Garami (drgaramiz@chello.com)
Attila Enyedi (drenyediatilla@gmail.com)
Tibor Flasko (flash@dote.hu)
Zsolt Horvath (horvathzsolt@med.unideb.hu)

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Author's response to reviews: see over
Dear „The Journal of Medical Case Reports Editorial Team”

We send you back the revised manuscript.

We have removed the dates found in Case presentation section, replaced the header "Disclosure of conflict of interest" with Competing interest.
We have restructured the competing interests section at the end of the manuscript, before the reference list.

We corrected the grammar and spelling errors, we did not perform other changes in the text.

We have attached the answers to the reviewers comments.

Yours sincerely

Csilla András
Dear Prof. Ganesamoni,

Thank you for your detailed and in-depth evaluation and for presenting valuable data about immune histochemical differential diagnosis of primary and metastatic adenocarcinomas of the bladder. It was of special interest the presentation of rare primary bladder adenocarcinoma and uroepithelial carcinoma types.

Taking into consideration all these data, with respect we still maintain our statement, that we have observed the late bladder and peritoneal metastases of our patients’ gastric cancer diagnosed 10 years before. We base our opinion on the fact, that the three tumor specimens had practically identical H.E. histological morphology and appearance. Even today, in the era of immune histochemistry, the H.E. picture is of determinative importance. Immune phenotype is valuable and gives decisive help in many cases, but only if it correlates with the H.E. picture and the disease clinics. In our case the rare primary bladder tumor variants, although their immune phenotype correlates more or less with our case, their H.E. morphology is markedly different from the one seen in our patient. The hepatoid adenocarcinoma, the signet cell carcinoma or the urothelial nested carcinoma presents different histological picture from our case. Numerous literature data are available on the immune phenotype of bladder adenocarcinoma. According to the WHO’s: „Pathology and genetics of tumors of the urinary system and male genital organs” (IARC Press, Lyon, 2004, pp. 128-130.), the majority of bladder adenocarcinomas are CK20 positive. This also supports us in our conviction that in our case the tumor seen in the bladder was of metastatic origin.

We have corrected the grammar and spelling errors.
Dear Prof. Herszényi,

First of all we would like to thank you for your careful review!

Our answers are the following:

Yes, we are certain that the two tumors (bladder and peritoneal metastasis) was not metastasis from colorectal carcinoma:

In our Institute the whole of the polyps bodies undergo histopathological examination, so we can be sure about the fact that in the adenomatous polyp of the patient carcinoma was not present. (Theoretically of course we can not exclude the presence of 1-2 mm invasive carcinoma in the area between the preparation sections, but this could be maximum of 1 mm thickness, pT1 Haggit 1 infiltration tumor in which case even the possibility of lymph node metastasis is slight and remote dissemination is to be excluded.

On the other hand the excised bladder and peritoneal tumor mass was CK7 positive, CDX2 negative which phenotype also pleads against colorectal origin.

Based on clinical data, the tumor excised from the bladder was localised in the wall subepithelially. We consider, that tumor arising as a part of peritoneal dissemination can not be resected endoscopically. To produce urological symptoms, the tumor should grow as a giant mass in the bladder.

We did not determine the Her-2 status in the absence of any therapeutic consequence. Herceptin treatment became available only later in time for Her2 positive metastatic gastric cancers.

The patient is non smoker, family oncological anamnesis is negative.

We corrected the grammar and spelling errors.
Dear Prof. Sabnis,

First of all we would like to thank you your careful review!

You had a comment regarding the description of the TUR and the appearance of the tumor in detail. Our answer is the following:

These kinds of lesions are intramural ones with intact mucosa. We experienced the same picture during diagnostic cystoscopy: a 2x4 cm large, solid mass was observed on the left wall of the bladder, close to the left ureteric orifice. The tumor was covered with elevated, slightly hyperemic, but normal looking urothelium. When we decided to perform a transurethral resection of this mass, our main goal was to identify the histological type. Due to the suspected cause of this tumor, we did not plan to remove it entirely. During the TUR (which was performed with Iglesias device with the aid of monopolar energy) we resected the mass deep in to the muscle wall of the bladder in order to get proper histological diagnosis and also trying to avoid perforation during the procedure. There was no severe bleeding or any kind of iatrogenic injury. At the end of the intervention, we assumed that there was still some residual tumor, but according to the possible histological diagnosis we decided to end the procedure leaving the residual cells for chemotherapy. PET CT revealed residual tumor in the bladder and chemotherapy was launched.

We corrected the grammar and spelling errors.
Dear Prof. Shenoy,

First of all we would like to thank you your careful review!

You had a comment regarding PET CT before cystoscopy.

Our answer is the following:

In Hungary, the health insurance does not cover PET CT examination in case of bladder tumor and therefore we did not perform this examination during our patients clinical investigation. The histopathological examination revealed bladder metastasis of the gastric cancer diagnosed 10 years before cystoscopy. We found the case rare and interesting. Our hospital may request university funded PET CT scan in such rare cases for scientific reasons, and so we performed it after the TUR operation. PET-CT presented only residual malignancy in the bladder, no distant metastases were suspected.

We corrected the grammar and spelling errors.

Dr András Csilla