MELIOIDOSIS MIMICKING PULMONARY TUBERCULOSIS

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Introduction

Melioidosis is caused by the soil bacterium *Burkholderia pseudomallei*. The bacterium is an oxidase-positive, motile gram-negative bacillus, showing bipolar staining. While most cases are considered to be from percutaneous inoculation, inhalation is also a well-recognized mode of infection1. Melioidosis is endemic in Southeast Asia, Northern Australia and the Indian subcontinent2. Sri Lanka is situated in the endemic region for melioidosis and the incidence of the disease is increasing3. It accompanies the pulmonary manifestations4. It tends to cause suppurative visceral lesions which may accompany the pulmonary manifestations4. Melioidosis can present with a variety of clinical manifestations. Clinical course may be acute, subacute or chronic. In subacute and chronic forms involving the respiratory system, the presenting features may resemble other chronic pulmonary infections including tuberculosis. Melioidosis tends to cause supplicative visceral lesions which may accompany the pulmonary manifestations5. It has been referred to as the ‘great mimicker’ by various authors5. Presentations mimicking tuberculosis are important clinical considerations as a significant number of patients are diagnosed clinically as tuberculosis where the results of their bacteriological tests are negative. We report a case of melioidosis with a clinical presentation similar to tuberculosis.

Case Presentation

A 29 year old army soldier serving in Nuwara Eliya for the past 5 years, presented to our unit with intermittent fever, loss of appetite and loss of weight of 3 months duration. He also complained of a mild intermittent cough of 2 months duration. Prior to his appointment to Nuwara Eliya he was engaged in paddy farming at Mahiyangana. He had a history of IgA nephropathy, detected 6 months previously, and was on daily low dose corticosteroids.

Examination revealed a febrile patient with a temperature of 39 °C. His pulse rate was 112/minute while the blood pressure measured was 140/90 mmHg. Upon admission the patient developed right sided flank pain and renal angle tenderness was elicited on the same side. The rest of the system examination was unremarkable.

The hemoglobin concentration was 10.5 g/dl and the white blood cell count was 32.5×10^9/mm³ comprising 74% neutrophils, 22% lymphocyte and 3% eosinophils. The platelet count was 464,000/mm³. Urine microscopy showed pyuria (field full pus cells/HPF), however the urine culture was sterile. The renal function tests were impaired revealing a blood urea level of 16.7 mg/dL and a creatinine value of 2.13 mg/dL. The serum electrolyte levels were normal. The liver function tests were within normal limits.

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CASE REPORT

**Presented as an abdominal wall fistula and later found to have an appendiceal mass**

**Table 1. Clinical presentation patterns of primary appendiceal neoplasms**

| Type of neoplasm  | Type of surgery | Clinical presentation |
|-------------------|-----------------|-----------------------|
| *Mucoceole*       | Acute           | Incidental            |
| *LAMN*            | Inflam          | Mass                  |
| *Adenocarcinoma*  | Unre **markable** | Other                  |
| *Neuroendocrine tumours* | Granuloma |                         |
| NET G1 (Carcinoid) | Other non neoplastic |                       |
| Others            | Non specific    |                        |
| Sessile serrated adenoma | Unremarkable |                         |

**Table 2. Correlation of gross appearances of appendices with microscopic features in appendicectomy specimens**

| Gross app | Type of neoplasm | Microscopic diagnosis |
|-----------|------------------|-----------------------|
| Mass      | Acute inlfam     | Granuloma inlfam      |
| Mucoceole | Inflam          | Other non neoplastic  |
| Inflamed  | Unre **markable** | Non specific          |
| Unremarked |                |                       |
| TOTAL     | 2907            | 7                     |

**Table 3. Correlation of gross appearances of appendices with microscopic features in colectomy specimens**

| Gross app | Microscopic diagnosis |
|-----------|-----------------------|
| Mass      | Acute inlfam          |
| Mucoceole | Inflam                |
| Inflamed  | Unremarked            |
| Unremarked|                      |
| TOTAL     | 93                   |

Of the mucinous neoplasms, 1 was an adenoma, 3 were LAMN and 5 were adenocarcinomas. Of the adenocarcinomas, four were mucinous type and one was unclassified. Gross appearances of these tumours were as follows, 3 had masses, 4 had thickened walls, 1 was ruptured with mucus on the serosa and 1 showed inflammation only. One had localized mucin in the right pelvic peritoneal cavity at the time of surgery.
classification, as mucinous adenoma, LAMN and mucinous adenocarcinoma. Presence of intraperitoneal mucin collections was recorded when indicated in the request form.

Results
There were 2907 appendicectomy specimens and 93 right hemi colectomy and total colectomy specimens which included an appendix. The mean age of the appendicectomy sample was 25.3 ± 14.1 years and 1572 (54%) were males. The mean age of the colectomy sample was 46.3 ± 19.8 years and 37 (39.8%) were males.

In the appendicectomy sample, the indication for surgery was suspected acute appendicitis in 2490 (85.7%), suspected appendicular mass in 38 (1.3%) and laparotomy performed for other reasons in 33 (1.1%); the indication was not mentioned in 346 (11.9%). In the colectomy sample, indications for surgery were malignancy elsewhere in the colon: 44 (47.3%), acute abdomen or suspected obstruction: 26 (28%), familial adenomatous polyposis: 3 (3.2%), appendicular masses: 2 (2.2%) and other reasons: (19.2%).

Grossly, in the appendicectomy specimens, there were 11 (0.4%) masses, 3 (0.1%) mucoceles, 1585 (54.5%) with features of inflammation only and 1308 (45%) were unremarkable. In the colectomy specimens, 3(3.2%) were appendicular masses, 1(1.1%) was unremarkable. None had evidence of nematode infestation. Correlations of gross appearances of appendices with microscopy in appendicectomy and colectomy specimens are given in Tables 2 and 3.

Of the 3000 specimens, 13 (0.4%) had a primary appendiceal neoplasm; 9 (0.3%) mucinous neoplasms, 3 (0.1%) neuroendocrine tumours grade 1 (NET G1) (formerly known as carcinoid tumour) and 1 (0.03%) sessile serrated adenoma. The mean age of those with a primary appendiceal neoplasm was 47.8 ±19.2 years. Melioidosis antibody titre was high positive with a titre of 1/5120 and blood culture yielded *Burkholderia* species, probably *B. pseudomallei*. The culture was sensitive to Meropenem and Ciprofloxacin.

The patient was commenced on initial intensive phase of the management with intravenous Meropenem 1 g every 8 hours while the ESR was 42. Chest radiography at that point showed a significant improvement (Figure 3). The therapy was continued for 6 months. The patient remains well up to now after completion of treatment which was 9 months. The patient was discharged on Cotrimoxazole and Ciprofloxacin. The maintenance dose of Prednisolone was continued as the therapy for IgA nephropathy.

Sputum for acid fast bacilli (AFB) was negative and sputum AFB culture was also negative. Tuberculin test carried with 5TU of PPD showed an induration of 12 mm. Sputum for acid fast bacilli (AFB) was negative and sputum AFB culture was also negative. The intensive phase was continued over 28 days and the patient was discharged on Cotrimoxazole and Ciprofloxacin. The maintenance dose of Prednisolone was continued as the therapy for IgA nephropathy.

Following discharge the patient was monitored biweekly with regard to his clinical status. At the end of 3 months of therapy the white cell count was 10×10°/mm^3^ while the ESR was 42. Chest radiography at that point showed a significant improvement (Figure 3). The therapy was continued for 6 months. The patient remains well up to now after completion of treatment which was 9 months. The patient was discharged on Cotrimoxazole and Ciprofloxacin. The maintenance dose of Prednisolone was continued as the therapy for IgA nephropathy.
months ago. There is no evidence of relapse of the disease.

**Figure 3.** Chest radiography at the end of 3 months of therapy

**Discussion**

This patient’s clinical presentation and chest radiography closely mimicked tuberculosis. Repeatedly negative bacteriological tests for tuberculosis should alert clinicians to look for alternative diagnoses. The concomitant suppuration, which was pyelonephritis in our patient, along with the pulmonary lesions should raise the possibility of melioidosis. Since the detection of melioidosis in Sri Lanka is increasing, it is an important differential diagnosis to be considered in patients suspected of Tuberculosis as management of them differs and delayed treatment can significantly increase morbidity and mortality.

**References**

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The infection is known to have a prolonged latent period with possible reactivation into acute and fulminating infection. The reactivation of the latent disease is often associated with concurrent diseases such as diabetes mellitus, chronic lung disease and chronic renal failure, which are considered as risk factors for developing Melioidosis. Use of steroids is also associated with an increased risk of Melioidosis. The steroid therapy for IgA nephropathy in our patient, probably would have resulted in immune suppression leading to activation of latent *B. pseudomallei* infection, acquired previously. This case report highlights the importance of considering other differential diagnoses in patients suspected of Tuberculosis as management of them differs and delayed treatment can significantly increase morbidity and mortality.

appendiceal lesions due to their poor prognosis. Furthermore, according to the surveillance, epidemiology and end results (SEER) database, appendiceal adenocarcinoma has shown a 2.6 fold rise over the past 30 years. Although neuroendocrine tumours were the most well recognized incidental neoplasms of the appendix, mucinous neoplasms of the appendix are increasingly being recognized and in some published series these are the commonest primary appendiceal tumour group. The group mucinous neoplasms of the appendix comprises a spectrum of lesions: adenoma, low grade appendiceal mucinous neoplasm (those with questionable stromal invasion) and mucinous adenocarcinoma (those with unequivocal stromal invasion). Mucinous adenocarcinoma of the appendix is known to infiltrate the peritoneal surface replacing the peritoneal cells with tumour cells. It causes copious production and accumulation of mucus within the peritoneal cavity. This is an intractable stage with available treatment options and is known as pseudomyxomaperitoneii (PMP). Although a neoplasm diagnosed as an adenoma should not show malignant behaviour, the entire spectrum of mucinous neoplasms has been reported to be associated with PMP. However, the risk of PMP with mucinous adenoma is low and most reported cases have been associated with “ruptured mucinous adenoma” which may have represented mucinous adenocarcinoma with deceptive stromal invasion. The reason for this controversy is that the predictors of malignant behavior in mucinous neoplasms, in the absence of unequivocal destructive invasion, are not fully determined. These tumours usually have mild cytological atypia and notorious to have deceptive stromal invasion patterns. Therefore, currently there are no universally accepted diagnostic criteria for mucinous tumours with equivocal morphological features. Mucinous neoplasms with questionable stromal invasion have been named in many ways in different classifications, as low grade appendiceal mucinous neoplasm (LAMN), mucinous tumours of uncertain malignant potential, mucinous tumours of low malignant potential and borderline tumours of the appendix. LAMN is the presently recommended term by the World Health Organization (WHO) 2010 tumour classification.

Appendiceal neuroendocrine tumours include carcinoid tumors, goblet cell carcinoids and mixed neuroendocrine – adenocarcinoma. Lymphomas and mesenchymal malignant are less commonly encountered malignant appendiceal neoplasms. Benign mucosal lesions include hyperplastic polyps, diffuse mucosal hyperplasia and sessile serrated adenoma. Common non neoplastic incidental lesions include granulomatous appendicitis, parasitic infestations and endometriosis.

The frequency and the clinico-pathological profile of incidental appendiceal lesions in Sri Lanka have not been published. Therefore, we conducted the present study to analyze the appendiceal pathological lesions encountered in surgical specimens in a sample of Sri Lankan patients.

**Materials and methods**

This study is a retrospective review of 3000 consecutive appendicectomy specimens and appendices included in right hemicolectomy and total colectomy specimens, received at the Department of Pathology, Faculty of Medicine, University of Peradeniya, from 2001 to 2014. Histology of mucinous tumours were reviewed and reclassified according to WHO 2010 tumour