CASE REPORT

Paraneoplastic jaundice and prostate cancer

Ana Claudia Vieira,¹ Maria Joana Alvarenga,² Jose Carlos Santos,³ Alberto Mello Silva⁴¹Pneumologia, Hospital de Egas Moniz, Lisboa, Portugal²Medicina Interna I, Hospital de Egas Moniz, Lisboa, Portugal³Urologia, Centro Hospitalar Lisboa Ocidental, Lisboa, Portugal⁴Medicina Interna I, Hospital de Egas Moniz, Lisboa, Portugal

Correspondence to

Dr Ana Claudia Vieira,
anavieira33@hotmail.com

Accepted 29 March 2017

SUMMARY

Cholestasis has numerous causes. We present the case of a 78-year-old man with a common diagnosis in this age group and gender but with an unusual presentation. There are only 11 articles published of patients with jaundice due to a paraneoplastic syndrome associated with prostate cancer. Interleukin 6 and other proinflammatory cytokines appear to contribute to the pathophysiology of this syndrome. Our patient remains symptom free 4 months after treatment initiation.

BACKGROUND

Although there are only a few reported cases of the syndrome described in this case report, it is important to keep this syndrome in mind when an elderly male patient presents with jaundice of unknown origin.

CASE PRESENTATION

A 78-year-old man was admitted to our hospital complaining of jaundice, choloria, pale stools and productive cough with haemoptoic sputum in the previous 4 days. He also reported anorexia and unquantified weight loss in the last few months. He did not have pruritus, pain, symptoms of prostatism, fever and night sweats. He had no history of liver/biliary disease, alcohol abuse, smoking, toxic drug consumption, recent travel abroad or blood transfusion. He was on antihypertensive treatment with a combination therapy of perindopril/indapamide 4 mg/1.25 mg (which we stopped because of low blood pressure) and with carvedilol 6.25 mg for rate control because he had atrial flutter. He was not on therapeutic anticoagulation. His physical exam revealed jaundice, basal crepitations at the right lung and a right inguinal mass that appeared to be a lymphadenopathy approximately 3 cm in size and was painless and elastic. He had no other positive findings on the physical exam.

INVESTIGATIONS

Laboratory analysis on admission revealed: haemoglobin 12.7 g/dL, international normalized

ratio (INR) 1.3, total serum bilirubin 12.3 mg/dL (normal <1.40 mg/dL), conjugated bilirubin 9.5 mg/dL (normal <0.3 mg/dL), aspartate transaminase 175 U/L (normal <40 U/L), alanine transaminase 188 U/L (normal <41 U/L), alkaline phosphatase 950 U/L (normal 40–130 U/L), γ -glutamyltranspeptidase 900 U/L (normal 10–71 U/L), total serum proteins 5.2 g/dL (normal 6.4–8.3 g/dL), albumin 3.3 g/dL (normal 3.5–5.2 g/dL), sedimentation rate 67 mm/h (normal <30 mm/h); serum protein electrophoresis showed an inflammatory/infectious pattern. Urine analysis was positive for bilirubin and haemoglobin. Serologic tests for hepatitis A, B and C were negative. The patient's chest radiograph revealed a right basal hipotransparency. Abdominal ultrasonography revealed multiple retroperitoneal, lumbo-aortic and mesenteric root lymphadenopathies. No abnormal findings of the liver and pancreas and no dilatation of the intrahepatic or extrahepatic biliary ducts were found. Pelvic ultrasonography showed a ureteric obstruction with left mild hydronephrosis and a large and heterogeneous prostate. The thoracoabdominal-pelvic CT scan showed retrocaval, lumbo-aortic and iliac lymphadenopathies, enlarged prostate gland, thickening of the bladder wall and left ureteric obstruction probably due to a proliferative process of the prostate. It also revealed areas of hyperdensity and hypodensity on the iliac wings. Once again, it showed a normal pancreas and liver, without dilatation of the biliary ducts. The pulmonary parenchyma had areas of bilateral ground glass and fibrous lesions with bronchiectasis in the upper lobe of the right lung. An excisional biopsy of the right inguinal lymphadenopathy found in the physical exam was performed and revealed lymph node metastases of prostate adenocarcinoma (figure 1). Prostate-specific antigen (PSA) value was >1000 ng/mL (normal <4.00 ng/mL). Calcium and phosphorus levels were normal. Interleukin-6 levels were also measured: 263.1 pg/mL (normal <17.0 pg/mL). We asked for a urologist consultation and carried out a digital rectal examination which found an enlarged and painless prostate hardened at the base. We assumed the diagnosis of prostate adenocarcinoma and the patient started therapy with bicalutamide 50 mg daily. The bone scintigraphy revealed multiple bone metastases: skullcap, all segments of the vertebral column, pelvis, rib cage, shoulder blades, sternum and proximal portion of both femurs (figure 2).

TREATMENT

After treatment with aminocaproic acid, the patient had no more haemoptoic sputum or haemoptysis due to pulmonary bronchiectasis. During

Figure 1 Lymph node metastases of prostate adenocarcinoma.

CrossMark

To cite: Vieira AC, Alvarenga MJ, Santos JC, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2016-218001

Figure 2 Bone scintigraphy with multiple bone metastases.

hospitalisation, laboratory analysis always showed elevated levels of conjugated bilirubin, transaminases, alkaline phosphatase and γ -glutamyltranspeptidase. We decided not to start therapeutic anticoagulation because of the history of haemoptysis. Two weeks after being discharged from the hospital, the patient started goserelin injections and stopped bicalutamide.

OUTCOME AND FOLLOW-UP

At the time of follow up, there was an improvement in the laboratory results: bilirubin 4.90 mg/dL (before 12.3 mg/dL), conjugated bilirubin 3.79 mg/dL (before 9.5 mg/dL), alanine transaminase 152 U/L (before 188 U/L) and γ -glutamyltranspeptidase 537 U/L (before 900 U/L). Nevertheless, the patient still had jaundice and choloria. Six weeks after treatment initiation, the patient no longer had jaundice, choloria or any other symptoms and his laboratory analysis showed a decrease in total serum bilirubin from 12.3 to 1.83 mg/dL (normal <1.40 mg/dL), conjugated bilirubin from 9.5 to 1.24 mg/dL (normal <0.3 mg/dL), aspartate transaminase from 175 to 50 U/L (normal <40 U/L), alanine transaminase from 188 to 58 U/L (normal <41 U/L), γ -glutamyltranspeptidase from 900 to 456 U/L (normal 10–71 U/L) and PSA value from >1000 to 283 ng/mL (normal <4.00 ng/mL). As expected, the patient still showed a considerable increase in alkaline phosphatase 1726 U/L (normal 40–130 U/L) because of bone metastases. Fourteen weeks after treatment initiation, aspartate transaminase, alanine transaminase and bilirubin levels were in the normal range and γ -glutamyltranspeptidase level was 260 U/L.

Our patient remains symptom free 4 months after hospital discharge.

DISCUSSION

Elevation of conjugated bilirubin is known to be due to biliary obstruction (extrahepatic cholestasis), impaired canalicular excretion (intrahepatic cholestasis) and hepatocellular injury/diseases (that usually cannot be separated from the previous two cholestatic syndromes).¹ When it comes to biliary obstruction (eg, cholelithiasis, lymphoma, intrinsic and extrinsic tumours),

the diagnosis can be done using imaging techniques. We ruled out this diagnosis at the beginning of the study of this case. As for intrahepatic causes, as the patient had no history of alcohol abuse, toxic drug consumption, recent travel abroad or blood transfusion, the only diagnosis that could be considered was a paraneoplastic syndrome associated with malignancy. In fact, it is believed that paraneoplastic syndromes can cause a reversible form of cholestasis known as Stauffer syndrome.¹ After the diagnosis of prostate cancer, this hypothesis became even more likely. It has been associated with prostate cancer and with renal cell carcinoma (more frequently), gynaecological malignancies and malignant lymphoproliferative diseases. The hepatic dysfunction that occurs in renal cell carcinoma has been associated with tumour production of cytokines, namely IL-6.² IL-6 has proinflammatory activity; for example, it induces production of acute-phase proteins, it also stimulates the proliferation and maturation of many types of cells and has a pyrogenic activity.³ Cholestasis may be due to a failure of bile formation at the hepatocyte or incapacity to secrete bile. The proinflammatory cytokines appear to be related with inhibition of hepatobiliary transporter gene expression leading to hyperbilirubinaemia and cholestasis.⁴

After the initiation of the treatment for prostate cancer, there was an improvement in the patient's symptoms and in the laboratory hepatic values. These findings support our main diagnostic hypothesis: jaundice due to a paraneoplastic syndrome associated with prostate cancer. After a study of the literature, we found only 11 articles with cases similar to ours where cholestasis was attributed to a paraneoplastic manifestation of prostate cancer.^{5–15}

Although there are only a few reported cases of this syndrome, it is important to keep this diagnosis in mind when an elderly male patient presents with jaundice of unknown origin.

Learning points

- Prostate cancer is a common diagnosis in elderly male patients. It is important to consider it in the differential diagnosis of jaundice mainly in this group of patients.
- Stauffer syndrome is a paraneoplastic syndrome that causes a reversible form of cholestasis. It is more frequently associated with renal cell carcinoma but has also been associated with prostate cancer.

Acknowledgements The authors would like to thank the Department of Anatomical Pathology, Hospital de Egas Moniz for contributing one of the images in this article.

Contributors ACV and JCS contributed to the planning, conduct, reporting, conception, design and acquisition of data for the article. MJA contributed to the acquisition of data and revision of the article. AMS contributed to the revision of the article. The Department of Anatomical Pathology, Hospital de Egas Moniz, contributed one of the images in this article.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Roy-Chowdhury N, Roy-Chowdhury J. Classification and causes of jaundice or asymptomatic hyperbilirubinemia. 2016 <http://www.uptodate.com/contents/classification-and-causes-of-jaundice-or-asymptomatic-hyperbilirubinemia> (accessed 23 June 2016).

2. Michael A. Clinical manifestations, evaluation, and staging of renal cell carcinoma. 2016 <http://www.uptodate.com/contents/clinical-manifestations-evaluation-and-staging-of-renal-cell-carcinoma> (accessed 23 June 2016).
3. Blay JY, Rossi JF, Wijdenes J, *et al.* Role of interleukin-6 in the paraneoplastic inflammatory syndrome associated with renal-cell carcinoma. *Int J Cancer* 1997;72:424–30.
4. Trauner M, Fickert P, Stauber RE. Inflammation-induced cholestasis. *J Gastroenterol Hepatol* 1999;14:946–59.
5. Reddy AN, Grosberg SJ, Wapnick S. Intermittent cholestatic jaundice and nonmetastatic prostatic carcinoma. *Arch Intern Med* 1977;137:1616–8.
6. Morís de la Tassa J, Claros González I, García-Alcalde Fernández ML, *et al.* [Cholestasis and prostatic carcinoma. description of a case and review of paraneoplastic cholestasis]. *Med Clin* 1991;96:22–5.
7. Karakolios A, Kaspis C, Kallinikidis T, *et al.* Cholestatic jaundice as a paraneoplastic manifestation of prostate adenocarcinoma. *Clin Gastroenterol Hepatol* 2003;1:480–3.
8. Koruk M, Büyükbirber M, Savaş C, *et al.* Paraneoplastic cholestasis associated with prostate carcinoma. *Turk J Gastroenterol* 2004;15:53–5.
9. Cole A, Mendelblatt D, Aguayo J, *et al.* Metastatic prostate cancer (with prostate-specific antigen of 9996) presenting as obstructive jaundice. *Am J Med Sci* 2000;319:118–22.
10. Taylor J, Lindor K. Metastatic prostate cancer simulating sclerosing cholangitis. *J Clin Gastroenterol* 1993;16:143–5.
11. Shah SH. Paraneoplastic liver dysfunction in prostate cancer. *J Pain Symptom Manage* 2006;32:511–3.
12. Nguyen V, Gurney H, van der Poorten D. Paraneoplastic hepatic dysfunction in metastatic prostate cancer: the role of cytokine dysregulation. *J Clin Oncol* 2011;29:e21–e23.
13. Kuramoto T, Senzaki H, Koike H, *et al.* Cholestatic jaundice as a paraneoplastic manifestation of prostate cancer. *Case Rep Urol* 2013;2013:1–3.
14. Okano A, Ohana M, Kusumi F. Idiopathic cholestatic jaundice may be a paraneoplastic manifestation of underlying malignancy: a case of prostate cancer. *Clin J Gastroenterol* 2014;7:278–82.
15. Kato D, Okwara C, Moreland C, *et al.* Hepatic dysfunction as a paraneoplastic manifestation of metastatic prostate adenocarcinoma. *J Investig Med High Impact Case Rep* 2014;2:232470961453992.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow