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Introductory Chapter: Bile Duct Cancer

Luis Rodrigo and Adolfo Suarez

1. Epidemiology and associated diseases

Cholangiocarcinoma (CC) is the most characteristic malignant tumour affecting to the bile ducts. It is a rare neoplasm that originates in the cells of the biliary epithelium. In the USA, it has a mean incidence of 1 case/100,000 inhabitants/year.

They are classified into three groups, with respect to their location within the biliary tree: (1) intrahepatic, (2) the upper and middle thirds and (3) the distal part of the common bile duct.

Intrahepatic tumours are the least frequent. They behave like primary hepatic tumours. Perihilar, or Klatskin, tumours are the most frequent, accounting for 60–80% of the total.

Their incidence increases with age, more cases appearing in patients aged between 50 and 70 years, with a clear predominance in men.

The diseases most frequently associated with it are primary sclerosing cholangitis (PSC), choledochal cysts, chronic infections with the parasite *Clonorchis sinensis* (typical of Asian countries and with a predominant intrahepatic location) and the presence of cholelithiasis and choledocholithiasis. The presence of PSC is an important risk factor, given that it occurs in 30% of cases. In many patients, no known risk factors are found.

2. Clinical presentation

Presentation depends fundamentally on the location of the tumour, although more than 90% of cases exhibit obstructive jaundice as their main sign. Other associated symptoms are episodes of cholangitis (which occur frequently after manipulation of the biliary tract), weight loss, abdominal pain, rebel pruritus and altered liver function test values, with elevated serum levels of bilirubin, alkaline phosphatase (AP) and gamma-glutamyl transpeptidase (GGT).

Transaminases can be quite elevated. The levels of serum tumour markers type CEA and CA 19-9 are usually raised, although they are of little diagnostic use due to their lack of sensitivity and specificity for this purpose. There are currently no other markers available that are useful for diagnosing or following up these tumours.

3. Diagnostic procedures

Abdominal ultrasound (AU) produces results of varying quality, depending on the location of the tumour. Distal tumours can be confused with primary pancreatic or periampullary neoplasms. Hilar tumours are usually infiltrative,

characteristically causing dilation of the intrahepatic bile duct and collapse of the extrahepatic duct.

Computerised axial tomography (CAT) can help identify the type and stage of an existing tumour.

Magnetic resonance cholangiography (MRC) is the current imaging technique of choice for studying the bile duct, providing information simultaneously about the bile duct and its locoregional extension.

Endoscopic ultrasound (EU) is especially useful in tumours located in the distal third of the duct, enabling the tumour to be sampled and its cytology determined.

Endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous cholangiography (PC) are currently reserved for the palliative treatment of obstructive jaundice, through the placement of biliary prostheses.

4. Classification

The classification of bile duct tumours is controversial and complex. Perihilar tumours are customarily divided into four types, depending on their extension and type of surgical resection, following the Bismuth-Corlette classification [1–3].

The working group of the Memorial Sloan-Kettering Cancer Center in New York has proposed a new classification that is better correlated with the prognosis, but which is very complex and does not take into account the current concepts of resectability.

In general, it is considered appropriate to separate perihilar tumours and those of the distal bile duct into separate groups.

5. Treatment

Resectability is determined by the absence of metastases, including retropancreatic nodes, non-invasion of the great vessels and the possibility of performing a surgical resection with free margins. Some groups recommend to do an exploratory laparoscopy prior to the indication of surgery, to rule out the presence of dissemination.

The discovery of lymph node involvement below the hepatoduodenal ligament indicates inoperability.

The placement of a biliary prosthesis before surgery is controversial. While some groups consider that it ameliorates the jaundice, allows the collection of biopsies and facilitates access to the bile duct after surgery, others postulate that it makes complications, especially cholangitis, more likely to arise [4–6].

The type of resection depends on the location of the tumour. In distal tumours, a cephalic duodenopancreatectomy is performed. This should be carried out in a reference centre to reduce the likelihood of perioperative morbidity (30%).

In hilar lesions, the resection should be individualised with respect to the extent of the tumour. A liver resection should normally be carried out that includes segments IV and V, extended according to the size of the tumour mass in order to ensure disease-free resection margins.

Liver transplantation is not a feasible therapeutic option because of the high rate of recurrence that occurs during follow-up.

In cases in which resection is not possible, it is advisable to drain the bile duct through catheters that are carefully placed through endoscopy or inserted percutaneously. Endoscopic drainage is considered easier and safer in distal tumours, while the percutaneous approach is more effective in proximal tumours. The most

common short-term complication is cholangitis, although this can be prevented by giving antibiotics before placement. In the long term, the obstruction of the prosthesis, either by tumour progression, biliary detritus or food debris, prevents the flow of bile through the duct, and the jaundice reappears.

There is currently not enough scientific evidence available to make firm recommendations about the use of adjuvant therapy after surgery. The Guidelines of the European Society of Medical Oncology (ESMO) suggest the use of chemotherapy and/or palliative radiotherapy after non-curative resections and of chemoradiotherapy after curative resections.

Neoadjuvant therapy is not usually recommended because of the deterioration that patients usually present at the time of diagnosis [7–10].

6. Prognosis and prevention

The prognosis of bile duct cancer is bad. Malignant tumours of the bile duct are usually diagnosed at advanced stages, with infiltration of neighbouring organs such as the liver, gallbladder, adjoining vessels and distant metastases, which often contraindicates surgery. Average survival is 12–24 months. Distal tumours have a better prognosis, with a 5-year survival of 15–25%.

Screening programmes have not proved to be effective for the early detection of these tumours. However, in carriers of PSC, it is advisable to undertake periodic surveillance using imaging techniques (e.g. MRC) and the determination of CA 19-9 serum levels, although none of these procedures is sufficiently specific [11, 12].

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