B.D., a 55-year-old woman with increasing abdominal pain and bloating accompanied by a 23-pound weight loss, was found to have multiple liver lesions during a computed tomography (CT) scan on March 21. A liver needle core biopsy conducted April 3 showed the adenocarcinoma and the following pathology report: Immunoreactive to cytokeratin, 19; cytokeratin, 7; monoclonal antibody epithelial-related antigen, 31; and anti-cytokeratin, 5.2. Also immunoreactive to estrogen receptor. Gross cystic disease fluid protein, chromogranin, cytokeratin 20, hepatocyte antigen, caudal-related homeobox 2, mesothelin, and thyroid transcription factor-1 were negative.

This immunohistochemical profile and histologic findings are nonspecific but suggest a breast or possibly a gynecologic primary. Less likely is a tumor of pancreatobiliary origin. The human epidermal growth factor receptor 2 (HER2) protein expression was 3+ (normal: 0–3+). Tumor marker carcinoembryonic antigen (CEA) was greatly elevated at 21,828 ng/ml (normal: 0–4 ng/ml). Positron-emission test (PET) scan was negative for other areas of disease. Esophagastroduodenoscopy and colonoscopy were negative.

A mammogram was performed on April 22 and showed a 1 cm lesion in the left breast. B.D. was admitted to the hospital on April 23 with failure to thrive, jaundice, decreased oral intake, and constipation. She was in liver failure with a bilirubin of 5.3 (normal: 0–1.4 mg/dl), alkaline phosphatase of 721 (normal: 20–145 U/L), aspartate aminotransferase of 620 (normal: 3–70 U/L), alanine aminotransferase of 155 (normal: 3–78 U/L), calcium level of 11 (normal: 8.4–10.4 mg/dl), and total protein of 7.1 g/dl (normal: 5.9–8.3 g/dl).

B.D. had a prior history of smoking one pack per day when she was aged 19–21. She drank one glass of wine per month. In addition, one of her sisters was diagnosed with breast cancer in her early 40s.

B.D. received two infusions of carboplatinum one week apart. She also received a dose of herceptin; however, she experienced progressive liver and renal failure and died on May 8, only 48 days after her initial presentation with liver masses on CT scan.

**Overview**

Oncology nurses often see cancers that are unusual or rare. Diagnosis and tumor identification are possible but, unfortunately, some patients develop a cancer of unknown primary (CUP). CUP often is metastatic at diagnosis and, because of the rarity of the disease, presents a challenge for oncology nurses educating their patients. Symptoms of metastatic cancers, such as lung or breast, can be taught, but CUP presents with no known primary and often multiple symptoms of metastatic disease (pain or weight loss). This unknown can be scary for patients and nurses. This article will review CUP, diagnosis, pathology, treatment, and nursing considerations.

**Epidemiology**

CUP accounts for about 2%–3% of all cancer diagnoses (Hainsworth & Greco, 2008b). An estimated 31,490 cases with 45,090 deaths occurred in 2008 (American Cancer Society, 2008)—the difference between figures is from lack of specificity in recording the underlying cause of death on certificates (Tan, Amar, & Perry, 2007). The average age at diagnosis was about 60, with more men being affected than women (Cancer.net, 2008). CUP is defined as "histologically confirmed metastases in the absence of identifiable primary tumor despite a standardized diagnostic approach" (Pentheroudakis, Briasoulis, & Pavlidis, 2007, p. 418). Workup of this metastatic disease often will not identify a primary site. Biopsy of a mass often results in a pathologic diagnosis, possibly identifying a specific tissue type that may help with the development of a treatment regimen. On autopsy, common identifiable sites of primary tumor are hepatobiliary tree, lung, and pancreas (Hainsworth & Greco, 2008b).

Because many patients have metastatic disease at presentation, such as lung, bone, liver and lymph nodes, they often are very ill, have poor performance status, and can decline fairly rapidly (Hainsworth & Greco, 2008b). Nonspecific symptoms may include weight loss, fatigue, and anorexia (Pentheroudakis et al., 2007; Tan et al., 2007). Favorable prognostic factors include tumor in lymph nodes, soft tissue, less sites of metastatic disease, female, good performance status, normal lactate dehydrogenase, normal albumin, and normal...