CASE REPORT

Primary manifestation of hepatocellular carcinoma as a cervical mass

Boyunda kitle ile ortaya çıkan hepatoselüler karsinom

Emin KARAMAN, M.D.,[1] Harun CANSIZ, M.D.,[1] Engin ACIOĞLU, M.D.,[1] Dilek YILMAZBAYHAN, M.D.[2]

Metastasis of hepatocellular carcinoma to the head and neck region is unusual and its exact frequency is unknown. A 72-year-old male patient presented with a mass on the left side of the neck. Clinical examination showed multiple, painless, immobile lymphadenopathies in the cervical region. Computed tomography revealed both an irregular mass in the cervical region and hepatomegaly accompanied by a lobulated liver contour. The patient was diagnosed as having hepatocellular carcinoma following an excisional biopsy from the cervical mass and fine needle aspiration biopsy from the liver.

Key Words: Carcinoma, hepatocellular; head and neck neoplasms.

Hepatoselüler kanserin baş-boyun bölgesine yayılımı çok nadirdir ve sıklığı tam olarak bilinmemektedir. Yetmiş iki yaşındaki erkek hasta boynun sol tarafında gelişen kitle nedeniyle kliniğimize başvurdu. Klinik muayenede servikal bölgede ağrısız, hareketsiz kitleler halinde çok sayıda lenfadenopati saptandı. Bilgisayarlı tomografide servikal bölgede düzensiz kitle görüldü, karaciğer lobüle yapıda ve büyüktü. Boyundaki kitleden yapılan eksizyonel biyopsi ve karaciğerden yapılan ince iğne aspirasyon biyopsisi sonucunda hepatoselüler karsinom tanısı kondu.

Anahtar Sözcükler: Karsinom, hepatoselüler; baş-boyun neoplazileri.

Hepatocellular carcinoma is the most common primary malign tumor of the liver in adults. It is associated with hepatitis B infection. Hepatocellular carcinoma may involve adjacent and distant regions by haematogenous and lymphogenous ways.[1] Head and neck metastasis of hepatocellular carcinoma is unusual. We reported a patient presenting only with a mass localized in the upper cervical region. Systemic evaluation revealed multiple lesions both in the liver and adjacent lymph nodes. Histopathological comparison of excisional biopsy from the cervical mass and fine needle aspiration biopsy from the involved region of the liver revealed metastasis of hepatocellular carcinoma to the neck.

CASE REPORT

A 72-year-old male patient who was referred to our clinic, presented with a mass localized on the left side of the neck. The patient was neither a smoker nor a drinker and had no pertinent medical history. He had become aware of the mass three months before admission and stated that it had increased in size. Clinical

examination revealed multiple lymphadenopathies on the jugulodigastric cervical region. They were painless, immobile and adhesive to adjacent tissue. The largest one was 3x2 cm in diameter. Endoscopic examination was performed and there was not significant pathological lesion in the nasopharynx, oropharynx, hypopharynx and larynx. Esophagoscopic examination did not reveal a pathological lesion. Cardiovascular, respiratory, abdominal and pelvic routine systemic examinations were normal.

Posterior-anterior thorax radiogram, routine blood biochemical tests, hemogram, erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and prothrombin time (PT) results were within normal ranges.

Cervical and thorax computed tomography (CT) was performed. Cervical CT revealed solid masses on the left jugulodigastric cervical region which were 35x21x19.5 mm, 30x18x15 mm, 20x16x12 mm, 25x18x15 mm, 20x18.5x16 mm in diameter and close to each other and compatible with multiple lymphadenopathies. They had lobulated contours and showed peripheral contrast-enhanced (Fig. 1). Thorax CT revealed no pathology but the right hepatic lobe that was included in the cross-sections of the thorax CT had a non-homogeneous, hypodense view and lobulated contour. Hence, abdominal CT was performed and it showed that the parts of the liver that exhibited a lobulated contour were larger than normal. Left hepatic lobe passed the midline. The posterior segment of the right lobe was involved completely and extended to the dome (Fig. 2). Hypodense areas were determined in the lesion. These findings were compatible with hepatocellular carcinoma. Also, two similar hypodense lesions were determined in the anterior segment of the right lobe, the largest one with a diameter of 3x3 cm. They were evaluated as intrahepatic metastases. Multiple lymphadenopathies were determined in retrocrural, coeliac, retrocaval, intraaortacaval, left paraaortic regions, the largest one with a diameter of 4x3 cm. A detailed biochemical assessment was performed for hepatic functions; Aspartate transaminase (AST) 57 U/L, alanine aminotransferase (ALT) 49 U/L, gamaglutamyl transpeptidase (G-GT) 194 U/L, alkaline phosphatase (ALP) 392 U/L, lactic dehydrogenase (LDH) 579 U/L, total protein 7.1 g/dl, alfa-fetoprotein (AFP) 300 ng/ml, total bilirubin 1.5 mg/dl, direct bilirubin 0.4 mg/dl. Blood urea, creatinine, total protein, albumin levels, PT and PTT measurements were within reference ranges.

Excisional biopsy of the cervical lymph node and fine needle aspiration biopsy from the liver guided by ultrasonography were performed under general anesthesia. Histopathological examination of cervical lymph nodes revealed low- differentiated carcinoma. Microscopic examination revealed large areas of necrosis, and tumor cells with hyperchromatic and pleomorphic nuclei, arranged around the capillary network (Fig. 3). LCA, CD3, CD20, cytokeratin 7 and cytokeratin 20 antibodies were assessed for a differential diagnosis. Negative results of immunos-
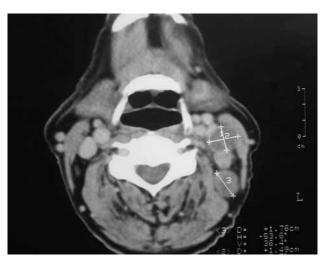

Fig. 1 - *Computed tomography showed multipl lympadenopathies localized on the jugulodigastric cervical region.*

Fig. 2 - *Abdominal computed tomography showed the complete involvement of posterior segment of the right hepatic lobe.*

taining and morphological findings were indicative of hepatocellular carcinoma. Histopathological examination of fine needle aspiration from the involved region of the liver confirmed the presence of hepatocellular carcinoma (Fig. 4).

DISCUSSION

The most common primary malign tumor of the liver is hepatocellular carcinoma in adults. Hepatitis B virus (HBV) infection is a risk for increased incidence of hepatocellular carcinoma. HBV infections may be symptomatic but mostly they are asympto-

matic and viral DNA eventually becomes incorporated into the host genome of infected hepatocytes which leads to malignant transformation and eventually hepatocellular carcinoma.[2] The other etiological factors that enhance the development of primary liver carcinoma are alcoholic, postnecrotic and hemochromatic cirrhosis, ingested carcinogens (aflatoxins and cycasin) and parasitosis (schistosomiasis or clonorchiasis). About 80% to 90% of all liver cell carcinomas develop in cirrhotic livers.[3-5]

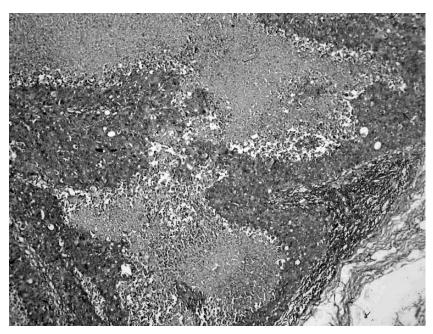Metastasis of hepatocellular carcinoma to the head and neck region is unusual. However in most

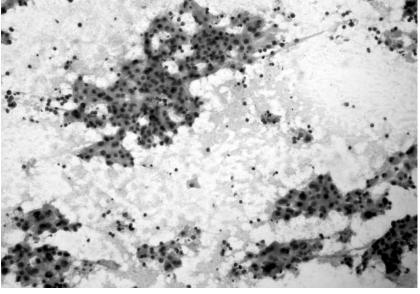**Fig. 3 -** *Microscopic view of excised cervical lymph nodes (H-E x 200).*

Fig. 4 - *Microscopic view of fine neddle aspiration of the hepatic region (H-E x 275).*

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of the reported cases, the first manifestations were metastatic lesions.[6,7] Our patient is an example for this situation. Hepatocellular carcinomas with extrahepatic metastases have been reported in 50% of all cases.[3,8] Distant metastases of hepatocellular carcinoma tend to occur in the lungs (51.6%), adrenal capsule (8.4%), and less frequently in bone, pancreas and kidneys.[9-12] Metastatic tumors in the head and neck regions are relatively rare.[13] Metastases to the head and neck can be haematogenous, lymphogenous or both.[1,14] In previous reports, hepatocellular carcinoma manifestations in the head and neck regions, presented with supraclavicular lymph node metastases, Virchow-Troisier's lymph node,[15] metastases in the esophagus,[12] mandible,[3,16] oral cavity,[6,14,17] nasal and paranasal sinuses,[7,10] temporal bone,[18] zygoma[19] and orbita.[20] Most of these cases were the first manifestations of the carcinoma.

The exact frequency of metastasis of hepatocellular carcinoma to the head and neck is not known. These metastases can be haematogenous. Previous studies reported that the most readily apparent route for haematogenous spread is via the caval venous system, then through the pulmonary circulation and from the heart to the sinuses through the arterial vessels to the head and neck. Significant increments in the intrathoracic pressure cause a retrograde flow from the usual venous channels back through the prevertebral and vertebral venous plexuses (Batson's plexus).[7,11,16] This retrograde flow may at times progress upwards as far as the base of the skull. Similar retrograde flow may be observed in the jugular venous system. With the rich intercommunication near the sinuses (pterygoid plexus, cavernous sinus, and superior portion of the pharyngeal plexus) the two pathways could very readily play a role in the metastasis of tumors to the oral cavity, mandible and paranasal sinuses.[7,10,11,16]

Metastases to the head and neck can also be lymphogeneous. Once they invade the lymphatic system, they spread along lymphatic channels to the hepatic lymph nodes in the porta hepatis, thence to the celiac nodes, and finally into the thoracic duct. Hepatic tumors situated close to the convexity of the right hemidiaphragm may spread via lymphatic vessels to glands in the mediastinum and thence to supraclavicular nodes via the thoracic duct of the right lymphatic duct. Malignant hepotocytes might also reach the thoracic duct indirectly as a result of spread from peritoneal metastases.[15] In the patient presented here, the primary tumor involved the liver extensively and almost diffusely, and the hepatic, peripancreatic, celiac and paraaortic lymph nodes were invaded by tumor, making it likely that this was the route by which malignant cells reached the thoracic duct.

For two different pathways have been proposed to explain the involvement of adjacent supraclavicular lymph node from the upper end of the thoracic duct. The first one, involves the upper end of the thoracic duct itself and direct invasion from here to the lower end of the internal jugular lymphatic trunk and thence along the efferent lymphatic duct of the adjacent supraclavicular lymph node. Secondly, pressure changes in the thoracic duct by respiratory effort or the occlusion of thoracic duct entrance to the venous circulation may affect refluxing up to the lumen of the internal jugular lymphatic duct and the efferent lymphatic duct.[15] In our review of the literature we could not find jugulodigastric lymphatic chain involvement in metastatic hepatocellular carcinoma. In all these similar case reports, the first manifestation of neck metastases of hepatocellular carcinoma were determined in the supraclavicular region where it was localized very close to the upper end of the thoracic duct. In the patient presented in this article, the lesion was placed in the upper deep jugular lymphatic chain (jugulodigastric region). To the best of our knowledge, refluxing up to this level from the thoracic duct without the involvement of supraclavicular lymph nodes has not been described previously in the literature.

Once metastasis of hepatocellular carcinoma to head and neck region has occurred, the prognosis of the patient is very poor.[11] Kanazawa and Sato[21] reported a mean survival rate of 21 weeks, ranging from two weeks to two years, after diagnosis of metastatic disease to the oral region. Our patient died one month after the operation during the chemotherapy period. Accordingly, in our opinion, the survival rate, which was reported for oral cavity metastases, may be applicable for all hepatocellular carcinoma metastases in the head and neck region.

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