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Iris metastasis from clear cell renal cell carcinoma: A case report

Wang TT *et al*. Iris metastasis from ccRCC

Abstract

BACKGROUND

Clear cell renal cell carcinoma (ccRCC) is a common type of tumor that can metastasize to any organs and sites. However, it is extremely rare for ccRCC to metastasize to the iris. Here, we describe a rare case of iris metastasis from ccRCC with a history of left nephrectomy in 2010.

CASE SUMMARY

A 62-year-old male was admitted to the hospital owing to blurred vision and red eyes and a mass was found on the iris in the right eye. B-scan ultrasonography revealed a well-bounded high-density lesion at the corner of the anterior chamber at a 3-4 o'clock position. Phacoemulsification with simultaneous intraocular lens implantation and iridocyclectomy was performed in the right eye. The lesion was confirmed to be metastatic ccRCC by histological and immunohistochemical analyses. The patient was still alive at 9 mo after surgical treatment. Ocular metastasis can be an initial sign with a poor prognosis. Timely detection and treatment may improve survival. Clinicians should pay attention to similar metastatic diseases to prevent misdiagnosis leading to missed treatment opportunities.

CONCLUSION

This report of the characteristics and successful management of a rare case of iris metastasis from ccRCC highlights the importance of a comprehensive medical history, histopathology, immunohistochemistry, and clinical manifest for successful disease diagnosis.

Key Words: Iris metastasis; Clear cell renal cell carcinoma; Diagnosis; Prognosis; Literature review; Case report

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Core Tip: Here, we report a rare case of iris metastasis from clear cell renal cell carcinoma (ccRCC). We found that a complete medical history, histopathology, and immunohistochemistry combined with clinical manifestations are crucial for a successful diagnosis of this disease. In addition, a total of 11 cases of iris metastasis from ccRCC were identified in the literature and are reviewed in this report.

INTRODUCTION

Renal cell carcinoma (RCC) is the most common type of renal tumor (approximately 90%), and clear cell RCC (ccRCC) is the most common subtype of RCC, accounting for approximately 75% of cases. More than 50% of patients with ccRCC are asymptomatic and rely on computed tomography (CT) for diagnosis[1]. While up to half of ccRCCs are confined to the kidney at presentation, approximately 30% develop metastases[2]. CcRCC can metastasize to any organs and sites including the eyes, but the most common sites of metastases are lung (50%) and bone (33%)[3]. It is very unusual for ccRCC to metastasize to the iris.

The iris is a rare location for cancer to metastasize and spread, and most instances occur with breast and lung cancers[4]. Iris metastasis is usually unilateral and unifocal; bilateral and multifocal involvement are considerably less common. Owing to its rarity, iris metastasis is often misdiagnosed. In patients with iris lesions and a history of RCC, the possibility of kidney cancer metastasis should be considered. The clinician should perform an iridocyclectomy promptly and confirm the diagnosis by pathology. In this article, we report a 62-year-old male who was diagnosed with iris metastasis from ccRCC. We hope this case will raise awareness of this rare disease, as clinical suspicion of this condition will lead to early diagnosis and treatment.

CASE PRESENTATION

Chief complaints

A 62-year-old male was admitted to the hospital owing to the discovery of a mass in his right eye 1 mo ago with no history of eye disease.

History of present illness

The patient had a medical history of blurred vision and red eyes.

History of past illness

A previous left nephrectomy with the diagnosis of ccRCC [World Health Organisation/International Society of Urological Pathology (WHO/ISUP) nuclear grading was not mentioned].

Personal and family history

The patient denied any family medical history.

Physical examination

The visual acuity of the left eye was 0.6 and that of the right eye was 0.4. The conjunctiva of the right eye was slightly congested, and the vessels of the nasal conjunctiva were tortuous and dilated. The cornea was clear. A keratic precipitate was visible behind the cornea and a red mass with a diameter of approximately 5 mm was visible at 2-5 o'clock in the front of the cornea. The depth of the anterior chamber was moderate. The iris texture was not clear and was partially posterior synechiae. The pupil was round, but slow to light reflex. Pigment was seen in the precrystalline capsule. There was no obvious abnormality in the left eye except the phacoscotasmus. The intraocular pressure was 14 mmHg in the left eye and 21 mmHg in the right eye.

Laboratory examinations

Complete blood counts, aspartate aminotransferase, alkaline phosphatase, bilirubin, serum electrolytes, creatinine, and urea were all within normal ranges.

Imaging examinations

B-scan ultrasonography revealed the central depth of the anterior chamber was approximately 3.14 mm and a well-bounded high-density lesion could be seen at the corner of the anterior chamber at 3-4 o'clock (Figure 1). Chest CT showed a lobulated uneven enhanced mass at the anterior basal segment of the lower lobe of the right lung, with clear boundaries and small streaks at the margin, indicating the high possibility of malignancy. Abdominal CT showed that the left kidney was absent and there was no obvious mass in the right kidney.

Pathological examination

The mass was received in several small pieces with a total diameter of 1 cm. Histologically, normal iris tissue could be seen around the tumor (Figure 2A). There was no fibrous envelope separation between the tumor and iris tissue. The tumor cells were large, cube-shaped, and in a solid nest-like arrangement. The cytoplasm was clear because it contained a lot of glycogen and lipids. The nuclei were round or ovate, and the nucleoli were visible (hematoxylin and eosin staining, × 400) (Figure 2B). There were abundant capillaries in the mesenchyme. Tumor cells were immunoreactive for CKpan (Figure 2C), vimentin, PAX-8 (Figure 2D), CD10 (Figure 2E), and CA IX, but negative for CK7, CD117, CK20, and TTF-1. The Ki-67 proliferation index was 10%.

FINAL DIAGNOSIS

The lesion was confirmed to be metastatic ccRCC (WHO/ISUP nuclear grade 2).

TREATMENT

To restore the patient's vision and make a clear diagnosis, phacoemulsification with simultaneous intraocular lens implantation and iridocyclectomy was performed after the clinician assessed the patient's condition in the right eye. During the operation, a lesion about the size of a peanut could be clearly seen on the surface of the iris. The

lesion was confirmed to be metastatic ccRCC. After the diagnosis was confirmed, the patient refused targeted drug therapy and transbronchial lung biopsy (TBLB) and discharged himself from the hospital against the advice of doctors.

OUTCOME AND FOLLOW-UP

The patient was still alive, with no recurrence noted, at 9 mo post-surgery.

DISCUSSION

RCC includes many subtypes, with the predominant ones being ccRCC, papillary renal tumors, and chromophobe renal tumors[5]. Of these three subtypes, ccRCC is the most common and has the worst prognosis because it is usually found at an advanced stage[4]. CcRCC may have no specific symptoms in the early stage, whereas symptoms such as hematuresis may appear in the advanced stage. However, a diagnosis cannot be made only by urine examination and should be assisted by imaging examination. More than 90% of kidney tumors can be detected by CT and such imaging can distinguish between benign or malignant tumors, as well as their relationship to surrounding tissue[1].

The preferred treatment for any nonmetastatic, solid, or Bosniak III or IV complex cystic kidney mass is surgical excision, preferably using a minimally invasive approach[1]. After local nephrectomy, tumors often recur near the surgical scar, and approximately 30% of nonmetastatic kidney tumors will metastasize to other organs after surgery[6]. Metastasis of RCC is hematogenous and lymphatic. The lung is the most common location of distant metastasis, followed by bone and liver. Ocular metastasis is rare, and iris metastasis has only been recorded in a few cases[3,4,6-8]. Both primary and metastatic renal tumors are reported to have VHL mutations, while primary tumors also have TERT promoter C228T mutation, but abnormal deletion of TERT appears in metastatic tumors[2]. The absence of TERT abnormality in metastasis supports the notion that an aberrant VHL protein is sufficient to confer metastatic capacity in ccRCC,

as proposed in tumors with low-grade histology. Metastasis of ccRCC to the iris may originate from low-grade clones in high-grade primary tumors[2].

Iris metastasis is extremely rare. In previous reports, the most common site of uveal metastases is the choroid, followed by the iris and ciliary body. This may be due to the posterior ciliary artery supplying a large amount of blood to the posterior choroid. Iris metastasis accounts for 7.8% of uveal metastasis[8]. The most common primary tumors with iris metastasis are breast cancer in women and lung cancer in men[3]. In addition, iris metastasis can also occur with esophageal squamous cell carcinoma[9], prostate carcinoma[10], kidney cancer[1-4,6,7], gastrointestinal malignancies[9], sarcoma and melanoma[11]. Nephrogenic iris metastasis accounts for < 1% of ocular metastasis and < 5% of iris metastasis[12]. After diagnosis of uveal metastatic cancer, more than half of patients have associated systemic metastasis, with the lungs being the most common site, followed by bones, liver, and central nervous system[2]. Our patient had suspected lung metastasis, but the patient refused TBLB, and we were unable to make a definitive diagnosis.

In the domestic and international literature, we found only 12 cases of iris metastasis from renal tumors, including our report (Table 1). This further confirms the rarity of nephrogenic iris metastases. The 12 patients were all male, aged between 54 and 70 years old. There were eight cases of blurred vision and decreased vision. The iris masses were 2-10 mm in size. Among them, eight cases had ccRCC as the primary tumor and one case had renal adenocarcinoma. The time from diagnosis of RCC, ccRCC, or renal adenocarcinoma to metastasis to the iris ranged from 1 to 13 years, and four cases were detected by iris metastasis as the first manifestation. There were four cases of ipsilateral metastasis and five cases of contralateral metastasis, and only one case of bilateral iris metastasis. There were three cases that only metastasized to the iris, compared with five cases that simultaneously metastasized to the iris and lungs and seven cases with metastasis to other organs. Four patients died between 2 and 9 mo after the diagnosis of iris metastasis owing to multiple site metastasis or cerebral infarction. Only five patients remained alive during the follow-up (6-18 mo).

The main clinical manifestations of iris metastasis are blurred vision, ocular pain, redness, photophobia[8], diplopia, exophthalmos, and periorbital swelling[9]. Visual acuity is usually poor when patients develop ipsilateral choroidal metastasis associated with retinal detachment, or with severe anterior chamber tumor implantation with secondary glaucoma[7]. When tumor cells spread to the anterior chamber, secondary glaucoma can occur owing to the spread of inflammation. Metastatic tumors may manifest as stromal nodules or ill-defined iris thickening. Only 10% of the iris mass is visible, with the mass being 1-12 mm in size and isolated, fragile, yellowish-white, pink, or red[8]. The pink or red color may be due to the abundance of capillaries in the tumor.

When a patient is known to have a primary tumor and a significant iris mass, the possibility of iris metastasis from the primary tumor should be considered and a timely biopsy should be performed to make a definitive diagnosis. However, when a patient has no exact primary tumor and there is no obvious iris mass, it is easy to miss the diagnosis of iris metastasis. Slit lamp examination, fluorescein angiography, and ocular ultrasound are highly warranted. In addition, early systemic examination is crucial to determine whether there are tumors in other organs. At this time, attention should be paid to the identification of other diseases of the eyes. Differential diagnoses of nonpigmented iris masses include iris choristoma, acquired iris cysts, unpigmented melanoma, sphincter-leiomyomas, granulomatous iridocyclitis, and xanthogranulomas[13].

When an ophthalmologist is unable to make an immediate diagnosis, slit lamp examination, fluorescein angiography, and ocular ultrasound should be performed first, even if these tests do not provide additional assistance in diagnosis. Positron emission tomography/CT can help identify benign or malignant lesions and indicate potential primary sites[9]. Ultimately, diagnostic tests for an iris mass include fine-needle aspiration biopsy and mass excision biopsy. When tumor cells are seen under the microscope, the corresponding immunohistochemistry is performed in combination with the patient's clinical symptoms, medical history, and imaging examination to obtain a final diagnosis and determine the primary tumor site.

Treatments for an iris mass include radiotherapy, laser therapy, chemotherapy, anti-vascular endothelial growth factor (VEGF), and ophthalmectomy. The current recommended treatment option is external beam radiation, which can damage the DNA of rapidly growing tumor cells and is effective in reducing the size of the lesion and improving or stabilizing visual acuity. Laser treatment-including transpupillary thermotherapy, laser photocoagulation with the use of argon or krypton, and photodynamic therapy-has significant curative effect. Chemotherapy, which uses different cytotoxic agents depending on the type of cancer, can lead to tumor shrinkage and sometimes even complete regression. VEGF-targeted treatment, such as bevacizumab, has been shown to be beneficial in patients with different types of cancers and has been used in clinical practice with significant efficacy[11]. In addition, systemic interferon therapy is effective for nephrogenic iris metastases, with a report showing that a tumor began to resolve after 3 wk of treatment and had completely resolved at 16 wk[7]. Therefore, conservative interferon therapy may be considered when a patient does not have visual loss, secondary glaucoma, or multiple organ metastasis.

CONCLUSION

Ocular metastasis is extremely rare and can be an initial sign with a poor prognosis of primary tumor. The prognosis of ocular mass is good after treatment, but systemic prognosis remains poor. The overall mean survival of iris metastasis is 20 mo and the median survival is 13 mo[8]. Timely detection and treatment may improve survival.

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