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Solitary Adrenal Metastasis: A Case Report of Aberrant Behavior of Prostate Cancer

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Abstract

Background: Metastasis of prostate cancer for the adrenal gland is not uncommon; however, a solitary metastasis to the adrenal gland is a rare case. The diagnosis of such cases is challenging.

Case presentation: A Caucasian male with prostate cancer under androgen deprivation therapy after radiotherapy for a locally advanced lesion. Positron emission tomography/Computed Tomography revealed an adrenal lesion. The mass was removed, and histopathological examination showed adenocarcinoma of prostatic origin. Prostate-specific antigen decreased dramatically after adrenalectomy.

Conclusion: Atypical sites of metastasis, like the adrenal gland, might be challenging in diagnosis, but beneficial outcomes could ensue after the optimum intervention.

Keywords: Adrenal; Adrenalectomy; Metastasis; Prostate Cancer; PSA Recurrence

List of abbreviations: ADT: Androgen Deprivation Therapy; FDG: Fludeoxyglucose; PCa : Prostate Cancer; PSA: Prostate Specific Antigen; mPCa: Metastatic Prostate Cancer; PET/CT: Positron Emission Tomography/ Computed Tomography

Introduction

Background

Prostate cancer (PCa) is the second most common cancer (excluding skin cancer) in males worldwide (Sung et al., 2021) [1]. The implementation of screening programs using prostate-specific antigen (PSA) has improved the early detection of localized disease, while metastatic and advanced cases have rarely been encountered. Metastasis occurs in 35% of autopsies of prostate cancer patients (Bubendorf et al., 2000) [2]. Among newly diagnosed PCa cases, 17% may develop metastasis (Scosyrev et al., 2012) [3]. The distribution of metastatic foci expresses the genetic background and phenotypic features of the primary lesion (Bubendorf et al., 2000; Ganeshan et al., 2017) [2,4]. Detection of metastases and their distribution pattern is a critical prognostic workup (Ganeshan et al., 2017; Nafissi et al., 2020) [4,5].

We report a case of metastatic PCa (mPCa) that followed an unusual course and distribution. Solitary metastasis to the left adrenal gland developed without remarkable clinical or biochemical manifestations for nearly a year. The patient was under a combination of radiotherapy and androgen deprivation therapy (ADT) and experienced biochemical response for 3 years after diagnosis. Only one case of similar behavior was reported in a patient with castrate-resistant PCa (Ashrafi et al., 2020) [6]. In our case, the patient has not been surgically castrated.

Case Presentation

A 66-year-old male patient presented to the urology clinic in April 2020 with chronic fatigue, loss of appetite, and weight loss, accompanied by rising PSA. The patient had locally advanced prostate adenocarcinoma and he started local radiotherapy on prostate, pelvic lymph nodes, and pelvic bones (35 sessions) without castration. It was finished on 12/2016. He has been on hormonal therapy since then (Bicalutamide and Goserelin). A Positron emission tomography / computed tomography (PET/CT), done 3 years later (with PSA levels < 0.1 ng/ml), revealed an asymptomatic left adrenal mass about 1×1 cm that has no metabolic activity, and no action had been taken.

The level of PSA started to rise gradually in Jan 2020 (Figure 1). Urinary tract infection, urine retention, and urethral instrumentation were excluded.

A whole-body PET/CT scan was done using intravenous fludeoxyglucose (F-18-FDG8 mCi). The left adrenal mass was about 5×4.2 cm and showed a low patchy metabolic activity (avidity to FDG). Prostatic tissue showed no metabolic activity. Internal iliac lymph nodes, abdominal lymph nodes, spleen, and liver were metabolically inactive. Kidneys and contralateral adrenal are normal. The right inferior pubic ramus showed metabolically inactive lesion, while the right superior ramus showed a non-united fracture. Scanning of lungs, pleura, supradiaphragmatic lymph nodes, cervical lymph nodes, parotid glands, orbits, and brain for metabolically active lesions was negative. Hormonal therapy was continued by the oncology team as it was, and Uro-surgical consultation was considered.

An enhanced CT examination of the abdomen was done at 7/2020, and it showed a slight increase in the size of the left adrenal mass (5.1×4.5 cm) (Figure 2). An osteolytic lesion involves the right inferior pubic ramus, a dense sclerotic lesion involves the right superior ramus, and a small dense lesion involves the left iliac bone. All bony lesions were not avid to FDG in the PET/CT scan at (6/2020).
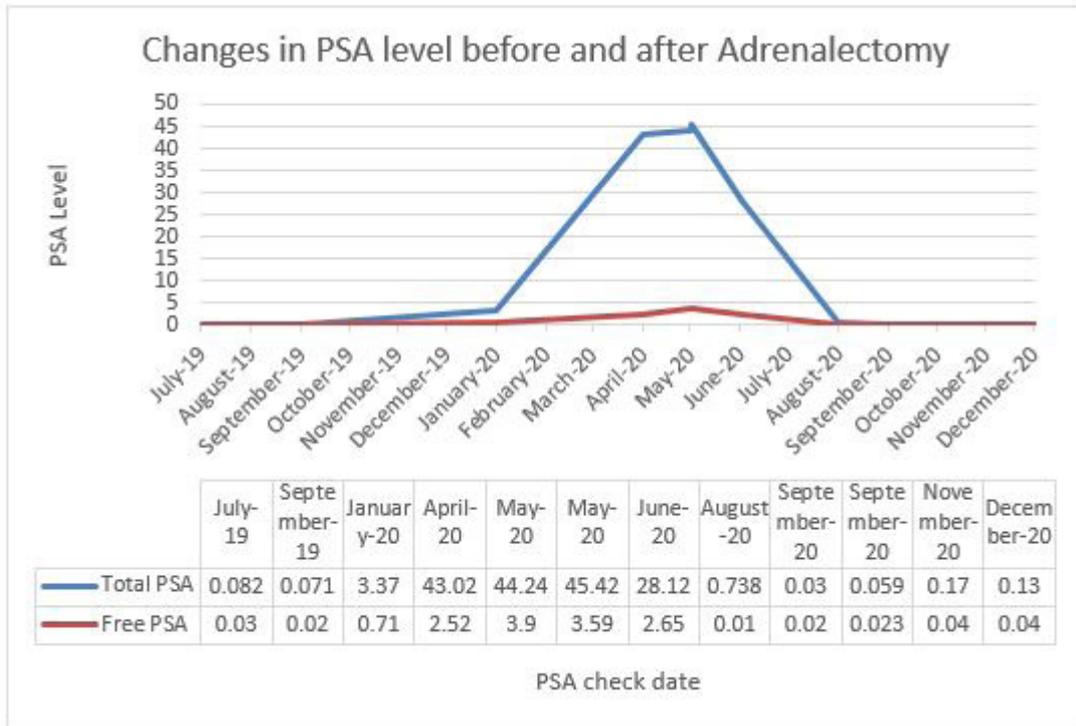
Figure 1: The course of PSA levels through the time period from 6/2019 to 12/2020
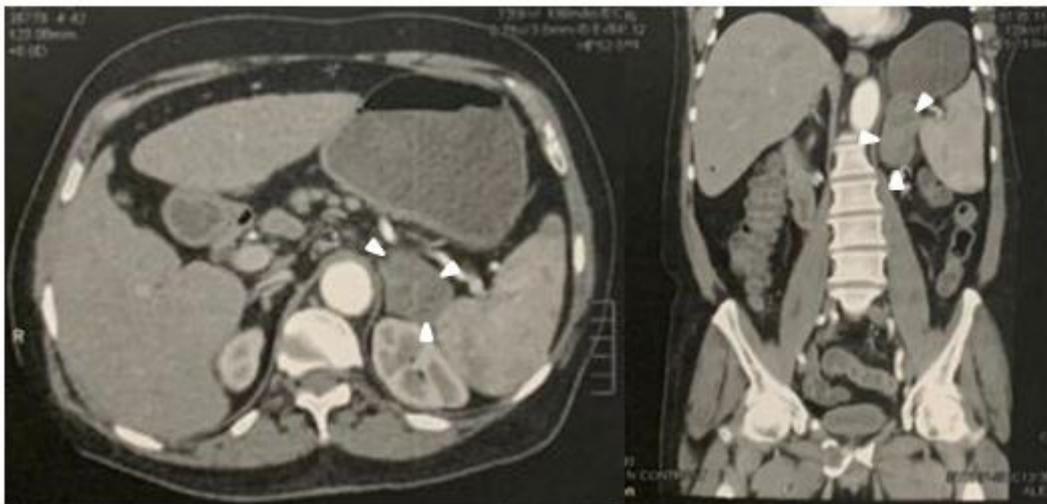

Figure 2: Enhanced PelviAbdominal CT shows left adrenal mass (white arrow heads) in axial and coronal images

We have done laparoscopic left adrenalectomy on 7/2020. The mass was about $11 \times 6 \times 5$ cm (Figure 3). The cut surface was pink-brown soft tissue, with focal nodularity. The histologic examination showed solid and cribriform growth patterns, focal areas of necrosis, capsular and vascular invasions, and neoplastic cellular features. The adrenal mass was immune stained using PSA, inhibin, and chromogranin A, and it was positive for PSA only, suggesting a metastasis from prostate cancer.

As shown in (Figure 1) (from 8/2020 to 12/2020), PSA levels declined dramatically after adrenalectomy. The follow-up of total PSA levels showed that it has never gone above 0.2 ng/ml. A follow-up enhanced MRI examination showed a benign-looking right hepatic focal lesion, enlarged lymph nodes (< 2.5 cm) at the celiac, porta hepatis, and right internal iliac groups. Bone mineral density (BMD) of spine vertebrae (L1 to L4) was moderately low (BMD = 0.91 g/cm², T-score = -1.3). The hormonal therapy was shifted to a combination of Goserelin and Abiraterone acetate.

Figure 3: Gross Morphology of the left adrenal mass after laparoscopic excision

A PET/CT follow-up has been done on 1/2021. It showed no metabolic activity at the prostate, left adrenal site, abdominal viscera, supradiaphragmatic lymph nodes, chest, orbit, or brain. The pubic rami lesions and internal iliac lymph nodes did not show any changes or metabolic activity.

Discussion

In this case, we have faced many challenges. First, the patient was biochemically responsive to radiation and hormonal treatment for 3 years, however, incidental imaging discovered a metastatic lesion. That early detection of the mass was not accompanied by endocrine symptoms, local prostatic symptoms, or a rise in the PSA levels. Second, after expectant management and close monitoring of the patient for one year, the PSA did not rise until the adrenal lesion was more than 4-fold its initial size. About 40% of visceral metastasis have normal PSA levels, and the median PSA level in anaplastic mPCa patients with adrenal metastasis is 1.9 ng/ml (Ganeshan et al., 2017) [4]. PSA in mPCa patients does not correlate with the pattern of visceral metastasis distribution (Vinjamoori et al., 2012) [7]. A cautious approach should lead to the interpretation of PSA levels during monitoring PCa patients.

The second challenge was that the adrenal is one of the least common sites of distant metastasis of PCa. According to autopsy studies, the most common sites of metastasis are bone (90%), followed by lung (45%), then liver (25%), and pleura (21%). Adrenal metastasis was found in 13% of metastatic cases (Bubendorf et al., 2000) [2]. Furthermore, adrenal involvement in a large population of mPCa (> 74800 cases) was less than 1% (Gandaglia et al., 2014) [8]. Examining images of 508 patients with PCa revealed only one case with metastasis to the adrenal gland (Long & Husband, 1999) [9]. The adrenal gland is invaded in 15% of 620 PCa patients with atypical metastasis sites (not bone or pelvic lymph nodes) (Vinjamoori et al., 2012) [7] and in 5.9% of patients with anaplastic PCa (Ganeshan et al., 2017) [4]. Therefore, routine workup of PCa patients may miss or underestimate an adrenal gland focus as a probable cause of biochemical relapse.

Invasion of the adrenal gland with PCa metastasis tends to be associated with multiple sites. The adrenal gland is involved in 0.3% of cases with solitary-site metastasis, in contrast to 4.2% of cases with multiple sites (Gandaglia et al., 2014) [8]. PCa patients with bone metastasis have a higher rate of adrenal involvement than patients without bone metastasis (Gandaglia et al., 2014) [8]. Sixty-eight

percent of patients with atypical sites of metastasis have associated bone metastasis. Regarding solitary visceral metastasis (including adrenal), only 27% have no associated bone foci, and 52% have no associated lymph node foci (Vinjamoori et al., 2012) [7]. Again, a case of a solitary metastasis in an uncommon site present with unanticipated behavior.

The return of biochemical response state after adrenalectomy might carry favorable prognostic indices. However, the explanation of the event is still questionable. Many hypotheses tried to model the behavior of PCa distant invasion (Batson, 1940; Bubendorf et al., 2000; Morgan-Parkes, 1995; Vinjamoori et al., 2012) [2,7,10,11]. In our case, there is no spinal involvement, no pelvic or abdominal involvement, no associated supradiaphragmatic organ invasion, and no other abdominal visceral invasion. Accordingly, this case does not follow either pathway of PCa distant invasion; retrograde approach via spinal vasculature, or cava-type pathway (Vinjamoori et al., 2012) [7].

Our argument is based on that the pattern of metastasis is affected by tumor size, stage, histologic grade (Bubendorf et al., 2000) [2], by the synchronous invasion of other organs (Vinjamoori et al., 2012) [7], and by the medical and surgical treatment that alter the tumor microenvironment (Hess et al., 2006) [12]. The complex bidirectional interaction between ADT, radiotherapy, local hormonal changes, and modification of adrenal hormonal profile can play a role in steering the circulating PCa cells into or away from distinct homing nests (Kassi & Moutsatsou, 2011; Mostaghel et al., 2019; Reilly et al., 2015; Xu et al., 2006) [13,14,15,16]. Furthermore, similar factors can modify the cell-cell and cell-connective tissue interactions in an unpredictable manner, so that PCa patients may present eventually with an atypical site of metastasis (Reilly et al., 2015; Xu et al., 2006) [15,16]. This multifactorial hypothesis was supported by the variability of both PCa molecular profile (Sabharwal & Sharifi, 2019) [17] and atypical sites of distant deposits; for example; orbit, parotid gland, breast, and muscle fibers (Long & Husband, 1999; Vinjamoori et al., 2012) [7,9].

Finally, the literature lacks strong evidence that recommends the best action for a solitary visceral metastasis in patients after definitive treatment of PCa. Developing such evidence is facing many methodologic challenges, and most of the available data are from case reports (Ohlmann et al., 2021) [18]. However, the importance of close monitoring of patients after ADT is obvious, and the pattern of PSA responses could be sedating in such cases.

Conclusion

The work-up for PCa patients after non-surgical treatment should be tailored on an individual basis. The changes that occur in relation to long-term therapeutic regimens might alter the natural course of the disease. Atypical sites of metastasis, like the adrenal gland, might be challenging in diagnosis, but beneficial outcomes can ensue after the optimum intervention. Investigating the mechanism of PCa metastasis is a critical step to reduce cancer-related mortality.

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Authors contribution

Both authors contribute equally to the preparation and writing of the manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

Patient consent was obtained.

Consent for publications

A written consent has been obtained from the patient.

Competing interests

There are no competing interests.

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