

FOAMY-GLAND VARIANT PROSTATIC ADENOCARCINOMA WITH PRIMARY HORMONE RESISTANCE: CLINICAL, PATHOLOGICAL AND THERAPEUTIC INSIGHTS

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ABSTRACT

Prostate cancer is a common cancer with high histological heterogeneity influencing the prognosis and management. Conventional acinar adenocarcinoma represents the most common histological form; however, some rare variants have been described, including foam cell adenocarcinoma, which represents an unusual variant of acinar adenocarcinoma, first described by Epstein in 1996. The available data regarding its clinically pathological characteristics and prognosis remain limited. We report the case of a 62-year-old patient with prostatic adenocarcinoma with foam variant diagnosed at a metastatic stage. The anatomopathological study highlighted a glandular proliferation composed of cells with abundant and foamy cytoplasm, associated with often pycnotic nuclei, which can constitute a diagnostic trap due to their sometimes slightly atypical cytological appearance. The clinical and histological data and therapeutic management modalities are detailed. This observation highlights the rarity of this histological variant and the importance of its recognition by pathologists, in order to avoid an underestimation of the tumor grade and a therapeutic delay. Knowledge of the morphological characteristics of prostatic foam cell adenocarcinoma is essential to ensure accurate diagnosis and appropriate oncological management.

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Introduction

Prostate cancer is one of the most commonly diagnosed cancers in humans and a major cause of cancer-related morbidity and mortality worldwide. Although conventional acinar adenocarcinoma represents the predominant histological form, this tumor is characterized by morphological and biological heterogeneity likely to influence prognosis and therapeutic strategies.

Among the rare histological variants is prostatic foam cell adenocarcinoma, considered a subtype of acinar adenocarcinoma and initially described by Epstein in 1996. This entity is distinguished by tumor cells with abundant cytoplasm, vacuolated or foamy, associated with sometimes discrete nuclear atypies. These morphological features can constitute a real diagnostic trap, exposing to an underestimation of the tumor grade, or even to confusion with benign lesions or reaction processes. Data concerning its clinically pathological characteristics, biological behavior and prognosis remain limited due to its rarity.

We report here the case of a prostatic adenocarcinoma with a foam variant diagnosed at a metastatic stage, focusing on clinical and pathological aspects, the diagnostic difficulties encountered and the oncological implications of this unusual histological form.

Case Presentation

A 62-year-old man (initials S.Y.A.) with no significant medical history presented with progressive bilateral sciatica pain and functional impairment of the lower limbs. Lumbar computed tomography revealed diffuse sclerotic bone lesions of the spine, raising suspicion for metastatic disease (Figure 1).



Figure 1: A: multiple bone lesions of the lumbosacral spine on lumbar CT. B: spinal compression of the L2

Laboratory tests showed a markedly elevated total prostate-specific antigen (PSA) level of 44.4 ng/mL, prompting referral to urology. Digital rectal examination revealed a firm, stone-hard prostate, suspicious for malignancy. Multiparametric MRI of the prostate demonstrated a 21 cm³ gland with an extensive lesion highly suggestive of clinically significant neoplasia (Figure 2).

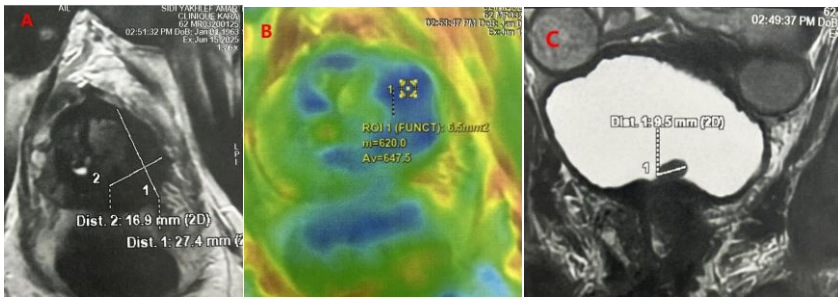


Figure 2: A: a large prostatic lesion range very strongly suspected of clinically significant neoplastic lesion (PI-RADS V2.1 5/5), of 27x17x35 mm interesting the left peripheral zone at the three stages, predominantly lateral, with peri-prostatic, of the neuro-vascular strip. B: MRI sequence in diffusion, area of interest ROI 1 suggestive of malignity (low ADC). C: prostatic lesion in continuity with a small nodular bud of the bladder floor of 09mm

Twelve systematic prostate biopsies were performed, eight of which were positive for adenocarcinoma. Histopathological analysis revealed an acinar prostatic carcinoma with a foamy (foamy-gland) cell component, initially scored Gleason 3 + 4 (ISUP grade 2), predominantly in the left lobe, with a 30 % grade 4 component and perineural invasion. On subsequent review, the Gleason score was revised to 5 + 4, confirming a high-grade tumor with a rare foamy gland variant (Figure 3).

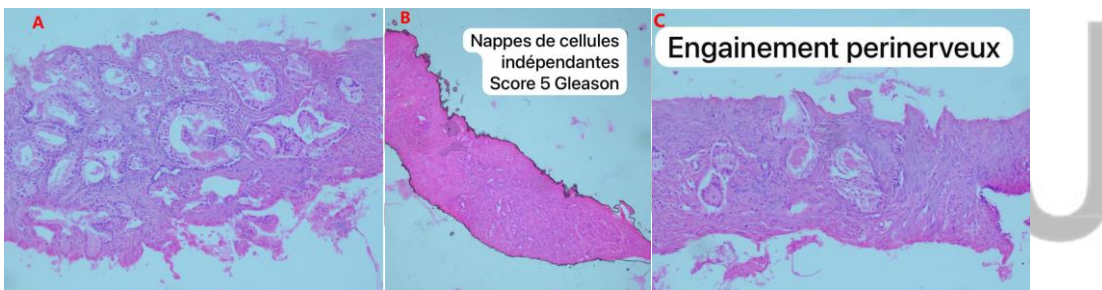


Figure 3: A: foam cells with high magnification. B: layers of independent cells scoring 5 gleason. C: perineural invasion

Staging evaluation with thoraco-abdomino-pelvic CT and bone scintigraphy showed multiple sclerotic bone metastases with spinal cord compression at T9 and T12. The case was staged as T4N1M1b according to the TNM classification. The patient began androgen deprivation therapy with a LHRH analogue on 02/07/2025 and received palliative radiotherapy (8 Gy) targeting spinal levels D8–D11 and L1–L4. Two months later, PSA paradoxically increased to 55.5 ng/mL despite castrate-level testosterone (0.27 ng/mL). After the second LHRH injection, repeat evaluation confirmed biological progression with persistently elevated PSA and testes-suppressed testosterone (0.025 ng/mL), accompanied by elevated lactate dehydrogenase (LDH) and alkaline phosphatase levels, indicating primary resistance to hormone therapy. On 04/11/2025, the patient presented with ECOG PS 2 , Karnofsky Score: 50% and paraparesis and lower limb paresthesia. Given the clinical and biochemical evidence of hormone-resistant disease, chemotherapy with docetaxel (50 mg/m² on days 1 and 15) was initiated, along with bone-targeted therapy using zoledronic acid following appropriate dental clearance. Early response to treatment was encouraging: within one month, PSA, LDH, and alkaline phosphatase levels significantly declined (Table 1).

parameters C1J1 C2J15

parameters	C1J1	C2J15
PSA total	96,12 ng/mL	13,55 ng/mL
Testostéronémie	0,025 ng/mL	
LDH	369 UI/L	217 UI/L
PAL	1620 UI/L	789 UI/L

Table 1: Evolution of biological parameters during systemic treatment

After two months of chemotherapy, the patient showed marked clinical improvement, achieving ECOG PS 1 Karnofsky Score: 80%, ambulating independently, with resolution of paraparesis and paresthesia. The patient continues treatment with a LHRH analogue, docetaxel, daily prednisone (10 mg), and zoledronic acid. Radiologic evaluation is scheduled for February 2026.

Discussion

Prostatic foam cell adenocarcinoma is a rare histological variant of acinar adenocarcinoma, accounting for less than 1-2% of diagnosed prostatic cancers. Initially described as a low-grade entity with deceptively banal cytology, this variant is now recognized as potentially aggressive, especially when associated with high-grade architectures, marked stromal reaction or early metastatic presentation.

From a prognostic point of view, the literature data are heterogeneous. The old series reported a behavior globally comparable to that of acinar adenocarcinomas with the same Gleason score. However, more recent studies, in particular those by Zhao and Epstein as well as the large series by Gao and Epstein (2023), have highlighted the existence of high-grade shapes, often associated with a cribriform architecture, an important stromal demobolasia, an early extraprostatic extension and a high incidence of bone metastases. In this series, nearly 75% of patients had an adverse outcome (metastasis or specific death), highlighting the pejorative evolutionary potential of certain forms of this variant.

The reported case perfectly illustrates this aggressive spectrum, with an inaugural bone metastatic presentation, complicated by a medullary compression, despite an intermediate initial Gleason score (ISUP 2). This discrepancy between the histological grade and the clinical course highlights the risk of prognostic underestimation in this variant, especially when the analysis relies solely on cytological atyp, often discrete, to the detriment of tumor architecture and the clinical context.

Therapeutically, there are no specific recommendations for the management of prostatic foam cell adenocarcinoma, and the treatment is based on advanced prostate cancer standards. Nevertheless, several authors have reported a heterogeneous response to hormone therapy, with cases of primary or early castration resistance. In the observation presented, the biological progression under hormone therapy, despite testosterone levels at the castration threshold, confirms this trend and suggests an aggressive tumour biology, close to that of hormone-resistant prostate cancers from the outset.

The early initiation of docetaxel-based chemotherapy resulted in a marked biological response (decrease in PSA, LDH and PAL), associated with significant clinical benefit, which joins the data suggesting that these aggressive forms could benefit from early therapeutic intensification. This observation reinforces the interest of a multimodal approach from diagnosis, particularly in high-risk metastatic forms.

Biologically and molecularly, recent data suggest that certain spume variants, particularly those associated with marked demoplasia, exhibit unfavorable molecular alterations, such as PTEN loss and nuclear accumulation of p53, known to be associated with rapid progression and a lower response to hormonal treatments. Although these analyses were not performed in our case, the observed clinical evolution is compatible with this adverse biological profile described in the literature.

Finally, this entity poses a real diagnostic challenge. The deceptively banal cytologic aspect, the abundance of foamy cytoplasm, the possible aberrant expression of basal markers and the significant stromal reaction can lead to diagnostic errors or undergrading. Specialized anatomopathological review, as in our case, appears essential to confirm the diagnosis, adjust the Gleason score and guide the therapeutic strategy.

Conclusion

Prostatic adenocarcinoma with foam cells is a rare histological variant, whose clinical behavior may be significantly more aggressive than its initial cytological characteristics suggest. The immediate metastatic presentation, the primary resistance to hormone therapy, and the good response to early chemotherapy observed in our case highlight the importance of a global evaluation integrating clinical, radiological, and histological data, beyond the single Gleason score.

The early recognition of this variant by pathologists is crucial in order to avoid an underestimation of the evolutionary potential and a therapeutic delay. In the future, a better molecular characterization of these tumors could allow identifying prognostic and predictive markers of response, paving the way for more personalized therapeutic strategies. Multicentric studies and broader series are necessary to better define the actual prognosis and optimize the management of this rare entity.

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