



## Editorial

# Prostate Cancer Before 50: A Wake-Up Call

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Prostate cancer is the second most common malignancy in males and the fourth most common malignancy overall globally.<sup>1</sup> Prostate cancer is a disease occurring in older males ( $\geq 60$  years); however, recent studies show an increased trend in young patients (age  $\leq 50$  years).<sup>2–4</sup> While the majority of prostate cancers in younger patients are less aggressive than those in older patients, emerging evidence indicates that biological factors, particularly genetic alterations, rather than chronological age alone, determine disease aggressiveness.<sup>5</sup> Younger patients with prostate cancer may present with biologically aggressive variants driven by specific molecular features rather than chronological factors. Studies demonstrate that aggressive variants occur in approximately 15 to 20% of early-onset cases.<sup>6</sup>

We present a case of a 46-year-old male patient, presented with persistent backache and was found to have metastatic prostate cancer with widespread sclerotic skeletal metastases and spinal cord compression. Decompressive laminectomy with biopsy confirmed metastatic poorly differentiated adenocarcinoma of prostatic origin. Next-generation sequencing identified an SLC45A3(1)–ERG(4) gene fusion, a rearrangement associated with unfavorable outcomes and representing a distinct molecular subtype.<sup>6,7</sup>

Initial serum prostate-specific antigen (PSA) was markedly elevated. Gallium-68 (<sup>68</sup>Ga)–prostate-specific membrane antigen (PSMA) positron emission tomography-computed tomography confirmed extensive skeletal and nodal metastases. The patient underwent bilateral orchidectomy followed by palliative radiation and systemic therapy including abiraterone with prednisolone, enzalutamide, and three cycles of <sup>177</sup>Lu–PSMA radioligand therapy.

Despite initial responses, the patient experienced progression with rising PSA levels and worsening neurological symptoms. Repeat laminectomy and biopsy 2 years after initial diagnosis revealed squamous cell carcinoma, indicating histological transformation, a recognized mechanism of therapeutic escape through lineage plasticity.<sup>8</sup>

Clinicians should be careful with younger symptomatic individuals, especially if they have unexplained back pain or vertebral lesions. Current guidelines (United States

Preventive Services Task Force, National Comprehensive Cancer Network, European Association of Urology)<sup>9,10</sup> do not recommend routine PSA screening below the age 50. However, selective evaluation may be appropriate in symptomatic or genetically predisposed individuals, balanced against the established limitations of PSA screening including modest impact on disease-specific mortality and minimal effect on all-cause mortality.<sup>11</sup>

The presence of SLC45A3–ERG fusion suggests genetically driven disease with implications for prognosis and treatment. A molecular profiling for mutations in TP53, PTEN, and RB1 (negative in this case), may inform therapeutic strategies.

Early-onset cases with aggressive features warrant prompt multidisciplinary care, genetic counseling, and consideration for clinical trial enrolment, particularly when standard treatments show resistance.

We propose that selective early PSA screening may be appropriate in specific circumstances like symptomatic individuals (bone pain, urinary obstruction, or neurological symptoms suggestive of metastatic disease), men with strong family histories, and those with known genetic predispositions (BRCA2 mutations or Lynch syndrome). This approach maximizes the likelihood of detecting clinically notable disease.

Future research should focus on identifying biomarkers to stratify risk in young men and developing screening strategies that maximize benefit while minimizing harm. Until such evidence emerges, clinical judgment should guide evaluation of symptomatic individuals while avoiding unnecessary screening.

**Patient's Consent**

Patient consent has been obtained.

**Conflict of Interest**

None declared.

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