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Case Report Open Access

Autoimmune Haemolytic Anemia Associated with Testicular Non Seminomatous Germ Cell Tumor (NSGCT): A Unique Para Neoplastic Presentation

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Abstract

Para neoplastic syndromes (PNS) are relatively rare and often an interesting systemic manifestation of malignancy. PNS are remote clinical or biochemical effects triggered by altered immune responses to neoplasm, not explained by the local extension or mass effect. PNS may presage the diagnosis or develop anytime during the course of malignancy. Depending on the organ systems affected PNS may be classified as neurological, endocrine, mucocutaneous and/or hematological.

Anemia is a common complication seen in patients with malignancy and is associated with increased morbidity, poor tolerance to treatment and worse clinical outcomes. Etiology of anemia of malignancy is multifactorial like nutritional, anemia of chronic disease, drug induced, direct involvement of bone marrow, blood loss and hemolytic anemia. Identification of the underlying cause of anemia and appropriate management impacts clinical outcomes. Autoimmune hemolytic anemia (AIHA) as PNS is commonly seen with hematological malignancies but such association with solid malignancies particularly like testicular tumors is very rare. Here we discuss a clinical profile and management of Para neoplastic autoimmune hemolytic anemia in a patient with testicular nonseminomatous germ cell tumor (NSGCT) and review of literature. Here we illustrate an unique Para neoplastic presentation of AIHA in association with testicular NSGCT. Such association needs to be verified after excluding other more common etiologies.

Case Report

A 37-year-old young male patient with no comorbidities presented with complaints of swelling and ulcer on the right side of scrotum and radiating pain along right lower back to thigh [1]. He also complained of fatigue and breathlessness on exertion limiting his day to day activities. General Physical examination revealed pallor, tachypnea, tachycardia, pedal edema and Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 3. Local examination confirmed right testicular swelling with ulcerated lesion over the right side of the scrotum. Rest of the systemic examinations was normal. PET CT scan showed metabolically enhancing right testicular mass lesion, multiple brain parenchymal, hepatic, right adrenal, and pancreatic, and bone lesions with enlarged Para-aortic lymph nodes as shown in Figure 1. MRI Brain confirmed multiple ring enhancing space occupying lesions in the brain. USG guided biopsy with immunochemistry from liver lesions revealed atypical tumor cells positive for SALL4, OCT 3/4, CK, CD30 and negative for beta-HCG and GLYPICAN 3, suggestive of metastatic germ cell tumor, predominantly embryonic type as shown in Figure 2. Tumor markers at baseline were, Alfa-fete protein (AFP) of 1330 ng/mL, beta-Human Chorionic gonadotropin (bHCG) of 3755 mIU/mL and Lactate Dehydrogenase (LDH) of 1140 IU/L. Based on imaging findings, tumor markers and histopathology the tumor was staged as stage IIIC, poor risk testicular NSGCT according to International Germ Cell Cancer Collaborative Group (IGCCCG) risk classification. Baseline blood parameters as shown in Table 1 revealed a hemoglobin level of 5.7 g/dl, white blood cell count of 27200/µl, platelet count of 376 × 103/µl, mean corpuscular volume of 74 fl, and a corrected reticulocyte count of 4.2%. Peripheral smear showed normocytic normochromic anemia with moderate anisopoikilocytosis, marked polychromatic with spherocytosis and nucleated red blood cells, fair number of microcytes and few tear drop cells. WBC series show neutrophil with left side shift and platelets were adequate, morphologically normal [2]. Biochemistry panel showed serum total and direct bilirubin of 3.2 mg/dl (0.4-1.3 mg/dL) and 0.8 mg/dl, serum lactate dehydrogenase of 680 IU/L (240- 460 IU/L), vitamin B12, 369 pg/mL (225-1100 pg/mL) and direct Coombs test was positive for immunoglobulin G, CD 3a. Serum protein electrophoresis showed no abnormal monoclonal band spike (Table 2).

Management and Patient Course

After confirming the diagnosis of AIHA, the patient was started on corticosteroid, Tab Prednisolone 1 mg/ Kg once daily per orally after meals. Baseline Hemoglobin was 5.7 g/dl at presentation. Despite initiation of steroids, the patient required repeated weekly blood transfusions in the first two months after diagnosis. Patient received palliative radiotherapy to the brain and lumbar vertebra for symptomatic brain and bony metastasis at presentation. In view of extensive disease at presentation, and poor PS orchiectomy was deferred and started with chemotherapy on the fourth week of diagnosis. Chemotherapy included a 21 day cycle of Bleomycin, Topside, Cisplatin (BEP) based regimen.

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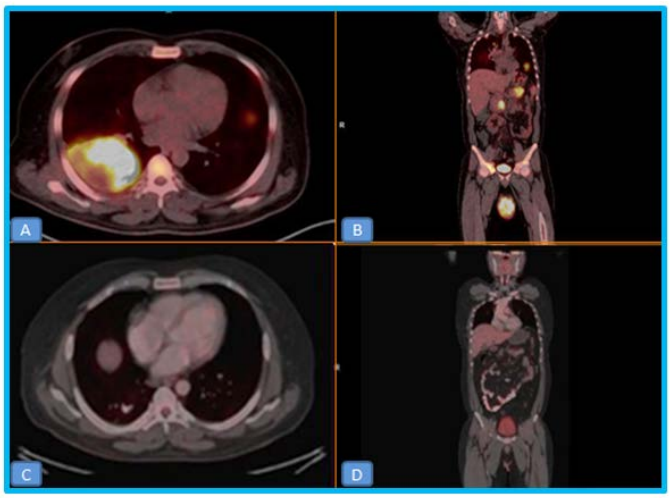

Figure 1: PET-CT at diagnosis (A & B) showing metabolically enhancing right testicular mass lesion, right adrenal, pancreatic, bone lesions with enlarged Para-aortic lymph nodes and following 3 cycles of chemotherapy (C & D) showing metabolic resolution all the lesions.

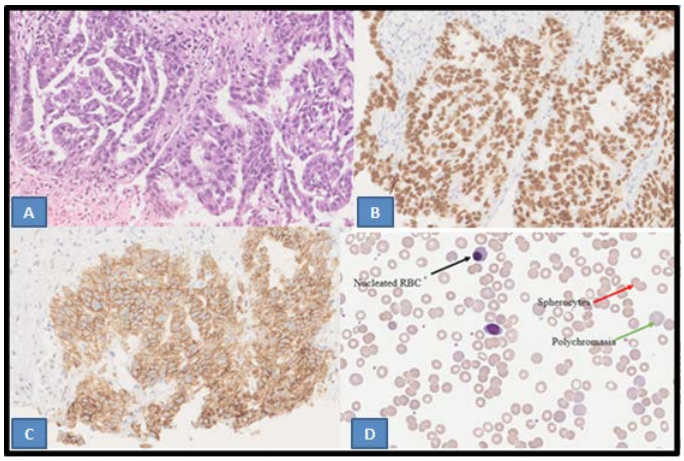

Figure 2 A: H & E stained slides under 20X, tumor cells in glands and papillae, have moderate eosinophilia cytoplasm, moderately pleomorphic vesicular nuclei with frequent mitosis. (B & C) tumor cells with immuno-histochemistry studies showed SALL 4 positivity (B) & CD 30 positivity (C) & (D) showing peripheral smear suggestive of hemolysis .

Hemoglobin consecutively started improving significantly with the chemotherapy cycles, and by the end of 2 cycles of chemotherapy his transfusion requirements stopped [3]. Hemoglobin was improved to 9.7 by 3 weeks after the completion of chemotherapy and corticosteroid dose was tapered gradually, suggesting diagnosis of malignancy related AIHA-PNS. Subsequently, he underwent right High inguinal orchiectomy with scrotum-entomb, as the scrotum was also involved at presentation. After that, he also underwent liver segmentectomy and right video assisted transthoracic surgery (VATS) guided non-anatomical pulmonary wedge metastasectomy. Post surgery AFP 3.25 ng/mL and HCG of < 2.39 mIU/mL. Patient is on regular follow up and is doing fairly well with no post treatment sequelae at one year follow up with Hemoglobin of 13 and no evidence of disease recurrence [4].

Discussion

This is a rare and interesting case of warm antibody AIHA associated with widely metastatic NSGCT. AIHA is commonly seen in patients with hematological malignancies [5]. However, an association

Table 1: Baseline Lab parameters.

	On admission	Reference range
White cell count (per µl)	27200	4000–11000
Hemoglobin (g/dl)	5.7	12.0–18.0 (men)
Hematocrit (%)	19	35.0–54.0
Red cell count (per pl)	2.55	4.5–6.5
Mean corpuscular volume (fl)	74	76.0-96.0
Platelet count (per µl)	3,76,000	150,000–450,000
Differential count (%)		
Neutrophils	85	40–75
Lymphocytes	10	20–45
Monocytes	2	01-Aug
Basophils	0	00-01
Eosinophils	2	01-Jun
Sodium (mmol/l)	139	135–145
Potassium (mmol/l)	4.5	3.5–5.5
Chloride (mmol/l)	103	95–110
AFP (ng/ml)	920	< 10
Blood urea nitrogen (mg/dl)	34	Jun-20
Creatinine (mg/dl)	2.84	0.7–1.4
Calcium (mg/dl)	7	8.5–10.5
Total protein (g/dl)	7.5	6.4–8.2
Albumin (g/dl)	2.41	3.6–5.6
Aspartate aminotransferase (U/liter)	41.9	0–40
Alanine aminotransferase (U/liter)	13.97	0-37
Alkaline phosphatase (U/liter)	344.6	108–306
Total bilirubin (U/liter)	3.2	0.0–2.0
Conjugated bilirubin (U/liter)	0.8	0.0–0.2
Lactate dehydrogenase (U/liter)	614	85–240
M spike (g/dl)	Not seen	
Reticulocyte count (%)	7.9	0.5–2.5
Prothrombin time (seconds)	16	12.0–15.0
International normalized ratio (seconds)	1.1	
Activated Prothrombin thromboplastic time (seconds)	66.5	30
Folic acid (ng/ml)	4.8	4.0–18.0
Vitamin B12 (ng/l)	669	193–986
Iron level (µg/dl)	96	65–175
Transferrin (mg/dl)	191	200–360
Saturation (%)	20	20–44
Ferritin (µg/l)	93	5–244
ANA	Negative	

Table 2: Correlation of tumor markers and markers of hemolytic anemia during disease course.

	At diagnosis	After 1st cycle of chemotherapy	After completion of chemotherapy	After completion of treatment
AFP (<10.0 ng/ml)	1330	18.5	2.42	4.09
BHCG (mIU/ml)	3755	4.75	< 2.39	< 2.39
LDH (240- 460 U/L)	1140	377	248	148
Hemoglobin (g/dl)	5.7	7.6	9.7	10.7
Reticulocyte count	7.90%	4.80%	2%	2%
Bilirubin (mg/dl)	3.2	2.6	1.4	1.2

between AIHA and malignant solid cancers is less commonly reported, with a notably rare occurrence in NSGCT [2, 6]. In 2016 NE nova et al reported, only 14 (1.29%) out of the 1083 patients with solid tumors were associated with autoimmune Para neoplastic syndromes and only three had AIHA [6]. Joe et al. compiled 52 case reports of AIHA associated with solid malignancies, commonly associated solid malignancies are renal cell carcinoma and Kaposi sarcoma and only 3 cases were associated with testicular tumors.

The pathophysiology of hemolysis in PNS-AIHA is said to be related to the destruction of RBC by cross reacting antibodies formed against the tumor itself [1, 5]. Alternatively, the tumor may release the substance which alters the RBC membrane and makes it antigenic. To label AIHA as PNS, an underlying malignancy must be present and the diagnosis of AIHA must be made using Coombs test and presence of anti-erythrocyte antibodies as seen in our case [2, 6]. In our case, patient peripheral smear, indirect hyperbilirubinemia, increased reticulocyte count, LDH, with positive direct Coombs test for immunoglobulin G, CD 3a in the background of NSGCT suggest AIHA as PNS.

The therapeutic options for AIHA management are corticosteroids, splenectomy, rituximab, and thereafter any of the immunosuppressive drugs [5, 7, 8]. Management of AIHA associated with solid malignancies is not well defined, are often refractory to steroids and resolve rapidly following treatment directed at underlying malignancy such as surgical resection or chemotherapy [2, 9]. In our case despite steroids, there was minimal improvement in anemia. Management of testicular tumors involves upfront high inguinal orchiectomy followed by chemotherapy with BEP. We treated our patient with BEP based regimen upfront due to poor general condition, for which he responded well and resolution of anemia paralleled resolution of cancer.

Conclusion

AIHA is a well-known Para neoplastic phenomenon in lymph proliferative disorders but, an association between AIHA and malignant solid cancers is less commonly reported, with a notably rare occurrence in NSGCT. AIHA in solid malignancies are often refractory to steroid therapy and treatment of underlying malignancy is crucial for the management.

References

1. Henry K (2019) Para neoplastic syndromes: Definitions, classification, pathophysiology and principles of treatment. Semin Diagn Pathol 36:204-210.
2. Puthenparambil J, Lechner K, Kornek G (2010) Autoimmune hemolytic anemia as a Para neoplastic phenomenon in solid tumors: A critical analysis of 52 cases reported in the literature. Wien Klin Wochenschr 122:229-236.
3. Canale D, Feldman R, Rosen M, Harvard MB (1975) Autoimmune hemolytic anemia associated with seminoma. Urology 05:411-414.
4. Autore F, Pasquale R, Innocenti I, Fresa A, Sora' F, et al. (2021) Autoimmune Hemolytic Anemia in Chronic Lymphocytic Leukemia: A Comprehensive Review. Cancers 13:5804.
5. Nenova IS, Valcheva MY, Beleva EA, Tumbeva DY, Yaneva MP, et al. (2016) Autoimmune Phenomena in Patients with Solid Tumors. Folia Med (Plovdiv) 58:195-199.
6. Barcellini W, Fattizzo B (2021) How I treat warm autoimmune hemolytic anemia. Blood 137:1283-1294.
7. Hariz A, Hamdi MS, Boukhris I, Cherif E (2019) Autoimmune haemolytic anaemia in pancreatic adenocarcinoma: a potential paraneoplastic presentation. BMJ Case Rep 12:e229807.
8. Loh KP, Kansagra A, Asik A, Ali S, Dahiya S (2015) Paraneoplastic Autoimmune Hemolytic Anemia in Ovarian Cancer: A Marker of Disease Activity. Rare Tumors 7:5598.
9. Honecker F, Aparicio J, Berney D, Beyer J, Bokemeyer C, et al. (2018) ESMO Consensus Conference on testicular germ cell cancer: diagnosis, treatment and follow-up. Ann Oncol 29:1658-1686.