stings would be required to deliver a lethal dose of hymenoptera venom for a non allergic adult weighs 70 kg [2]. Ninety-nine percent of the alkaloid component of red fire-ant venom is made up of 2, 6, di-substituted piperidines that have hemolytic, antibacterial, insecticidal, and cytotoxic properties. Venom alkaloids do not generate IgE antibody responses and thus do not appear to be responsible for allergic reactions [3]. Anaphylaxis is more common and severe in subsequent stings [4]. Serious complications like laryngospasm, seizures, rhabdomyolysis and acute renal failure were reported [5].

Allergic angioedema typically occurs within several minutes of exposure to insect stings. In the above case angioedema started after 5 hours of exposure without pruritus and urticarial rash suggesting non allergic etiology due to excess bradykinin release. The close differential diagnosis is C1 esterase inhibitor deficiency, either hereditary or acquired, causing angioedema. This was ruled out in the above case by normal C1 esterase inhibitor level. The etiology of red ants' ingestion was concluded also on the basis of recurrent presentation on exposure to the same.

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Precocious Puberty as Initial Presentation in Mediastinal Tumour

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Numerous disorders can cause precocious puberty in children, and germ cell tumours (GCT) are one of the rare causes . We report two cases of mediastinal malignant GCTs who presented with precocious puberty. Both patients had bulky and advanced disease, were aggressively treated with neo-adjuvant chemotherapy and surgery, and are surviving and free of disease.

Key words: *Germ cell tumour, Mediastinum, Precocious puberty.*

Isosexual precocious puberty is an uncommonly seen phenomenon, and this can occur due to various causes – central type due to stimulation of the hypothalamo-pitutary-gonadal axis or peripheral type due to sex hormone secretion independent of hypothalamic stimulation. Tumors are rare causes of sexual precocity, and initial presentation of mediastinal germ cell tumors (GCT) as precocious puberty is very uncommon.

CASE REPORT

Case 1: 10-year-old boy was referred to us with history of change in voice noted by parents one year back, followed sometime later by appearance of pubic hair and sudden increase in stature. He had been evaluated with multiple investigations including CT scan abdomen, bone scan and MRI of head, which were normal. Meanwhile, patient developed cough and breathlessness, and chest *X*-ray revealed mediastinal mass, from which trucut biopsy was done. On examination, the boy was pale and tachypneic, had decreased breath sounds over right axillary and mammary areas, and firm hepatomegaly. His phenotype was normal, and he had enlarged gonads, thick pubic hair and deep voice. Complete blood counts and liver and renal function tests were normal. CT scan showed large soft tissue opacity occupying the anterior and middle mediastinum, opacification of right upper lobe of lung and rounded well-defined soft tissue masses in both lung fields suggestive of metastases. Ultrasound scan of abdomen showed hypoechoic area in right lobe of liver suggestive of metastases and right sided pleural effusion. Thyroid function tests, FSH, estradiol and testosterone were normal. Serum tumour markers revealed β-HCG of more than 50,000 mIU/mL and AFP of 269 ng/mL. The biopsy slide review was suggestive of germ cell tumour.

Patient was treated with chemotherapy using

ifosfamide, etoposide and carboplatin, with good clinical response, as assessed with decreasing tumour marker levels, reduction in symptoms, decrease in mass size and disappearance of liver lesion. After 6 courses of chemotherapy, patient underwent resection of residual mediastinal mass. Follow-up CT scan of chest after 3 months showed no tumor or lung metastases, and tumor markers were normal. Patient is on regular follow-up for past 7 years, and is doing well.

Case 2: 11 year-old-boy was referred for evaluation of persistent vomiting, abdominal pain and chest pain of one month duration. His parents had also noticed change of voice and darkening of skin color recently. On examination, patient was febrile and tachypneic, with facial suffusion. He had enlarged cervical lymph nodes, enlarged tender liver and bilateral crackles on chest auscultation. He also had generalized hyperpigmentation, deep voice and gynecomastia. *X*-ray and CT chest showed large anterior mediastinal mass compressing the SVC and neck veins, and multiple nodular mass lesions in both lungs suggestive of metastases. Blood hemogram and biochemistry were normal, as were USG of abdomen and MRI scan of brain. Karyotype was reported as 46 XY, Serum AFP was 4.9 ng/mL and β-HCG was 771 mIU/mL. CT guided FNAC from mediastinal mass was diagnostic of germ cell tumour.

Patient received chemotherapy with cisplatin, bleomycin and etoposide every 3 weeks. After 4 cycles of chemotherapy, his tumor markers were normal (AFP 4.6 ng/mL, β-HCG 7.5 mIU/mL) and chest scan still showed residual tumour with calcification and multiple lung metastases. He received two more courses of cisplatin and etoposide, and then underwent excision of residual mediastinal mass. Post-op scans showed multiple mediastinal nodes and pulmonary metastases, which disappeared on follow-up scans 6 months later. 3.5 years post treatment, he is free of disease.

DISCUSSION

Cause of precocious puberty may range from variant of normal to pathological causes with significant risk of morbidity and mortality like malignant germ cell tumors [1]. These tumors are infrequent in children, occurring at a rate of 2.4 cases per million children, representing approximately 1% of cancers diagnosed in persons younger than 15 years. [2] Only 1-2% of all GCTs in children occur in the mediastinum [3].

Mediastinal GCT patients may present with chest pain, dyspnea, superior vena cava syndrome, cough, weight loss, fever, night sweats, dysphagia, shoulder or arm pain and hoarseness, or can be an incidental finding of routine chest *X*-ray [3]. Nonseminomatous mediastinal GCTs may produce bioactive substances like alpha-fetoprotein and/or β-HCG, which may cause gynecomastia and precocious puberty due to elevated testosterone levels, secondary to stimulation of the testes by β-HCG [4,5].

About 40 cases of mediastinal GCTs presenting as isosexual precocious puberty in patients with Klinefelter syndrome are reported [7]. However, it is rarely reported in boys with normal phenotype. Both our patients did not have Klinefelter syndrome.

Nonseminomatous mediastinal GCTs are faster growing and metastasize earlier than mediastinal seminomas [3]. Both our patients had advanced stage of disease at presentation. Histopathologically, HCG-secreting thoracic tumours reported are teratomas, choriocarcinomas, polyembryomas and teratocarcinomas [4,6,7]. In both our patients, histopathology after surgical resection was teratoma with nonviable elements and treatment changes.

Intensive cisplatin-based chemotherapy followed by resection of residual tumor was shown to yield survival rates of 48-73% in nonseminomatous MGCTs [3]. Surgical resection should include all gross disease with en bloc resection of all involved structures that can be sacrificed [10]. Though GCTs in general have a good outcome with treatment, prognosis of mediastinal GCT is not that satisfactory, especially with advanced stages. [10] This is because MGCTs are not as sensitive as other GCT to chemotherapy and bulky disease increases risk of poor outcome in the short term owing to respiratory failure [3].

There is a significant interaction between age and primary site in GCT, suggesting that patients older than 12 years of age with thoracic tumors are a biologically distinct group, at higher risk of mortality from tumour progression [8]. An intergroup POG/CCSG randomized trial found that these tumours often have incomplete regression with chemotherapy alone. Aggressive attempt at complete tumor resection should be offered to all patients even if bulky tumor persists after induction chemotherapy, with expectation of a significant salvage rate [9]. Both our patients were treated aggressively, and are free of disease three years post treatment.

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