Rare manifestations of Wegener's granulomatosis

To the Editor: Wegener's granulomatosis (WG) is a necrotizing granulomatous small-vessel vasculitis.[1] The frequency of cardiac involvement in WG varies from 6 to 12 percent.[2] However, the occurrence of ascites and hemorrhagic effusion in WG were not reported in a MEDLINE search.

A 19-year-old man was referred to Baqyatollah hospital with a history of fever and polyarthritis for two weeks. The patient presented with weight loss, productive cough, and hemoptysis. His temperature was 39°C, heart rate 95/min and the respiratory rate was 28/min. A diffuse, coarse crackle was audible over both lungs. Severe joint inflammation was noted. His chest X-ray showed multiple pulmonary infiltration (Figure 1). He was treated for pulmonary abscess with clindamycin and ceftriaxone. The fever subsided gradually, but the polyarthritis, tachycardia, and tachypnea continued. Ultrasound study of the abdomen (Fiugure 2), showed mild splenomegaly and ascites. Moderate pericardial effusion was noticed by echocardiography. In the chest CT-scan, multiple isodense masses were found. Because of his severe clinical condition a high-dose steroid was given. Subsequently, marked hematuria, granular casturia and proteinuria developed.

C-ANCA (cytoplasmic antineutrophil cytoplasmic antibody) was positive. Pericardial effusion presented with a bloody appearance and the WBC count was 15000/mm^3. Culture and PCR examinations were negative. No organism grew in ascites fluid culture. The WBC count in ascitic fluid was 2500/mm^3, with a PMN value of 75%. A CT-guided lung biopsy was performed. Multiple foci of necrosis and infiltration of macrophages and neutrophils were seen. The diagnosis of WG was made, and combination therapy of high-dose steroid with cyclophosphamide was prescribed. In a few days, his general condition began to show signs of improvement. All clinical, laboratory, and imaging abnormalities also improved. He was discharged after 30 days.

WG is a disease manifested by necrotizing granuloma of the upper respiratory tract, lung, and renal involvement[3] with a 5-year survival rate approaching 95%.[2] Hemopericardium and ascites are a rare clinical picture not previously reported in WG.

Morteza Rajai MD
Baqiyatallah Medical University
Department of Internal Medicine
Tehran, Iran
m.rajai@gmail.com

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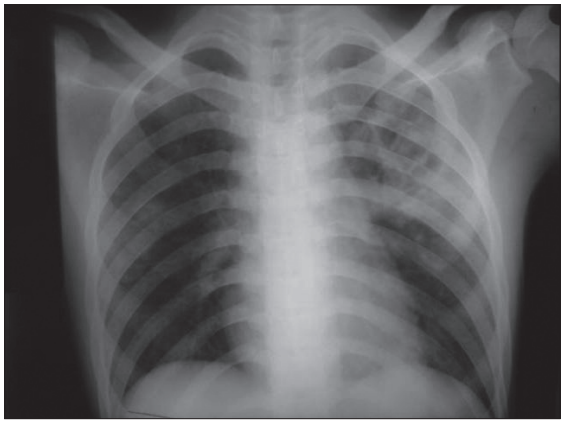

Figure 1. Chest X-ray showing multiple pulmonary infiltrations.

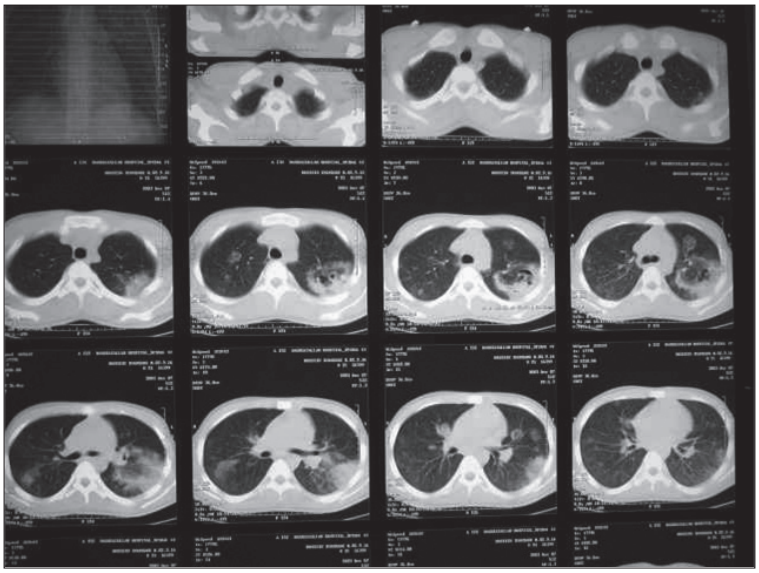

Figure 2. Chest CT scans showing multiple isodense masses.

What explains discrepant gender identity outcome in 46,XX individuals with 11-hydroxylase deficiency?

To The Editor: I read with great interest the report by Bin-Abbas et al[1] of two 46,XX siblings with 11-hydroxylase deficiency (11-OHD) raised male with divergent gender identity (GI) outcome in adolescence. The authors conclude "that the extent of external genitalia virilization, particularly the degree of hypospadias, and not the duration or the level of prenatal and postnatal androgen exposure, is the main gender identity determinant" in 46,XX patients with CAH. I applaud the authors for having based their decisions for and against gender-reassignment in these two siblings on a careful psychiatric evaluation with extensive counseling, but I am concerned that their theoretical conclusions regarding the determinants of GI may lead some clinicians to problematic unifactorial decisions regarding gender assignment and re-assignment.

Clearly, the "extent of external genitalia virilization" determines gender assignment at birth in newborns with normal genital development, and to a considerable extent also in newborns with ambiguous genitalia, especially when sophisticated diagnostic techniques are not readily accessible, as it is common in resource-poor communities. However, the association of the degree of masculinization of the external genitalia with gender identity development is comparably weak, not only in 46,XY, but also in 46,XX individuals, and genital-status-based gender assignment in infancy does not firmly determine GI outcome later. Otherwise we would not see gender dysphoria and patient-desired gender re-assignment in 46,XX 21-OHD-CAH, which occurs—albeit with relatively low incidence—in both female- and male-assigned patients.[2] In my reading of the literature and my clinical experience with 46,XX CAH patients raised female, patient-initiated gender change to male occurs more frequently in patients born with Prader stage 3-4 (clitorophallus with hypospadias) than in patients born with Prader stage 5 (completely masculinized external genitalia). The existence of non-intersex patients with female-to-male transsexualism who typically have entirely normal female genitalia also speaks against a determining role of the external genitalia for GI development.

So, which factors should one consider in explaining the different outcome in the two 11-OHD siblings of Bin-Abbas et al? First of all, the remarkable difference between the siblings in genital development may indicate behaviorally relevant differences in androgen exposure of the developing brain. Given that the two siblings are offspring from the same parents, it is highly likely (albeit not absolutely certain) that the molecular abnormality of the 17-OHD gene is identical in both. Nevertheless, the high local androgen concentration required at the early critical period of genital differentiation for the formation of a penile urethra[3] was apparently not present in the older sibling, although later in development the androgen levels were high enough to promote substantial growth of a clitorophallus. We do not know how late during the fetal development of this patient the androgens increased to that level. The statement that the older sibling, in contrast to the younger one, "behaved as a female since early childhood", raises the question whether the systemic androgen level influencing the sexual differentiation/masculinization of the brain during its hormone-sensitive period of prenatal development was lower in this sibling than in the younger one. Mammalian research has provided ample evidence that both dose and duration of androgen exposure during the homone-sensitive pre- or perinatal period of brain development affect later behavioral masculinization. This principle is likely to apply to humans as well. Research of my team in 46,XX individuals with 21-OHD CAH has clearly shown a dose-response relationship of syndrome severity (which is associated with the degree of androgen excess) with gender-related behavior (GR),[4] and related research in both non-human primates and humans makes it likely that these GR effects are primarily prenatal rather than postnatal in origin.[5,6] However, unlike the early critical period of genital differentiation, the hormone-sensitive period of sexual differentiation of the brain is much longer and extends far into the second half of pregnancy.

Our studies show considerable variability of GR in individuals with a given degree of CAH severity, as one also sees it in non-intersex males and females, so that prenatal androgen production is certainly not the only biological factor that explains interindividual differences in behavioral masculinization. In addition, one has to consider potential variations in systemic androgen metabolism, e.g., by aromatization,[7] or in androgen utilization due to androgen receptor modulation by trinucleotide repeats in the androgen receptor gene,[8] also the possibility of CNS-limited variations of endocrine processes such as production of neurosteroids and the action of steroid co-activators and co-inhibitors,[9,10] and last but not least, contributions from non-steroid related genetic effects on temperament.[11]

Although psychosocial factors

contribute to GR,[12] the markedly masculinized GR of 21-OHD CAH girls appears to be rather unresponsive to parental gender-normalizing pressure,[13] and recognition of children's gender by their peers is not primarily based on genital status.[12] However, gender-related behaviors and interests that are atypical for the assigned gender are salient among the commonly given reasons for gender dysphoria and patient-desired gender-change by both intersex and transsexual patients in later adolescence and adulthood. On the other hand, core GI as male or female can accommodate considerable variations of GR, and my own team's research has shown a lack of correlation of GI and GR in 21-OHD girls,[14] which makes it unlikely that the processes underlying the development of GI and GR are identical. Many individuals with a marked degree of gender-atypical GR do not suffer from gender dysphoria, while others with a similar degree do, and we still cannot pinpoint the etiological difference. Overall, it currently appears more likely that it is the confluence of a variety of interacting biological, social, and psychological factors rather than one prominent factor among these that pushes a given child or adolescent towards gender dysphoria or actual gender-reassignment. Thus, when deciding for the newborn with a disorder of sex development on the gender assignment with optimal prognosis for stable GI development, we need to consider whether and to what extent the genital status at birth permits inferences on the androgenization of the brain, which varies considerably between syndromes, and to take into account all other known relevant factors including psychosocial and cultural ones. In cases of potential gender re-assignment after infancy, a comprehensive evaluation of the patient's gender status (GR, GI, and any indications of gender dysphoria) must be added.

Heino F. L. Meyer-Bahlburg
Psychiatry
Columbia University
1051 Riverside Drive, NYSPI Unit 15
New York, New York 10032
United States
T: 212-543-5299
F: 212-543-6003
meyerb@childpsych.columbia.edu

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Medical chaperoning at a tertiary care hospital in Saudi Arabia: Prevalence and patient preference

To the Editor: The prevalence of medical chaperoning and the related patient preference in Saudi Arabia (or other Islamic/Arab countries) have not been well documented. We examined these issues in the out-patient clinics of a tertiary care hospital in Riyadh, Saudi Arabia, using a questionnaire that was completed during a personal interview. The study protocol, including verbal consent, was approved by the Research Ethics Committee of the institution. Two hundred thirty-nine patients were approached and 224 (94%) agreed to participate (15 declined for undeclared reasons).

Two hundred and five participants (2 males and 203 females, 92%) were seen by a physician of the opposite gender; 78 (38%) and 53 (26%) of which did not have a chaperone during the current medical interview and exam, respectively. When not present, a chaperone was rarely offered by medical staff (2%) and never requested by the patient. Of the 224 participants, 72 (32%) and 48 (21%) recalled that a chaperone was absent during previous medical interviews and exams, respectively. Table 1 shows chaperoning according to types of clinic and medical encounter. A significant association was found between the presence of a chaperone and clinic types for both interview and exam. There was also a significant association between the presence of a chaperone and types of medical encounter for all clinics ($P<0.0001$) and in the case of Family Medicine

and Polyclinics ($P<0.0001$). Of the 78 participants interviewed by a physician of the opposite gender in the absence of a chaperone, 77 (99%) were not offered a chaperone by the hospital staff and none requested one. Similarly, of the 53 participants examined by a physician of the opposite gender in the absence of a chaperone, 52 (98%) were not offered a chaperone and none requested one.

Ninety-one percent of chaperones during an interview were patient relatives. Relatives and staff nurses contributed equally during an exam (38% and 39%, respectively). Fifty-six percent and 21% of chaperones during an interview or exam, respectively, were males.

Figure 1 depicts the preference of the 224 participants regarding chaperoning. Fifty-one percent and 85%, respectively, of the participants who did not have a chaperone viewed the presence of a chaperone as commendable/preferred during interview and exam. The reasons most commonly cited for preferring a chaperone during an interview/ exam were religious (53%/ 63%), psychological (50%/ 49%), and social (22%/ 25%) and for preferring not to have one were psychological (58%/ 38%) and privacy and confidentiality (52%/ 63%). The prevalence of chaperoning in our study (62% during an interview and 74% during an exam) is consistent with the results of previously reported studies in other parts of the world, which were mostly physician-based rather than patient-based.[1-3]

In contrast to previous reports,[1-3] we found that family members comprised the majority of chaperones. This could be due to inadequate nursing staff or to the social norm that most female patients are usually accompanied by family members. Compared to previous reports,[4-6] our study showed a higher rate of patient preference for chaperoning, which is likely related to different social norms and religious values. Given this degree of preference, our observation that the patients who had a medical encounter without a chaperone were rarely offered a chaperone and never asked for one raises concerns about the training of hospital staff and the knowledge of patients about their rights. The results of the study may not be generalizable to all patients in Saudi Arabia. We studied only outpatient clinics in one hospital. Further, although we aimed to study both male and female patients, our participants were 97% females.

Several bodies have developed guidelines and policies for chaperoning.[7-9] The standards of practice regarding chaperoning at KFSH&RC

Table 1. Chaperoning according to types of clinic and medical encounter.

Clinic	Interview Number (%)		Exam Number (%)	
	Yes	No	Yes	No
Cardiovascular	20 (61)	13 (39)*	26 (79)	7 (21)*
Family Medicine & Polyclinics	10 (24)	32 (76)*	11 (26)	31 (74)*
Medicine	32 (78)	9 (22)*	29 (71)	12 (29)*
Neurosciences	19 (79)	5 (21)*	24 (100)	0 (0)*
Obstetrics & Gynecology	8 (47)	9 (53)*	16 (94)	1 (5.9)*
Surgery	14 (64)	8 (36)*	21 (96)	1 (4.5)*
Oncology	17 (90)	2 (11)	18 (95)	1 (5.3)*
Orthopedic Surgery	5 (100)	0 (0)	5 (100)	0 (0)
Kidney Transplant	2 (100)	0 (0)	2 (100)	0 (0)

*The P value of Fisher's exact test for the association of chaperone presence and types of clinic is $P<0.0001$ for both interview and exam.

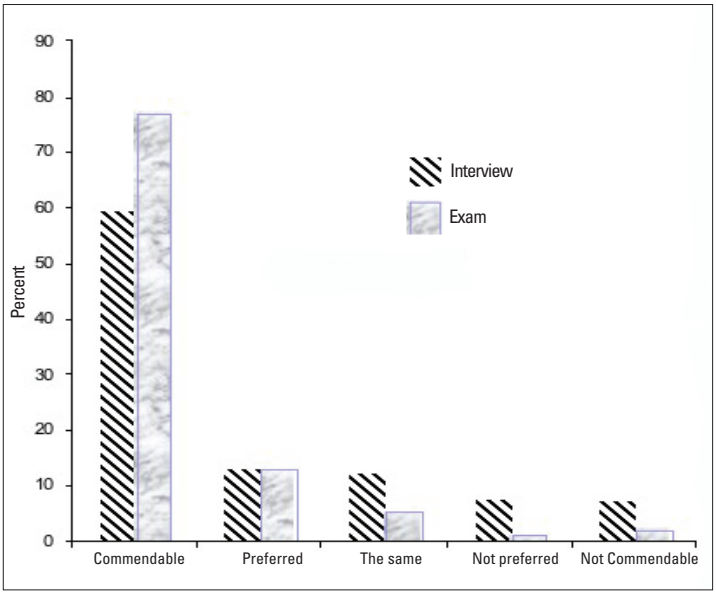

Figure 1. Patient's view of chaperoning during medical encounter.

are not clearly stated. Since there is a strong patient preference to have a chaperone during medical encounters, clear policies and guidelines should be developed and more resources should be allocated to educate both patients and hospital staff on patient rights. Further studies in other hospitals in Saudi Arabia will assist in determining the over all degree of deficiency in chaperoning as well as the preferences of patients and may help set national guidelines.

Eman Al Gaai, Husaam Al Sayed and Muhammad M Hammami

Centre for Clinical Studies and Empirical Ethics
King Faisal Specialist Hospital and Research Centre
Riyadh, Saudi Arabia

Correspondence:
Muhammad M Hammami, MD, PhD
Centre for Clinical Studies and Empirical Ethics
King Faisal Specialist Hospital and Research Centre
PO Box 3354 (MBC 03)
Riyadh 11211, Saudi Arabia
T: +966-1-442-4527
F: +966-1-442-7894
muhammad@kfshrc.edu.sa

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